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Abstracts

O1.

SERUM CYTOKINE PROFILE IN PATIENTS WITH BEHÇET'S DISEASE

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Introduction. Behçet's disease (BD) is a multi-systemic disorder characterized by relapsing oral–genital ulcers, uveitis, and involvement of vascular, gastrointestinal, neurological and musculoskeletal system. Although BD aetiology is not fully understood, several data showed that impaired immune response observed in BD patients is characterized by enhanced serum cytokines levels that might provide diagnostic or activity markers for the disease.
Objectives. The aim of the study was to investigate the serum levels of a panel of twenty-five cytokines in patients with Behçet's disease (BD) compared with Healthy Controls (HC) and to correlate their concentration with the status of disease activity.
Materials & Methods. 54 serum samples from 46 BD patients (17 males, 29 females, mean age 45,5±11,3 years) and 19 age- and sex- matched HC were recruited. A panel of twenty-five serum cytokines (APRIL/TNFS13, BAFF/TNFSF13B, sCD30/TNFRSF8, sCD163, Chitinase3-like1, gp130/sIL-6Rb, IFNb, sIL-6Ra, IL-10, IL-11, IL-19, IL-20, IL-26, IL-27 (p28), IL-28A/IFN-lambda2, IL-29/IFN-lambda1, IL-32, IL-34, IL-35, LIGHT/TNFSF-14, Pentraxin-3, sTNF-R1, sTNF-R2, TSLP and TWEAK/TNFSF-12) were simultaneously quantified using a Bio-Rad cytokine bead arrays. BD patients were included in active-BD group when they had at least two of the following clinical findings: uveitis, oral aphthosis, genital aphthosis, cutaneous disease, central nervous system involvement, vascular involvement, gastrointestinal involvement. Statistical approaches included Mann-Whitney test or Student's t-test, one-way analysis of variance (ANOVA) and correlations were calculated using Spearman's correlation (two-tailed p-value) as well as Pearson's correlation test when required.
Results. The results revealed that serum concentrations of Chitinase3-like1, gp130/sIL-6Rb, IL-11, IL-26, sTNF-R1, sTNF-R2 were significantly higher than in HC. Moreover, Spearman's rho's test showed moderate positive correlations between sTNF-R1, sTNF-R2 and gp130/sIL-6Rb (Spearman rho 0.706 and 0.783 respectively) and between sTNF-R1 and sTNF-R2 (Spearman rho 0.7308). Additionally, based on BD disease activity, serum levels of sTNF-R1 ($p<0.01$) and sTNF-R2 ($p<0.01$) resulted higher in both active- and inactive-BD than HC, while Chitinase3-like1 ($p<0.05$) and gp130/sIL-6Rb ($p<0.01$) serum levels were significantly higher in inactive-BD and IL-26 ($p<0.01$) in active-BD than HC.
Conclusions. Our findings support a key role for IL-6 as well as TNF cell activation in BD pathogenesis, in particular as a feature of inactive disease patients. Moreover, in active-BD patients enhanced IL-26 serum levels were found, supporting the potential involvement of Th17 activation pathway in the disease activity.

References

1. HAMZAOUI K, HAMZAOUI A, GUEMIRA F, BESSIOUD M, HAMZA M, AYED K: Cytokine profile in Behçet's disease patients. Relationship with disease activity. *Scand J Rheumatol* 2002.
2. LOPALCO G, LUCHERINI OM, VITALE A, TALARICO R, LOPALCO A, GALEAZZI M, LAPADULA G, CANTARINI L, IANNONE F: Putative Role of Serum Amyloid-A and Proinflammatory Cytokines as Biomarkers for Behçet's Disease. *Medicine* (Baltimore). 2015.

O2.

OCULAR DISEASE PHENOTYPING FROM MULTIPARAMETER CELL ANALYSIS BY MACHINE LEARNING ALGORITHMS

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Background. Current analysis of cell populations in body fluids from patients with ocular diseases relies strongly on cytometry, which measures the expression of markers on each cell. However, cell heterogeneity can be a difficult challenge for current single-cell biology, and it can be difficult to distinguish between complex ocular diseases. A recent study1 combined multiparameter single cell analysis with machine learning classification to accurately predict patients with Behçet's Disease (BD) and patients with sarcoidosis on the basis of five markers on CD8+ cells. We have now extended the numbers of patients analysed and incorporated patients with other ocular diseases.
Methods. Peripheral blood mononuclear cells (PBMC) was isolated from patients with BD (n=-100), sarcoidosis (n=15) isolated idiopathic uveitis (n=15) and birdshot uveitis (BU; n=15) and healthy controls (n=45). PBMC were labelled with a 15-colour antibody panel and the data was collected using flow cytometry and subsequently compensated using FlowJo. Compensated data was then analysed by two machine learning algorithms, Supercell, which randomly allocates multiple single cells into a supercell and calculates a single score value for all parameters which are then compared between patient groups to identify differences; and quantile-based analysis which compares each parameter against all others to identify the most significant phenotype which can discriminate between patient groups.
Results. The results show that all disease groups can be distinguished from healthy controls via supercell and quantile-based analysis. In patients with BD this was based on markers including IL22, TNF-α and IL-23R supporting previous findings by protein and genomic studies. Patients with ocular BD could be distinguished from patients without eye involvement by markers such as TNF-α,IL23R and IL17. Between diseases patients with BD could be distinguished from patients with Birdshot uveitis IL22 and CCR7.
Conclusions. Flow cytometry has been a hugely influential technique in advancing our understanding of the cellular basis of ocular disease. Novel machine learning algorithms increase the range of analysis to distinguish between diseases with a similar aetiology. The ability to apply such techniques to include other parameters such as gender, genetics and therapy have exciting potential.

Reference

CANDIA J *et al*. *PLoS Comp Biol* 2013; 9: e1003215

O3.

EXPRESSION OF HOMING MAKERS ON PERIPHERAL BLOOD LYMPHOCYTES IN BEHÇET'S DISEASE PATIENTS AND HEALTHY CONTROLS

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Background. Behçet's Disease (BD) is characterised by significant mucosal pathologies including recurrent oral aphthous ulcerations, genital ulcers and ocular inflammation as well as skin involvement. Some of the sites of pathology (ocular, oral and genital mucosa) are considered as immune privileged sites so that disregulation of homeostatic process must contribute to the symptoms experienced by patients, including recruitment of inflammatory cells into the tissues initiating the inflammatory profile characteristic of the disease.
In recent years the role of the unconventional γδ T cell population has been re-examined in many diseases. While these cells represent only a small proportion of circulating lymphocytes their role in maintaining both homeostasis and driving inflammatory processes warrants careful scrutiny in the context of BD.
Vγ9Vδ2(+) (Vδ2) T cells proliferate and accumulate in mucosal tissues following microbial activation and these cells have been demonstrated in the ulcer bed of oral ulcers in BD patients. Vδ2T cells produce proinflammatory cytokines in response to bacterial species, especially to those capable of producing phosphoantigens, many of which are resident in the oral microflora. We hypothesized that circulating Vδ2T cells can home to mucosal tissue (and /or skin) and contribute to inflammation. We have hypothesized that oral mucosal sites have homing receptors for β7 and CLA which may be responsible for the homing (tropism) of γδ T cells to oral mucosa (or skin) and drive the inflammatory processes in BD.
Methods. Peripheral Blood Mononuclear Cells were stimulated with IL-2, and the microbial phosphoantigen (1-hydroxy-2-methyl-2-buten-4-yl 4-diphosphate [HDMAPP]) and medium alone for seven days. Flow cytometry was performed to detect the expression of β7 and CLA by Vδ2+ and αβ T cells. Data obtained by flow cytometry was analysed using Flow Jo software.
Peripheral blood lymphocytes were also investigated for their binding to mucosal addressin cell adhesion molecule-1 (MadCam-1) in vitro.
Results. Both unstimulated Vδ2+ and αβ T cells from BD showed greater expression of β7 and CLA compared to HC revealing the potential for homing to mucosa and skin. The stimulated Vδ2+ and αβ T cells from both BD and HC exhibited increased β7 (up to 80%) but CLA was down-regulated in stimulated BD samples. Stimulated HC appeared to segregated into two distinct populations; one showing high CLA expression and other with lower expression of CLA.
Conclusion. Stimulation of PBMCs with HDMAPP upregulated the expression of β7 by Vδ2+ and αβ T cells in both BD and HC. However, the mean expression of β7 in BD was higher than HC suggesting that the cells were already primed in BD for migration to the mucosal site. CLA was down regulated in stimulated BD but inconsistent results obtained for HC reveals there might be some ethnic background involvement.

O4.

DENSE GENOTYPING OF IMMUNE-RELATED LOCI IMPLICATES HOST RESPONSES TO MICROBIAL EXPOSURE IN BEHÇET'S DISEASE SUSCEPTIBILITY

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Background. Recent genetic studies have identified multiple susceptibility loci exceeding genome-wide significance. However, these genetic factors do not fully explain the apparent disease heritability. Pathogenic and opportunistic infections have been proposed as important environmental factors contributing to both the development and exacerbation of Behçet's disease. The purpose of this study was to densely genotype loci associated with immune-related diseases to identify novel susceptibility loci for Behçet's disease.
Methods. 1,900 Turkish Behçet's disease patients and 1,779 controls were genotyped using the Immunochip. After strict quality control, we performed association tests. For novel loci with association test $p<5\times10\text{-}5$, additional SNPs in the region were imputed using 1000 Genomes Project data as a reference. For replication, the lead SNP genotyped by the Immunochip in each novel locus with $p<5\times10\text{-}5$ in the Turkish population was genotyped in 982 cases and 826 controls from Iran. We also replicated disease associations with imputed previous GWAS data from 608 Japanese cases and 737 controls.
Results. HLA-B*51 was the strongest associated marker and rs1050502 the strongest associated SNP. rs1050502 is located in exon 2 of HLA-B and the risk allele T is a tag SNP for HLA-B*51. Outside of the MHC region, we identified 4 novel loci, IL1A-IL1B, ADO-EGR2, IRF8, and CEBPB-PTPN1, which exceeded genome-wide significance in Turks. In addition, we confirmed four previously reported loci, IL10, CCR1, IL12A, and FUT2. Genotyping Iranian samples and meta-analysis with Turkish data replicated associations of three loci, ADO-EGR2, IRF8 and CEBPB-PTPN1. Comprehensive meta-analysis of the regional imputed genotype data of Turks and Japanese replicated two loci, ADO-EGR2 and IRF8, and revealed two additional novel loci, RIPK2 and LACC1. The lead SNP, rs4402765, for IL1A-IL1B is also the most significantly IL1A expression-associated variant in a lymphoblastoid cell eQTL database. The eQTL database also showed decreased expression of RIPK2 and CEBPB associated with the risk allele of the lead SNP for each locus. Homozygosity for ancestry specific FUT2 non-secretor alleles, rs601338 (p.Trp143Ter) in Turks and Iranians and rs1047781 (p.Ile129Phe) in Japanese, showed strong disease association. The non-secretor genotype has been associated with Crohn's disease and gut microbiome composition.
Conclusion. Here, we conducted an Immunochip study in the largest Behçet's disease discovery cohort ever with multiple populations for replication. This study provided robust evidence for HLA-B*51 as the primary source of the strong disease association in the HLA region and identified 6 novel loci (IL1A-IL1B, RIPK2, ADO-EGR2, LACC1, IRF8, and CEBPB-PTPN1) with genome-wide significance for Behçet's disease. Our findings that the disease-associated alleles of IL1A, RIPK2 and CEBPB are associated with decreased gene expression and that disease-associated FUT2 structural variants are hypofunctional suggest that an impaired host response to the microbiome may contribute to Behçet's disease susceptibility

O5.

GENOME-WIDE SCREENING OF LOCI ASSOCIATED WITH CLINICAL MANIFESTATIONS OF BEHÇET'S DISEASE

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Objective. Behçet's disease (BD) is a chronic systemic inflammatory disorder characterized by four major symptoms: recurrent ocular symptoms, oral ulcers, genital ulcers, and skin lesions. BD is occasionally associated with inflammation in other tissues, such as joints, the vascular system, the gastrointestinal tract, the central nervous system, and epididymis. The etiology of BD is still uncertain, but the disease is currently thought to be triggered by various genetic as well as environmental factors. It is well established that BD is strongly associated with the human leukocyte antigen (HLA) class I allele, HLA-B*51, in many different ethnic groups. Recent genome-wide association studies (GWASs) have reported several susceptibility loci/genes for BD, including UBAC2, HLA-A*26, IL10, IL23R-IL12RB2, ERAP1, CCR1, KLRC4, STAT4, and GIMAP. The purpose of this study was to identify loci specifically associated with clinical manifestations of BD using a GWAS.
Materials and Methods. We used previous GWAS data with a Japanese population (612 BD patients and 740 healthy controls) using Affymetrix GeneChip Human Mapping 500K Array Set (500,568 SNPs) (Nat Genet 2010;42(8):703-6.). After sample and SNP quality control, a total of 309,362 autosomal SNPs from 611 patients and 737 controls were used for statistical analyses to identify loci affecting specific disease manifestations (oral ulcer, skin lesion, ocular lesion, genital ulcer, arthritis, epididymitis, gastrointestinal lesion, vascular lesion, and central nervous system lesion). In order to be considered a candidate, we required SNPs to have $p<00001$ and OR ≥1.40 in patients with a specific disease manifestation but $p>0.05$ and OR <1.1 in patients without the manifestation.
Results. We identified 40, 25, 36, and 31 candidate risk loci for oral ulcer, skin lesion, ocular lesion, and genital ulcer, respectively. We also identified 28, 37, 36, 35, and 89 candidate risk loci for arthritis, epididymitis, gastrointestinal lesion, vascular lesion, and central nervous system lesion, respectively. The candidate loci for each major symptom include some HLA loci, whereas no HLA loci were associated with minor symptoms.
Conclusions: Preliminary results of the ongoing study point out to risk loci for clinical manifestations of BD. To confirm the findings, future validation studies with other independent populations are needed.

O6.

HOMOZYGOSITY FOR A SINGLE ERAP1 ALLOTYPE GREATLY INCREASES BEHÇET'S DISEASE RISK IN HLA-B*51 CARRIERS

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Background. Endoplasmic reticulum aminopeptidase-1 (ERAP1) trims intracellular proteasome-processed peptides, a step required for efficient loading of many peptides onto HLA class I molecules prior to transport to the surface of nearly all cell types. These HLA-peptide complexes play important roles in immune surveillance through their interactions with cytotoxic T cells and natural killer cells. The class I HLA type, HLA-B*51, has been identified in multiple populations as the most significant genetic risk factor for Behçet's disease and several ERAP1 gene variants have been found to interact with this factor. The ERAP1 protein has numerous missense variants that collectively influence its peptide specificity and enzymatic activity. In this study we determined the haplotypes of ERAP1 variants and the encoded ERAP1 allotypes found in the Turkish population and determined their association with Behçet's disease risk.
Methods. Ten ERAP1 missense variants, 8 directly genotyped on the Immunochip and 2 imputed from the ERAP1 region genotypes using Impute2 and 1000 genomes phase I reference haplotypes, were determined in 1876 individuals with Behçet's disease and 1761 controls from Turkey. HLA-B*51 types were imputed with Immunochip HLA region genotypes using SNP2HLA and 10,450 reference HLA marker and classical HLA type haplotypes as reference. Haplotypes and Pearson chi squared disease association tests were determined with SNP Variation Suite 8.4.

Results. The 10 ERAP1 missense variants with minor allele frequency greater than 1% defined 8 haplotypes or protein allotypes with greater than 1% frequency in the Turkish population. One allotype with 5 non-ancestral amino acids was recessively associated with disease (p=3.13 x 10-6, odds ratio 2.55, 95% CI 1.70 to 3.82). This association was enhanced in individuals who carry HLA-B*51 (p=4.58 x 10-8, odds ratio 3.05, 95% CI 1.64 to 5.66) and absent in individuals who did not carry HLA-B*51 (p=0.82). Individuals who carry HLA-B*51 and are also homozygous for the ERAP1 haplotype had substantially increased disease odds compared with those with neither risk factor (p=4.8 x 10-20, odds ratio 10.96, 95% CI 5.91 to 20.32).
Conclusion. The disease-associated ERAP1 allotype likely contributes to Behçet's disease susceptibility by altering its peptidase activity and or substrate specificity, suggesting that either an over production of ERAP1 allotype specific disease promoting peptides or inadequate production of disease-protective peptides contributes to disease susceptibility. Identifying the nature and source of such peptides, for example, are they self-derived or do they originate in pathogenic or commensal organisms, would be an important step towards elucidating the mechanism by which HLA-B*51 contributes to Behçet's disease risk.

O7.

POST-THROMBOTIC SYNDROME IS INCREASED AND VENOUS DISEASE SPESIFIC QUALITY OF LIFE IS IMPAIRED IN PATIENTS WITH VASCULAR BEHÇET'S DISEASE WITH NO BENEFIT OF ANTICOAGULANT USE

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Objective. Deep venous thrombosis (DVT) is the most common form of vascular involvement in Behçet's disease (BD). Chronic post-thrombotic syndrome (PTS) develops in up to one-half of patients with DVT and is associated with impaired quality of life (QoL). We aimed to evaluate PTS, venous disease spesific QoL and the associated factors in patients with VBD.
Method. This study included 94 patients (Male/Female:75/19) with VBD and 29 age and gender-matched individuals, (Male/Female: 18/11) with DVT associated with non-BD causes. Villalta scale was used to assess of PTS. Venous Disability Score (VDS) and Venous Clinical Severity Score (VCSS) were used for the assessment of venous disease. Venous disease-specific QoL was measured through Venous Insufficiency Epidemiological and Economic Study Quality of Life/Symptom questionnaire (VEINES-QoL/Sym). Behçet Syndrom Activity Score (BSAS) questionnaire was used to assess disease activity.
Results. A high presence of PTS (61.7%) was observed in VBD (Table 1). The rate of anticoagulant usage was significantly lower (63% vs 100%, p=0.001), and the number of DVT attacks were significantly higher in VBD (1.6 vs 1.3, p=0.001) compared to non-BD. When VBD patients with PTS were compared to VBD patients without PTS, VEINES-QoL and VEINES-Sym VCSS were significantly worse in VBD with PTS. BSAS was also significantly higher in patients with PTS. An inverse correlation was observed between VEINES-QoL and BSAS in multivariate analysis. There were no differences between anticoagulant users and non-users regarding the presence of PTS and scores of all venous assessment tools in VBD.

Table I. Venous assessment and quality of life parameters in studi groups.

	Vascular Behçet Disease (n=94)	Non-Behçet group (n=29)	P value
PTS, n (%)	58 (% 61.7)	21 (%84)	0.036
VEINES-QoL	87,80±16,55	72,31±19,67	0.001
VEINES-Sym	38,83±8,95	32,72±10,32	0.002
VCSS	4,74±4,33	6,43±4,53	0.015
CEAP	2,09±1,68	2,25±1,51	0.468
VDS	1,04±0,59	1,48±0,58	0,001

PTS:Post-thrombotic syndrome, VEINES-QoL/Sym: Venous Insufficiency Epidemiological and Economic Study Quality of Life/Symptom questionnaire, VCSS: Venous Clinical Severity Score, CEAP:Clinical, Etiologic, Anatomic, Pathophysiologic) classification, VDS: Venous Disability Score

Conclusion. A high presence of PTS and impaired venous disease spesific QoL, symptom severity and venous disability scores was observed in VBD in our study. Venous disease spesific QoL negatively correlated with general disease activity. Any additional benefit of anticoagulant treatment on development of PTS and venous QoL was present. Our results suggest that successful control of disease activity might decrease development of PTS, improve venouse disease spesific QoL as well as preventing the relapses in VBD.

O8.

AN OUTCOME SURVEY OF 100 PATIENTS WITH CEREBRAL VENOUS SINUS THROMBOSIS DUE TO BEHÇET'S SYNDROME FOLLOWED UP AT A SINGLE, DEDICATED CENTER

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Background and objectives. Behçet's syndrome (BS) is a well-recognized cause of cerebral venous sinus thrombosis (CVST). We assessed the outcome of a large cohort of patients with CVST due to BS attending a single dedicated center.
Methods. We identified 100 (81 M/19 F) BS patients out of 8000 who were diagnosed as having CVST. Their outcome was evaluated between Feb and Dec 2015. All contacted were called back to the outpatient clinic for a clinical, neurological and ophthalmological examination and cranial MRI /MR venography.
Results. The mean age of the patients at the onset of the symptoms was 28±10 years. A total of 48 patients developed CVST before or at the onset of ISG fulfillment, while 52 developed CVST after a median 3 [2-8] years of ISG fulfillment. Detailed radiological information was not available in 3 patients. Cranial MRI did not show any abnormality in 8 patients, although all had symptoms of acute onset of intracranial hypertension with bilateral papilledema. In the remaining, superior sagittal (n=47) and transverse sinuses (n=46) were most commonly involved followed by sigmoid sinus (n=26) and jugular vein thrombosis (n=15).
A total of 59 (53 M/ 6 F) patients had vascular involvement in addition to CVST. In about half (32/59), CVST preceded any type of additional vascular involvement. Eye involvement was seen in 37 patients, parenchymal CNS involvement in 8 (all later than CVST) and gastrointestinal involvement in 5.
Seven patients died, due to causes unrelated with CVST such as hepatic encephalopathy due to Budd-Chiari syndrome (n=3), pulmonary artery involvement PAI (n=2), sepsis and suicide (n=1). Six patients were lost to follow-up after a single visit. By the end of the study, all remaining 87 patients were alive and contacted with a median follow-up time of 11 [IQR: 6-15] years. Only 6 patients had a relapsing CVST course. A total of 81 (95 %) patients received immunosuppressive treatment and 5 underwent shunting surgery/or embolization.
By the end of Dec 2015, a total of 50 patients were re-evaluated at the clinic. None had symptoms of intracranial hypertension. Ophthalmological examination showed that 17 patients had complications such as bilateral optic atrophy (n= 3), bilateral papilledema (n= 5), bilateral optic disc pallor (n=4) and fibrotic scars around optic disc (n= 5). Sensorineural type hearing loss was detected in 4 patients. Neurological examination was found to be normal among 43 patients with isolated CSVT, whereas abnormal in the remaining 7 patients with concomitant parenchymal CNS involvement.
Cranial MR/MR venographies were abnormal in 36 (72 %) patients showing occlusion/ irregularity/ hypoplasia or collaterals in the sagittal or transverse sinus. In the remaining 14, these were found to be normal.
Conclusions. CVST due to BS is closely associated with vascular involvement elsewhere in the body and may be considered as a risk factor for future vascular involvement. CVST relapses are rare; however, the course is not uneventful: visual acuity or field may be impaired totally or partially because of optic disc atrophy; in addition hearing deficits may occur.

O9.

A LOW BALANCE BETWEEN MICROPARTICLES EXPRESSING TISSUE FACTOR PATHWAY INHIBITOR AND TISSUE FACTOR IS ASSOCIATED WITH THROMBOSIS IN BEHÇET'S SYNDROME

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Background. Thrombosis is common in Behçet's Syndrome (BS), and there is a need for an understanding of causation and for better biomarkers to enable thrombotic risk assessment.
Objectives. We investigated whether plasma microparticles expressing Tissue Factor (TF) are increased in BS and how TF positive MPs relate to numbers of MP expressing Tissue Factor Pathway Inhibitor (TFPI).

Methods. This was a case-control study comparing 88 BS patients with 72 healthy controls. The BS group contained 21 patients with a thrombosis history (Th+) and 67 patients without (Th-). MPs were identified by size and annexin V binding using flow cytometry, and were further analyzed with antibodies to surface antigens.
Results. Total MP numbers were increased in BS compared to HC, as were MPs expressing TF and TFPI (all $p<0.0001$). Amongst BS patients, the Th+ group had increased total and TF positive MP numbers (both $p<0.0002$) compared to the Th- group, but had a lower proportion of TFPI positive MPs ($p<0.05$). Consequently, the ratio of TFPI to TF MP counts (TFPI/TF) was significantly lower in Th+ versus Th- BS patients ($p=0.0002$), and no patient with a TFPI/TF MP ratio >0.7 had a history of clinical thrombosis.
Conclusions. We conclude that MP expressing TF are increased in BS and more so in patients with a history of thrombosis. An imbalance between microparticulate TF and TFPI may be pathophysiologically important for thrombosis in BS and may contribute to improved identification and appropriate treatment of thrombotic risk.

O10.

EARLIER USE OF INFLIXIMAB FOR THE UVEITIS OF BEHÇET'S SYNDROME APPEARS TO BE ASSOCIATED WITH BETTER OUTCOME

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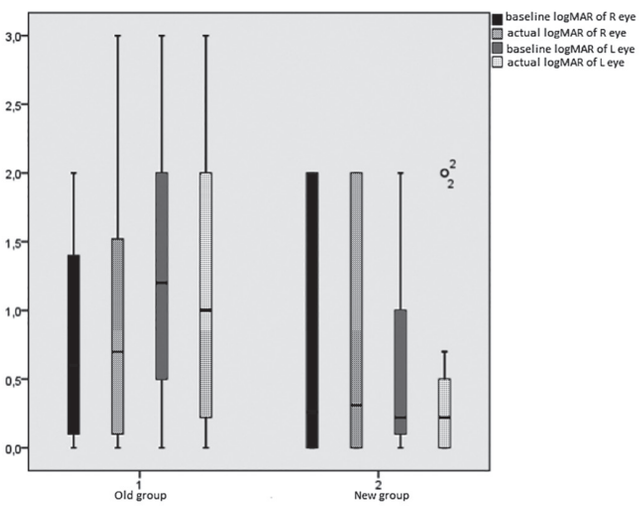
Background. New data suggest a better visual outcome for Behçet's Syndrome (BS) compared to earlier reports (1,2). This improvement may have resulted from the introduction of more effective therapeutic agents like anti-TNFs, but perhaps also from their more efficacious use. However, whether the disease characteristics and treatment responses of BS patients starting specifically anti-TNF therapy for uveitis have changed over time is not known.
Objective. To compare the clinical characteristics and treatment responses of BS patients who started infliximab (IFX) for uveitis before and after 2013.
Methods. The charts of 17 patients (15 men, 2 women; age at the initation of IFX: 33.8±7.5 SD years) receiving IFX (5 mg/kg) for uveitis at our centre after 2013 (New Group) were reviewed retrospectively. The data were compared with those of 43 patients starting IFX before 2013 (Old Group) (3).
Results. Similar to the patients in the old group, the patients in the new group also had severe, sight-threatening posterior uveitis that was refractory to previous treatment with conventional immunosuppressives (azathioprine=15, cyclosporin A=15, interferon alfa=13, cyclophosphamide=2 and steroids). The duration of previous immunosuppressive treatment was significantly shorter (median: 26 months; IQR: 10-53 months) in the new group compared to that of the old group (median: 60 months; IQR: 25-84 months; $p=0.012$). The duration of uveitis until the initiation of IFX was also shorter in the new group (median: 39 months; IQR: 16-94 months) than the old group (median: 72 months; IQR: 45-132 months) but this did not reach statistical significance ($p=0.075$). There was no significant difference between groups regarding the baseline visual acuity (VA) at the time of initation of IFX in the right eye (Median LogMAR for new group: 0.3, for old group: 0.7; $p=0.8$) but the baseline VA of the left eye of the new group (median LogMAR: 0.22; IQR: 0.05-1) was significantly better compared to that of the old group (median LogMAR: 1.2; IQR: 0.5-2; $p=0.005$). The percentage of patients with no useful vision (LogMAR>1) in at least one eye was 47% in the new group and 67% in the old group ($p=0.23$). Information on outcome was available for 14 patients in the new group. The duration of IFX treatment was 13.8±7.9 SD months (median 11.5 months). Ten patients (71%) had at least one attack in the right, left or both eyes before IFX, while all patients except one (93%) became attack free under IFX. The mean VA of the left eye improved significantly with IFX (Figure 1).



Discussion. Earlier use of IFX for BS uveitis appears to be associated with better outcome.

References
1. Chung YR. *et al*. *Ocul Immunol Inflamm* 2015 Apr; 23(2): 157-61.
2. Cingu AK. *et al*. *Ocul Immunol Inflamm* 2012 Dec; 20(6): 423-8.
3. Hamuryudan V. *et al*. *Arthritis Rheum* 2013; 65 Suppl. 10: 2626.

O11.

EVALUATION OF OCULAR DISEASE ACTIVITY USING BEHÇET'S DISEASE OCULAR ATTACK SCORE 24

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Background. ocular involvement in Behçet's disease (BD) is reported to range from 47 to 69% and is characterized by recurrent attacks of intraocular inflammation, including anterior and more often posterior uveitis or panuveitis. Evaluation of ocular inflammatory activity is difficult and usually based on frequency of ocular attacks, best-corrected visual acuity, location of inflammation. BD ocular attack score 24 (BOS24) – the new easily used objective scoring system for quantitative evaluation of disease activity related to ocular BD proposed by Japanese ophthalmologists (1).
Objective. to evaluate of ocular disease activity using BOS24 scoring system
Methods. 124 BD patients were enrolled in the study. All the patients met the criteria of the International Study Group for BD (1990). The disease activity was assessed by scoring system BDCAF. All the patients were examined by an ophthalmologist. 81 (65,3%) of these BD patients had ocular involvement. 61 (75,3%) BD patients with ocular involvement were men with mean age (M±m) 33,6±1,11 years. An ocular attack was defined as acute aggravation of intraocular inflammation with subjective symptoms of uveitis (conjunctival ciliary injection, floaters, blurred visions, etc.) and objective signs observed by slit-lamp microscopy and fundoscopy. For evaluation of ocular disease activity BOS24 scoring system used. The BOS24 consists of a total 24 points summarized from 6 objective parameters of ocular inflammatory symptoms, including anterior chamber cells, vitreous opacity peripheral fundus lesions, posterior pole lesions, subfoveal lesions and optic disc lesions. Simultaneous bilateral attacks (attacks in both eyes) were considered to be 2 attacks, 1 attack for each eye, and BOS24 was separately determined for each eye.
Results. 31 from 81 (38,3%) BD patients with ocular involvement had current ocular attack. Total amount of ocular attacks (eyes with intraocular inflammation) was 56. 25 (81%) patients with current ocular attacks had panuveitis and 6 (19%) – posterior uveitis. Total BOS24 was done for all BD patients with ocular attack. The average score BOS24 for the 56 ocular attacks before treatment was (M±m) 9,10±0,95 (from 2 to 19). All the BD patients were treated by systemic anti-inflammatory/ immunosuppressive drugs such as systemic corticosteroid

(100%), cyclosporine (53%), azathioprine (47%). The average score BOS24 significantly decreased to 2,67±1,40 (from 0 to 6) (p<0,001) after 8,92±3,47 (M±m) months treatment. The BOS24 before the treatment was positive correlated with number of ocular attacks during current year (R=0,89), severity of BD (R=0,37), skin (R=0,46) and vascular (R=0,28) involvement and was negative correlated with duration of ocular involvement (R=-0,37).
Conclusion. BOS24 is useful objective scoring system for quantitative evaluation of ocular BD activities and the efficacy of treatment.

Reference

1. KABURAKI T, NAMBA K, SONODA KH, KEZUKA T, KEINO H, FUKUHARA T, KAMOI K, NAKAI K, MIZUKI N, OHGURO N; Ocular Behçet Disease Research Group of Japan. *Jpn J Ophthalmol* 2014 Mar; 58(2):120-30. doi: 10.1007/s10384-013-0294-0

O12.

CELLULAR IMMUNE RESPONSES IN BEHÇET'S DISEASE PATIENTS WITH UVEITIS DURING INFLIXIMAB TREATMENT

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Purpose. Infliximab is a chimeric IgG1 monoclonal antibody that blocks binding of TNF-α to its receptor, and various studies have shown remarkably beneficial effects of infliximab in the treatment of Behçet's disease (BD)-associated uveitis. However, recurrent uveitis was observed in some BD patients after initiation of infliximab treatment. It has been found that peripheral blood mononuclear cells (PBMCs) obtained from BD patients produce proinflammatory cytokines, and Th1-, Th2-, and Th17-related cytokines when stimulated with interphotoreceptor retinoid-binding protein (IRBP) that is one of retinal self-antigen. In this study, we examined the quantitative changes of proinflammatory cytokines, and Th1-, Th2-, and Th17-related cytokines produced by PBMCs from BD patients with uveitis before and after treatment with infliximab when stimulated with IRBP. Furthermore, we compared cytokine production between BD patients with recurrent uveitis during infliximab treatment and those in whom recurrent uveitis was not observed after initiation of infliximab treatment.
Methods. Eight BD patients who were treated with infliximab more than 1 year were enrolled in this study. BD patients were also classified into a group with recurrent uveitis (BD-recurrent uveitis group) in which recurrence of uveitis was occasionally observed even after initiation of infliximab treatment and a group with remitted uveitis (BD-remitted uveitis group) in which uveitis did not recur after initiation of infliximab treatment. Ten healthy subjects were enrolled as controls. PBMC were collected from BD patients before and one week after infliximab infusion, and from healthy controls at any time. PBMCs were cultured in vitro with various concentrations of IRBP, and levels of proinflammatory (IL-1β, IL-6, and TNF-α), Th1- (IFN-γ and soluble CD40 ligand: sCD40L), Th2- (IL-4, IL-10, and IL-31), and Th17- (IL-17A, IL-17F, IL-21, and IL-22) cytokines in cultures were measured by Bio-Plex kit® (Bio-Rad Laboratories Inc.)., IL-10, IL-17F, and IL-22 were reduced after infliximab infusion in BD-remitted uveitis group but not in BD-recurrent uveitis group. α, TNFγ.
Results. All these cytokines except for sCD40L were higher in BD patients before infliximab infusion than in healthy subjects, and decreased in BD patients after infliximab infusion, but were still higher than in healthy subjects except for IL-4 and IL-10. In BD patients, all cytokines except for IL-6 were higher in BD-recurrent uveitis group compared with BD-remitted uveitis group before infliximab infusion, and decreased after infliximab infusion to a greater extent in BD-remitted uveitis group than in BD-recurrent uveitis group. Especially, IFN-.
Conclusions. Th1-, Th-2, and Th17-related cytokines by PBMCs upon IRBP stimulation were suppressed after infliximab infusion preferentially in BD patients without recurrent uveitis. Measurement of these cytokines by IRBP-stimulated PBMCs would be a clue to evaluate quantitatively the efficacy of infliximab treatment for uveitis in BD patients.

O13.

COGNITIVE IMPAIRMENT IN CHRONIC PROGRESSIVE NEURO- BEHÇET'S DISEASE: COMPARATIVE STUDY OF BRAINSTEM AND HIPPOCAMPUS REGION USING BRAIN MAGNETIC RESONANCE IMAGING

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Background/Purpose. Central nervous system involvement is one of the most serious complications in Behçet's disease (BD). This condition is referred to as neuro-Behçet's disease (NB) and can be classified into acute NB (ANB) and chronic progressive NB (CPNB) based upon differences in the clinical course and response to corticosteroid treatment. Brainstem atrophy is significantly more frequently observed in CPNB than in ANB. It is also noteworthy that cognitive dysfunction, in addition to truncal ataxia, is frequently observed in CPNB, and this cannot be accounted for by brainstem atrophy. In the present study, we examined volumes of the hippocampus in order to identify the responsible lesions for neurobehavioral changes in CPNB.
Methods. The subjects were 32 patients, including 13 with CPNB (11 males and 2 females, age 51.2±12.1 years old [mean ± SD]), 13 with Behçet's disease without NB (non-NB) (10 males and 3 females, age 54.4±11.4 years old), and 6 with Alzheimer's Disease (AD) (5 males and 1 female, age 78.8±7.5 years old). All patients with BD satisfied the international classification criteria for Behçet's disease. CPNB was defined as intractable, slowly progressive neurobehavioral changes and/or ataxia accompanied by persistent elevation of interleukin-6 of >20 pg/mL in cerebrospinal fluid on two different occasions at an interval of at least 2 weeks. All patients with AD satisfied the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria. Sagittal sections of T1-weighted images on brain magnetic resonance imaging (MRI) were obtained from each subject. The areas of the midbrain tegmentum and pons were measured on mid-sagittal sections of T1-weighted images using image analysis software (Image J ver.1.45: NIH, USA). Severity of gray matter loss in the hippocampal region and whole brain were investigated using Voxel-Based Specific Regional Analysis System for Alzheimer's Disease (VSRAD) software (Eisai Co., Ltd) to determine the degrees of hippocampal region atrophy (Z score) and whole-brain atrophy (WBAI).
Results. The brainstem area was significantly decreased in CPNB (461.8±87.3 [mean ± SD]) compared with those in AD (661.9±56.1) and non-NB (666.1±50.6) (Figure 1, A). VSRAD analysis showed that Z score was significantly increased in CPNB (1.46±0.70) and AD (3.13±1.21) compared with non-NB (0.77±0.40) (Figure 1, B). All patients with CPNB showed brainstem atrophy, but there was no significant correlation between the area of brainstem atrophy and Z score. Neither Z score nor WBAI was correlated with age in CPNB.
Conclusion. These results indicate that the hippocampus, in addition to the brainstem, is a common site for lesions in CPNB, accounting for the progressive cognitive dysfunction in this disease. The lack of correlation between brainstem atrophy and hippocampal atrophy suggests that predisposing factors might determine the lesion site in CPNB.

O14.

BEHÇET'S SYNDROME AND PSYCHIATRIC INVOLVEMENT: IS IT A PRIMARY OR SECONDARY FEATURE OF THE DISEASE?

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Background. Frequency of psychiatric disorders in Behçet's syndrome (BS) is a debated issue: while some experts attribute their presence to the chronicity of the illness, others think that they may be imputable to disease activity or to intrinsic features of the disease.
Objectives. The primary aims were to determine the frequency of psychiatric disorders in BS patients, both with neurological involvement or without; the secondary aims were: to investigate a possible association between disease activity/organ involvement and psychiatric profile of the BS patients and to compare the distribution of psychiatric disorders of patients with BS with those in patients with other chronic diseases.
Methods. One hundred and seven BS patients with a diagnosis of BS according the ISG criteria were studied. Demographic profile of the cohort studied are summarised in Table I. Psychiatric disorders evaluated were: bipolar disorder, obsessive-compulsive disorder, depression and sleep disorder. Age and sex

matched disease controls of systemic lupus erythematosus (SLE) and chronic arterial hypertension were included.
Results. Prevalence of psychiatric disorders are shown in Table II. No correlations were found between the presence of psychiatric disorders and disease activity/organ involvement. Moreover, the frequency of bipolar disorder resulted significantly higher than in disease controls (p<0.001).

Table I. Demographic profile.

	Neuro-BS (n)	BS without neurological involvement (n)
Number of patients	44	63
M/F	36/8	41/22
Mean age ± SD (min-max) (years)	43±7 (15-68)	42±8 (18-71)
Mean disease duration ± SD (min-max) (years)	9±2 (2-28)	10±2 (3-28)

Table II. Prevalence of psychiatric disorders.

	Neuro-BS n (%)	BS without neurological involvement n (%)
bipolar disorder	41 *(65)*	28 *(64)*
obsessive-compulsive disorder	29 *(46)*	20 *(43)*
depression	20 *(32)*	16 *(36)*
sleep disorder	5 *(11)*	10 *(16)*

Conclusions. Our results show a high frequency of psychiatric disorders in BS patients. This elevated prevalence both in BS patient with or without neurological involvement, in presence or absence of disease activity and in a higher frequency than in disease controls, strongly suggest that BS patients are characterised by a specific psychiatric profile.

O15.

THE COCHLEAR INVOLVEMENT IN BEHÇET'S DISEASE: CROSS SECTIONAL STUDY

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Introduction. The cochlear damage was a common symptom of Behçet Disease (B D) esteemed between 9 and 80% of cases. It was ranked second or third after cutaneous and ocular damage according to most studies.
Objective. To determine the frequency of cochlear involvement (CI) during BD and Identify their demographic, clinical and paraclinical particularities.
Patient and methods. We conducted a cross-sectional study including 55 patients with BD fulfilled the diagnostic criteria of the International Study Group on the BD, followed at Medicine Interne Department of the Hospital of Fattouma Bourguiba Monastir. All patients underwent clinical examination and cochleovestibular investigations. We compared the group with CI and its sub-groups to the control group consisted of patients with BD but without CI.
Results. The CI was objectified in 17 cases (31%). It was isolated in 12 cases (70.5%) and associated with vestibular dysfunction in 5 cases (29.4%). Deafness was bilateral and symmetric in 76.5% of cases, light in 70.6% of cases and focusing on high frequencies in 88.2% of cases. THE majority had sensorineural hearing loss (94.1%), classified deafness endocohléaire in 13 cases (81.25%) and retrocochlear in 3 cases (18.75%). Patients with CI were significantly older (p=0.048) with a late onset of BD compared to control patients (p=0.013). However, the duration of BD was longer in the group of sensorineural hearing loss compared to the control group without being statistically significant. The vascular injury was significantly less frequent in patients with CI and particularly those with sensorineural hearing loss. The frequency of the pseudofolliculitis necrotic was significantly higher in the group with sensorineural hearing loss (p=0.034).
Conclusion. CI is prevalent in BD, but remains underestimated. Therefore, all Behçet's patients should be regulary subjected to cochlear investigations to detect inner ear involvement.

O16.

PREDICTIVE VALUE OF BONE SCINTIGRAPHY FOR THE DETECTION OF JOINT INVOLVEMENT IN BEHÇET'S DISEASE: DERMATOLOGISTS' PERSPECTIVES

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Background. Behçet's disease (BD) is a chronic multi-organ inflammatory disease with joint involvement. It is very common for physicians in different clinical settings to experience BD patients with joint symptoms. Because non-specific arthralgia without objective signs of arthritis, such as swelling or effusion is frequent in patients with BD, an accurate diagnosis of joint involvement is often challenging, especially for non-rheumatologists. Considering the high frequency of BD-associated arthritis and the importance of early detection, finding a useful and simple imaging technique for detecting articular involvement is a high priority for physicians in many fields.
Objectives. The aims of this study were to analyse the correlation between bone scintigraphy findings and clinical symptoms and to validate the diagnostic specificity achievable in this context by supplementing the dermatologist's clinical examination with bone scintigraphy.
Materials and methods. This study included 211 patients with BD (mean age 49.0±10.8 yr; M/F 53/158). The prevalence of joint complaints, based on clinical evaluations and positive bone scintigraphy results, was estimated for each of anatomic sites, and agreement between bone scintigraphy findings and clinically evaluated joint complaints was assessed using Cohen's kappa (κ) statistic. Furthermore, a patient subset (n=104) whose joint complaints and scintigraphy findings were mutually compatible was re-evaluated by a rheumatologist to determine the level on diagnostic specificity attained by combining bone scintigraphy with clinical examinations of dermatologists.
Results. The total kappa value (211 patients) was 0.604, indicating fair agreement between joint complaints and scintigraphy results. Individual analysis of eleven joint categories revealed that there were statistically significant correlations in wrist (κ=0.677), shoulder (κ=0.661), and foot joints (κ=0.618). Of the 104 cases referred to a rheumatologist, 95 (91.34%) were confirmed as having BD-associated articular involvement. Joints acral areas (*e.g.*, foot, hand, wrist, and shoulder) that had the highest kappa value correlations also ranked highest in diagnostic specificity.
Conclusion. Bone scintigraphy is simple to perform and may be useful to assess joint involvement in BD patients, especially for specific anatomic sites. By improving diagnostic specificity in BD-associated arthritis, the capacities of physicians in various fields to effectively manage this unique and chronic inflammatory disease is heightened, allowing proper control of joint symptoms and prevention of destructive arthritis through early detection.

O17.

DIETARY AND NON-DIETARY TRIGGERS OF ORAL ULCER RECURRENCES IN BEHÇET'S DISEASE

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Background. Recurrent oral ulcers (OU) are a highly consistent feature of Behçet's disease (BD), but their pathophysiology is not well understood. Certain foods or other external factors admittedly play a role in BD-related OU recurrences. However, the proportion of patients among whom we can identify a specific triggering factor of their OU recurrences and the nature of these factors remain unknown.
Objectives. To study the role of dietary and non-dietary factors as triggers of BD-related OU recurrences.
Methods. A 23-item self-reporting questionnaire was given to in- and outpatients with BD who attended 7 French hospital departments of internal medicine over 12 months. Patients were enrolled if they agreed to participate and if they had a history of OU that had not definitively abated to ensure patients' ability to provide accurate information. The questionnaire consisted of 13 questions collecting general information (e.g., demographic characteristics, dietary habits, age at onset and severity of OU). Six open-ended, dichotomous (Yes or No) or scaled questions (Yes, I am sure, Yes, that's possible, No, that's highly unlikely, or I

don't know) collected information on potential OU-triggering factors. In particular, the questionnaire evaluated the effect of 6 general triggering situations (i.e., fatigue/stress, dental care, tooth brushing, menstruation, infection, and food), 24 selected food items, of 8 physicochemical properties of food (*i.e.*, salty, sweet, bitter, sour, astringent, hard, hot, cold), and of fast eating. The results are given as proportion of positive responses; for scaled questions, the response Yes, I am sure was considered positive.

Results. Among 101 questionnaires distributed, 87 were returned and 81 were usable. Among the 81 patients (mean age 41 years, 62% male), 79 (96%) fulfilled the ICBD classification criteria, 75% had a non-French origin and 83% consumed European-style food. The mean time since OU onset was 19 years; 53 patients (65%) reported >50 OU lifetime attacks and 42 (52%) qualified their OU recurrences during the previous 12 months as "very discomforting" or "discomforting". Among the 6 general situations suggested, 50 patients (62%) recognized ≥1 as a "sure" trigger of OU recurrence: fatigue/stress (37%) and food (32%) were the most frequent triggers. Among the 24 suggested foodstuffs, walnuts (48%), pineapple (42%), peanuts (32%), Emmental cheese (30%), almonds (24%), lemon (22%), and other cheeses (21%) were the most frequently reported. Sourness was the most frequently reported "sure" physicochemical OU-triggering food characteristic (13%). The corresponding open-text responses and subgroup analyses of the patients with >50 OU lifetime episodes or with "very discomforting" or "discomforting" OUs over the previous 12 months were highly consistent.

Conclusion. Most patients can identify triggering factors for their BD-related OUs, with fatigue/stress and food representing the most frequent triggers. The management of OU must take into account such external factors. The histamine-rich or histamine-liberating properties of the commonly cited OU-triggering foods suggest a hypersensitivity mechanism.

O18.

ORAL HEALTH CAN BE IMPROVED BY ORAL HYGIENE EDUCATION IN BEHÇET'S DISEASE: A LONG-TERM FOLLOW-UP STUDY

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Objective. The aim of the study was to evaluate factors associated with the oral health of patients with Behçet's disease (BD) in long-term follow-up.

Materials and methods. In this retrospective study, non-selected 143 BD patients (F/M: 87/56, mean age:33.4_7.1 years) followed by clinical and laboratory assessments were included. Among them, 93 patients (F/M:57/36, mean age: 31.9_6.9 years) were followed with dental and periodontal indices and oral hygiene education in each visit regularly (Regular follow-up (RF) group), whereas 50 patients (F/M:20/30, mean age:37.3_6.7years) were not under regular oral hygiene control (comparative (CP) group). The mean follow-up periods were similar between the groups (RF: 5.2±2.9 years vs CP: 4.4±2.3 years, p=0.18).

Results. Although no significant differences were observed in periodontal indices between RF group and the comparative group at baseline (p>0.05), scores of plaque index, gingival index and sulcus bleeding index were found to be higher in the CP group (1.9±0.9; 1.8±1.1 and 2.2±0.9) than the RF group (1.2±1.03; 1.5±1.1; 1.6±1.2, respectively) at the end of current follow-up (p>0.05).

When groups are analysed separately, in the RF group, scores of dental and periodontal indices were similar at baseline (plaque index:1.1±0.9; gingival index:1.5±0.9; sulcus bleeding index: 1.5±1.01) and follow-up (p>0.05).

In contrast, indices were worse at follow-up (plaque index:1.9±0.9; gingival index: 1.9±1.1; sulcus bleeding index: 2.2±0.9) than baseline (1.3±0.9; 1.6±1.01; 1.8±1.1, respectively) at the CP group (p<0.05).

Morover, the number of natural teeth was decreased at follow-up (16.5±8.8) compared to that of baseline (21.8±5.7) at the CP group (p=0.005) whereas was almost the same at baseline (19.9±8.1) and follow-up (19.7±8.7) at the RF group (p=0.94).

The utilisation of dental services for emergency care were higher in the CP group (61.2%) than the RF group (41.9%) (p=0.02). As expected, the frequency of tooth brushing was higher in RF group (1.3±0.8) than the CP (0.4± 0.5) (p=0.000) at follow-up.

Conclusion. A stability in oral health was accomplished in BD patients by oral hygiene motivation and education in long-term follow-up. As oral ulcers affect oral health poorly, a more aggressive approach for better oral health should be aimed in all BD patients to eliminate microbial factors which are a part of pathogenic processes.

Key words. Oral health, oral hygiene and Behçet's disease.

O19.

PAPULOPUSTULAR LESIONS ACCORDING TO AGE, SEX AND BODY PARTS IN BEHÇET'S SYNDROME PATIENTS COMPARED HEALTH POPULATIONS AND DISEASED CONTROL

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Objective. To assess whether papulopustular lesions are different in Behçet's syndrome (BS) according to site, age, sex and medications when compared to rheumatoid arthritis (RA) and apparently healthy population (HP) subjects.

Methods. 209 consecutive BS patients who were routinely followed-up in our dedicated BS center were studied. Patients with RA (n=146) who were followed up in the rheumatology outpatient clinic of the same unit and HP (n=149) were used as controls. All subjects were clinically evaluated by the same dermatologist and all skin lesions (papules, pustules, comedones, folliculitis, cysts, nodules) on the face, trunk and legs were separately counted. Information regarding the demographic and clinical features of primary disease and medications were obtained from patients' charts.

Results. Demographic features and mean number of papulopustular lesions according to site of body were summarized in Table I. Mean number of total papulopustular lesions were similar between BS and HP and significantly higher than in RA (F: 21.7, p:0.0001). Results were similar when subgroups of men and women and age groups (<30, 31-50, >50) were analyzed separately. In all 3 groups the mean total number of papulopustular lesions were significantly lower in older ages (F:95.8, p:0.0001). Corticosteroid use did not impact the results. When we analyzed the number of papulopustular lesions on the legs separately we observed that BS patients had significantly more lesions on the legs when compared to the RA and HP (F:12.2, p:0.0001) due to the high number of pustules and folliculitis on the legs of BS patients. When leg lesions were analyzed according to age, this difference persisted in age groups 31-50 and >50 (age 31-50, F:9.8 p:0.0001; age >50, F:6.2 p:0.002) but not in age group <30 (F: 0.8 p:0.45).

Table I.

	Behçet's syndrome	Rheumatoid arthritis	General population
Mean age (SD)	41±11	52±13	41± 15
Male/Female	78/131	21/125	74/75
Patients with steroid (n)	32 (15 M/17 F)	85 (13 M/72F)	-
N of patents with at least 1 papulopustular lesion	156/209	57/146	101/149
Mean n of total papulopustular lesion (SD)	5.9±7.8	1.5±3.0	6.6 ±9.0
Mean n of papulopustular lesions on the legs (SD)	0.6 ±1.4	0.05±0.6	0.3 ±1.1
Mean n of papulopustular lesions on the face (SD)	2.3 ± 3.4	0.8 ± 1.9	3.2 ± 4.6
Mean n of papulopustular lesions on the back (SD)	3 ± 5	0.7±1.5	3.1 ± 4.9
Mean total n of papulopustular lesion in males (SD)	7.8 ± 9.2	2.8 ± 5	6.3 ± 9.7
Mean n of papulopustular lesions on the legs in males (SD)	1.1 ± 1.8	0.3 ± 1.5	0.3 ± 1.2
Mean total n of papulopustular lesion in females (SD)	4.8± 6.5	1.3 ± 2.5	6.7 ± 8.4
Mean n of papulopustular lesions on the legs in females (SD)	1.2	0.01 ±0.9	0.2 ± 0.9

Conclusions. As had been sporadically observed in the past and now confirmed in a controlled in a study among healthy and diseased controls in a sizeable study BS patients have significantly more papulopustular lesions on the legs when compared to HP and RA. Number of papulopustular lesions tend to decrease as the patient ages in BS similar to RA and HP but it is still higher on the legs among BS even when the patients are over the age of 50. We may consider including only the papulopustular lesions on the legs in future classification/diagnostic criteria for BS.

O20.

FECAL CALPROTECTIN AS A NON-INVASIVE BIOMARKER FOR INTESTINAL INVOLVEMENT OF BEHÇET'S DISEASE

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Background. The diagnostic and prognostic values of fecal calprotectin levels in patients with inflammatory bowel diseases, including Crohn's disease and ulcerative colitis, have been proven. However, little is known about the usefulness of fecal calprotectin (FC) measurement in predicting intestinal involvement of Behçet's disease (BD).
Methods. Forty-four consecutive patients with systemic BD who underwent colonoscopy for the evaluation of gastrointestinal symptoms were prospectively enrolled between November 2012 and March 2014 in a single tertiary medical center. Fecal specimens from the patients were obtained the day before bowel cleansing and 3 months after colonoscopy.
Results. Twenty-five patients showed intestinal ulcerations on colonoscopy (12 [48.0%) typical and 13 [48.0%) atypical ulcerations]. The median FC level in the intestinal BD group was significantly higher than that in the non-diagnostic group (112.53 [6.86-1604.39] vs. 31.64 [5.46-347.60] μg/g, respectively, p<0.001). Moreover, the typical ulceration group showed a significantly higher median FC level than the atypical ulceration group in patients with intestinal BD (435.995 [75.65-1604.39] vs. 71.42 [6.86-476.94] μg/g, respectively, p=0.003). Multivariate analysis revealed higher FC as an independent predictor of intestinal BD (OR=1.020; 95% CI=1.002-1.038; p=0.026). The cut-off level of FC for predicting intestinal BD was 68.89 μg/g (76% sensitivity and 79% specificity). The absolute changes between fecal calprotectin levels and the disease activity index of intestinal BD from initial diagnosis of intestinal BD to 3 months after diagnosis were significantly correlated (Pearson's correlation coefficient=0.470, p=0.027).
Conclusion. The FC level might serve as a non-invasive surrogate marker of intestinal involvement of BD.

O21.

BEHÇET DISEASE IN THE PEDIATRIC AGE: DATA ON 129 PATIENTS COLLECTED FROM AN ITALIAN COHORT

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Behçet's disease (BD) most often affects young adults, but occasionally can have its onset in childhood. Large series describing the disease in the pediatric age are scarce. The aim of our study was to collect information on clinical characteristics and treatment in pediatric patients (pts.) with BD in Italy. Demographic, clinical and therapy data from pediatric pts. with BD, enrolled in the Eurofever registry by Italian Pediatric Rheumatology Centers, have been analyzed. Patients enrolled met the international criteria (Lancet 1990) or were diagnosed by specialists as affected by Behçet's disease. 129 pts. were included in our study: 73 were males and 56 females. In about half of cases (n=64) a follow-up visit was also recorded, in addition to the baseline. Ethnicity was Caucasian for almost all (125/129). Mean age at disease onset was 9 years, mean age at diagnosis 13 years. A positive family history of BD was reported in 14 cases. At the baseline visit 94.3 % had muco-cutaneous symptoms; 41.5% ocular involvement; 35.9% musculoskeletal symptoms; 34.8% gastro-intestinal manifestations; 31.4% constitutional symptoms; 23.5% neurologic involvement. The most common mucocutaneous symptoms were recurrent oral aphtosis (93%); genital ulcers (27%), pseudo-follicolitis (17%), maculopapular rash (16%), erythema nodosum (13%), acneic or papulo-pustular lesions (12% each). Pathergy test was positive in 9 pts., negative in 68, not done in 7. Ocular involvement occurred in 37 pts.: 14 had anterior uveitis, 4 posterior uveitis 5 panuveitis, 8 retinal vasculitis, 5 papilledema, 5 papillitis, 3 episcleritis, 1 band keratopathy and keratitis. The most common musculoskeletal symptom was arthralgia (n=30), followed by myalgia (n=16), oligoarthritis (n=6), polyarthritis (n=5), and monoarthritis (n=2). Abdominal pain (n=30) and diarrhea (n=11) were the most common gastrointestinal symptoms (GI), followed by GI ulcers (n=4), and anal ulcers (n=2); 5 pts. had GI bleeding, one patient presented aseptic peritonitis and 2 patients gut perforation. Constitutional symptoms included recurrent fever in 22 patients, fatigue and malaise in 14. Headache was the most common neurologic symptom (n=17); 7 pts. had cranial nerve palsies, 3 presented vertigo, 1 optic neuritis and 1 aseptic meningitis. Moreover, 1 patient had ataxia and 1 presented hemiplegia and abnormal behavior. Venous thrombosis occurred in 3 pts. (thrombosis of transverse sinus in one of them). HLA-B51 was present in 39 pts., not done in 12. The main treatment used was systemic corticosteroids, followed by colchicine (n=31) and other immunosuppressants, ie azathioprine (n=6), metothrexate (n=5), cyclosporine (n=3), thalidomide (n=2), and cyclophosphamide (n=1). Infliximab was also used in one patient. During follow-up, other biologic agents were also used, ie Adalimumab (n=9) and Anakinra (n=1). This is one of the largest pediatric BD cohorts reported so far. Our data are similar to those of other pediatric series. The performance of the new Ped-BD criteria in our series is currently being evaluated, as well as possible correlations between clinical signs or symptoms at onset with immunosuppressive treatment.

O22.

IMPAIRED QUALITY OF LIFE IN PATIENTS WITH BEHÇET'S DISEASE IS ONLY IN PART RELATED TO DISEASE ACTIVITY.

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Background/Purpose. Behçet's disease (BD) has a chronic-relapsing course, could be debilitating and potentially life-threatening, and it has been associated with impaired quality of life (QoL). The objective of this study was to evaluate, through the Short Form 36 Questionnaire V2 (SF-36V2), the perception of health related QoL (HRQoL) in patients affected with BD and to identify major factors associated with its impairment.
Methods. Sixty-one patients (24 males, mean age 47.3±12.0 years and mean disease duration 14.0 ± 9.5 years) fulfilling the International Study Group (ISG) criteria for BD were enrolled. Patients with primary psychiatric illness were excluded. Each patient underwent clinical examination and completed the SF-36V2. The search for factors independently associated with impaired quality of life (defined as low results in the SF-36V2 domains) included univariate analyses and stepwise multiple regression models. Explanatory baseline variables were age, gender, disease duration, disease activity (Behçet's Disease Current Activity Form –BDCAF-, Physician and Patient Visual Analogic Scale – Phy-VAS and P-VAS, respectively-) and active clinical manifestations (categorized as present/absent). Sixty healthy subjects, 90 patients with Systemic Lupus Erythematosus and 50 patients with Rheumatoid Arthritis were enrolled and served as controls. P values less than 0.05 were considered significant.

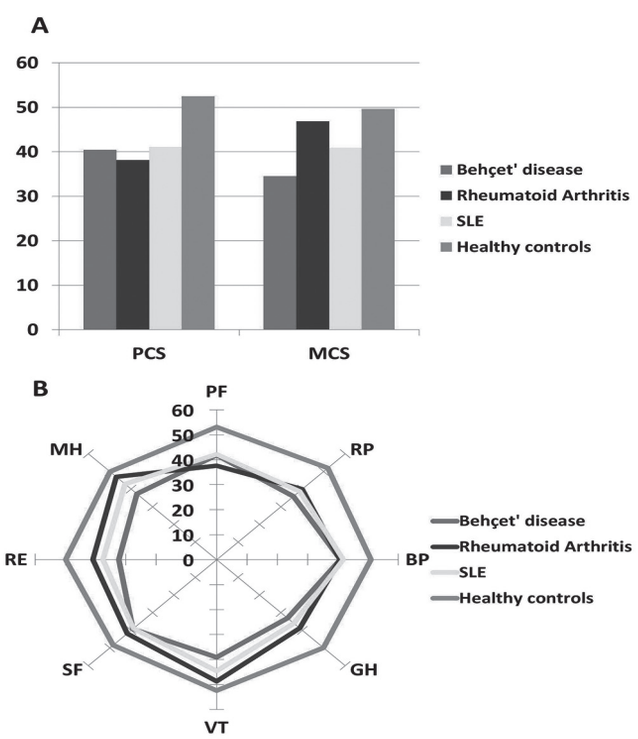

Fig. 1. A-B

Results. Patients with BD showed lower results in the mental component summary (MCS) scale and physical component summary (PCS) scale of the SF36V2 when compared with healthy controls (p<0.01). No differences were revealed comparing PCS score in BD patients (40.4±11.0) with PCS score in SLE (41.0±11.5) and RA (38.2±10.7) patients, whereas MCS score in BD patients (34.5±12.2) was lower than in SLE (40.9±12.0; p<0.01) and RA (46.8±12.9; p<0.01) patients (Figure 1A). This difference was explained by lower results in the mental health (MH), vitality (VT), role emotional (RE) and general health (GH) domains (figure 1B). The low results in PCS were independently associated with higher BDCAF results (p<0.001) whereas no factors independently associated with low MCS results were identified among those investigated.
Conclusions. Patients affected with BD reported of low QoL by means of SF36V2 compared with normal subjects and patients with other chronic systemic diseases. The low results in SF36V2 PCS were associated with high disease activity whereas causes of low results in MCS were not identified. Further studies are needed in order to identify major reasons for impaired mental quality of life in BD and to implement strategy to cope with that.

O23.

CORRELATION OF ESR, CRP, AND THE IRAN BEHÇET'S DISEASE DYNAMIC ACTIVITY MEASURE (IBDDAM) IN THE MAJOR MANIFESTATIONS OF BEHÇET'S DISEASE

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There is a correlation of ESR, CRP, and one of the Disease Activity Measures of Behçet's Disease, the Behçet's Disease Current Activity form (BDCAF), as shown by Melikoglu and TopKarci in Turkish patients.
The aim. of this study is to look for the same in Iranian patients, but with the IBDDAM instead of BDCAF.
Materials and methods. Patients (135) were selected as consecutive patients seen at the Behçet's Unit of the Rheumatology Research Center, Tehran University of Medical Sciences. ESR, CRP, and IBDDAM were calculated for patients having with the active manifestation of the day the patient was seen, and compared with the patients having the same manifestation in the past but not at the day of the evaluation. The t-test was used for the comparison. The number of cases (active and inactive), the mean, and the standard deviation (SD) is given. Then, items were compared by Mann-Whithney U Test and the p value is given. If the null hypothesis was rejected the figure was specified by *.
Results. Number of patients, active cases (AC), the mean and SD for ESR – CRP – IBDDAM were in oral aphthosis (OA): 59 (24.25, 22.4–13.3, 19.0–13.3, 15.5), and for inactive cases (IC) 76 (18.1, 20.3–8.4, 15.9–21.0, 27.0), p was 0.06, 0.03*, 0.5. In genital aphthosis (GA): AC 14 (34.1, 21.6–19.2, 18.0–6.5, 9.4), IC 73 (20.5, 10.5–17.5, 15.4–15.4, 22.2), p was 0.02*, 0.009*, 0.001*. Skin (Sk): AC 12 (30.7, 25.4–19.2, 25.1–14.7, 35.4), IC 23 (19.9, 16.5–9.8, 11.5–11.6, 13.9), p was 0.33, 0.46, 0.38. Pseudofolliculitis (PF): AC 6 (25.8, 21.0–15.3, 25.1–26.0, 49.4), IC 29 (23.1, 20.5–12.6, 16.2–9.9, 12.8), p was 0.36, 0.25, 0.22. Erythema nodosum (EN): AC 8 (37.0, 25.9–27.1, 27.8–3.4, 1.8), IC 27 (19.7, 17.0–8.9, 10.8–15.4, 25.7), p was 0.13, 0.12, 0.10*. Pathergy test (PT): AC 19 (20.95, 14.7–15.8, 23.6–20.6, 29.4), IC 49 (25.6, 27.1–11.6, 19.2–13.7, 17.5), p was 0.2, 0.09, 0.07. Eye Involvement (EI): AC 68 (11.9, 9.9–6.7, 13.6–31.7, 24.1), IC 24 (20.9, 25.4–12.6, 20.1–4.4, 6.7), p was 0.3, 0.5, 0.000*. Anterior uveitis (AU): AC 16 (16.4, 12.9–15.5, 23.3–44.4, 36.8), IC 52 (10.6, 8.4–3.9, 7.2–27.8, 17.5), p was 0.000, 0.000, 0.000. Posterior uveitis (PU): AC 60 (11.4, 9.3–6.1, 13.6–32.6, 24.8), IC 8 (15.7, 13.6–10.5, 14.4–25.0, 17.4), p was 0.000*, 0.06, 0.000* . Retinal Vasculitis (RV): AC 45 (10.2, 8.0–6.6, 15.5–38.8, 25.7), IC 23 (15.3, 12.2–6.7, 9.4–17.8, 11.8), p was 0.000*, 0.05, 0.000*. Vascular manifestations (VM): AC 10 (59, 28.1–38.8, 20.1–5.1, 3.6), IC 3 (21.3, 18.3–10, 17.3–3.0, 2.6), p was 0.05*, 0.11, 0.29. Joint Manifestation (JM): AC 17 (46.2, 21.8–20.2, 21.1–5.3, 5.6), IC 9 (19.0, 20.8–14.3, 22.0–5.9, 7.9), p was 0.001*, 0.43, 0.56. Neurological Manifestations (NM): AC 2 (18.0, 4.2–2.0, 2.8–6.5, 0.7), IC 1 (7–3–42), p was 1, 1, 1.
Conclusion. ESR and/or CRP were significantly higher in active cases of OA, GA, AU, PU, RV, VM, JM, and NM. IBDDAM was higher in OA, GA, EI, AU, PU, and RV.

O24.

EFFECT OF INFLIXIMAB IN CHRONIC PROGRESSIVE BEHÇET'S DISEASE: INFLUENCES OF TIME OF INTRODUCTION ON THE OUTCOME OF THE PATIENTS

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Objectives. Chronic progressive neuro-Behçet's disease (CPNBD) is characterized by progressive deterioration leading to disability and death. It has been appreciated that methotrexate is effective for CPNBD. In addition, recent studies have demonstrated that infliximab is effective for patients with recalcitrant CPNBD who had inadequate responses to methotrexate. However, the appropriate timing for introduction of infliximab remains unclear. We therefore explored the effects of intervals before introduction of infliximab on the outcome of patients with chronic progressive NBD.
Methods. Eleven patients (8 males, 3 females, ages 35.2±9.3 [mean±SD]), who met the international classification criteria for BD with CPNBD and received infliximab, were followed up until October 2015. The functional disability of the patients was rated by Steinbrocker functional classification as used in rheumatoid arthritis. Correlation between the patients' outcome and the intervals before the introduction of infliximab was analyzed by Spearman's rank correlation test.
Results. All the 11 patients had received methotrexate prior to infliximab. The intervals from the onset to the introduction of infliximab and the follow-up periods were 26.6±35.1 months and 65.2±43.6 months [mean±SD], respectively. Among the 11 patients, 9 patients did not show progression after the introduction of infliximab, whereas 2 patients progressed. In the latter 2 patients, infliximab had been discontinued before the final follow-up. The functional disability grades of the patients after the introduction of infliximab were significantly correlated with the intervals from the onset of CPNBD to the introduction of infliximab (r=0.6177, p=0.0476).
Conclusion. The results indicate that the delay of the introduction of infliximab leads to the irreversible functional disability of the patients with CPNBD. Thus, it is recommended that infliximab should be administered as soon as possible for the patients with CPNBD who do not respond to methotrexate adequately.

O25.

INFLIXIMAB THERAPY FOR NEUROLOGICAL, VASCULAR, AND INTESTINAL INVOLVEMENT IN BEHÇET'S DISEASE: EFFICACY, SAFETY, AND PHARMACOKINETICS IN A MULTICENTER, PROSPECTIVE, OPEN-LABEL, SINGLE-ARM PHASE 3 STUDY

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Background. Behçet's disease (BD) is a multisystem disease characterized by mucocutaneous, ocular, neurologic, vascular, or gastrointestinal manifestations. Involvement of the nervous system (neurological BD [NBD]), the vascular system (vascular BD [VBD]), and the intestinal tract (intestinal BD) is rare, although such cases tend to have a poor prognosis.
Objectives. We conducted a multicenter, prospective, open-label, single-arm phase 3 study to determine the efficacy, safety, and pharmacokinetics of infliximab (IFX) in BD patients with these serious complications who had displayed poor response or intolerance to conventional therapy (ClinicalTrials.gov, NCT01532570).
Methods. IFX at 5 mg/kg was administered to 18 patients (3 NBD [2 acute and 1 chronic progressive], 4 VBD, and 11 intestinal BD) at Weeks 0, 2, and 6 and every 8 weeks thereafter until Week 46. In patients who showed inadequate responses to IFX after Week 30, the dose was increased to 10 mg/kg. We then calculated the percentage of complete responders according to the predefined criteria depending on the symptoms and results of examinations (ileocolonoscopy, brain magnetic resonance imaging, computed tomography angiography, positron emission tomography, cerebrospinal fluid, or serum inflammatory markers), exploring the percentage of complete responders at Week 30 as the primary endpoint.

Results. The percentage of complete responders was 61% (11/18) at both Weeks 14 and 30 and remained the same until Week 54. By BD type, the percentage of complete responders at Week 30 was 33% (1/3) among NBD patients, 100% (4/4) among VBD patients, and 55% (6/11) among intestinal BD patients. In acute NBD patients, IFX lowered the cell count and interleukin-6 concentrations in the cerebrospinal fluid and inhibited the onset of attacks. In a chronic progressive NBD patient, IFX lowered cerebrospinal fluid interleukin-6 concentrations along with inhibition of progression of clinical symptoms and brainstem atrophy. VBD patients showed improvement in clinical symptoms at an early stage (Week 2) with reductions in serum C-reactive protein (CRP) levels and erythrocyte sedimentation rate. Imaging findings showed reversal of inflammatory changes in three of the four VBD patients. Intestinal BD patients showed improvement in clinical symptoms along with decrease in serum CRP levels after Week 2. Consistently, scarring or healing of the principal ulcers was found in more than 80% of these patients after Week 14. Irrespective of the type of BD, all patients achieved improvement in quality of life, leading to the dose reduction or withdrawal of steroids. IFX dose was increased to 10 mg/kg in three intestinal BD patients, resulting in improvement of clinical symptoms, CRP levels, and visual analogue scale score. Safety and pharmacokinetics profiles were comparable to those in patients with rheumatoid arthritis or Crohn's disease.
Conclusions. IFX is effective and well tolerated in the treatment of NBD, VBD, and intestinal BD with poor response or intolerance to conventional therapy. IFX may therefore represent a promising new therapeutic option for use in BD patients with these serious complications.

O26.

EFFICACY AND SAFETY PROFILE OF ANTI-INTERLEUKIN-1 TREATMENT IN BEHÇET'S DISEASE

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Growing data have provided encouraging results on the use of interleukin (IL)-1 inhibitors in Behçet's disease (BD). This study was aimed at reporting the largest experience with anti-IL-1 agents in BD patients. We evaluated 30 BD patients receiving treatment with anti-IL-1 agents. The primary aims of the study were to evaluate the efficacy of anakinra (ANA) and canakinumab (CAN) in a cohort of BD. The secondary aims were to evaluate the overall safety profile of the treatments, explore the timing of response to therapy and any adjustment of dosage and frequency of drugs studied, and investigate predictive factors of response to therapy. The frequency of first line therapy was 90 % with ANA and 10 % with CAN. The overall number of subjects in complete remission after 12 months of therapy with anti-IL-1 drugs was 13: 6 maintained the initial therapy regimen, 1 maintained the same initial anti-IL-1 drug with further therapeutic adjustments, and the remaining 6 shifted from ANA to CAN. Among them, 3 used CAN for at least 12 months without therapeutic adjustments, 1 had therapeutic adjustments, and 3 had an overall history of a 12-month complete remission. Adverse events (AEs) were reported in 15 % patients who received ANA, represented in all cases by local cutaneous reactions, while no AE were observed in patients who received CAN; we did not observe any serious AEs (SAEs) during the follow-up period. Our data have confirmed that the use of anti-IL-1β drugs is efficacious and safe with an overall acceptable retention on treatment.

Basic Science

P1.

INCREASED SERUM ANTIBODY TITER AGAINST HPV-16 ANTIGEN IN PATIENTS WITH BEHÇET'S DISEASE

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Objectives. It was reported that quadrivalent Human Papillomavirus (HPV) vaccine was significantly associated with Behçet's disease (BD). There was no report that HPV infection can be an one of the possible causes to develop BD. The objective of this study to evaluate whether the anti-HPV antibody titer in BD would increase.
Methods. Sera from 93 Korean BD patients, who fulfilled the diagnostic criteria of the International Study Group for BD were used for ELISA. The clinical activity of BD was evaluated at the time of blood sampling. HPV 16 L1 VLP antigen was used in this study for ELISA.
Results. Patients with BD had significantly higher antibody titer against HPV 16 (OD:0.210-3.675; mean 0.992) than that of healthy controls (OD:0.248-0.762; mean 0.517) (p<0.001). Using ROC analysis from analysis, the cut-off value for anti-HPV antibody titer of 0.578 OD was determined in order to differentiate BD patients from healthy controls. When we compared the clinical features of BD between the two groups, articular involvement of BD could be more likely in patients with anti-HPV 16 antibody titer <0.578 OD (p=0.035). In addition, patients with anti-HPV 16 antibiody titer <0.578 were significantly younger than patients with anti-HPV 16 antibody titer ≥0.578 OD.
Conclusion. There might be a possibility that HPV can be an one of the extrinsic triggering possible infectious agent for the development of BD.

P2.

IL-27 GENE POLYMORPHISMS IN IRANIAN PATIENTS WITH BEHÇET'S DISEASE

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Background. Behçet's Disease (BD) is a chronic systemic inflammatory disease of unknown etiology, principally characterized by relapsing periods of a broad range of clinical symptoms. Cytokines play fundamental roles in the pathogenesis of BD. Polymorphisms within cytokine genes have been found to play a pathogenic role in the development of autoimmune/inflammatory disorders. Interleukin 27 (IL-27), a new pro/anti inflammatory cytokine, is a great candidate for chronic inflammatory disease studies. The purpose of this study was to investigate a possible association between polymorphisms in the IL-27 gene and susceptibility to BD.
Methods. Fifty Iranian patients with BD and one hundred healthy individuals were examined for rs153109A/G and rs181206T/C IL-27 gene single nucleotide polymorphisms using RFLP-PCR and ARMS-PCR, respectively. Allele and genotype distributions were compared between groups using chi-square or Fisher's exact test.
Results. Frequencies of the rs153109AA genotype and rs153109A allele were statistically higher in BD patients comparing with the control group (p=0.034 and p=0.011, respectively). The genotype and allele frequencies of rs181206 T/C polymorphism in BD patients were not significantly different from those of healthy controls.
Conclusions. Present findings demonstrate for the first time that IL-27 gene rs153109 A/G SNP may be involved in susceptibility to BD in the Iranian population.

P3.

FUNCTIONAL ANALYSIS OF M1 AND M2 MACROPHAGE IN BEHÇET'S DISEASE

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Introduction. The recent GWAS have identified susceptible loci encompassing chemokine CCR1 and anti-inflammatory cytokine IL10, genes highly expressed in macrophages, suggesting its pathological roles in Behçet's disease (BD). Interestingly, reduced expression of CCR1 is associated with risk for BD. Recently, inflammatory macrophage M1 and anti-inflammatory M2 polarization has gained attention in the immunology field.
Objectives. To compare features of in vitro differentiated M1 and M2 macrophages from peripheral blood between BD and healthy controls (HC).
Methods. Differentiation into M1 or M2 macrophages (Mϕ) was induced in vitro from peripheral monocytes in the presence of GM-CSF or M-CSF, respectively. Expressions of CD68, CD163, and CCR1 were determined by real-time PCR and flow cytometric analyses. For the Mϕ that were treated with LPS for 24 hours, supernatants were analyzed for cytokine profiles using beads assay. GWAS identified IL10 SNP rs1518111 was genotyped.
Results. As previously shown, differentiated M2 expressed conventional M2 marker CD163 protein and mRNA, but not M1, confirming validity of our assay to differentiate M2. M1 Mϕ produced higher amounts of IL-6, whereas only M2 secreted IL-10 cytokine, although we could not find significant difference of cytokine production between HC and BD in our assay. Both mRNA and protein analysis of CCR1 revealed higher expression in M2 compared to M1 Mϕ. In comparison between HC, CCR1 protein in M1 was higher in BD. Finally, we found significant association between IL-10 mRNA expression and rs15181111 SNP genotypes in M2Mϕ from HC.
Conclusion. We found that CCR1 and IL-10 are highly expressed in M2Mϕ. GWAS-identified SNP genotypes could affect on expression of CCR1 and IL-10 in M2Mϕ, resulting in lower migration of anti-inflammatory cells to site of active inflammation.

P4.

SEQUENCING OF 16S RRNA REVEALS A DISTINCT SALIVARY MICROBIOME SIGNATURE IN BEHÇET'S DISEASE

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Objective. Behçet's disease (BD) is a multisystem inflammatory disorder characterized by recurrent oro-genital ulcers, mucocutaneous lesions and serious organ involvement. This study was undertaken to investigate the structure of the salivary microbiome in BD patients.
Methods. Stimulated saliva samples were collected from 31 BD patients and 15 healthy controls, and detailed oral health indices were recorded. In 9 BD patients a second oral health evaluation and saliva collection was performed following dental and periodontal treatment. High-throughput sequencing of the 16S rRNA V4 region in saliva samples was performed. Sequences were rigorously filtered and grouped into phylogenetically-related operational taxonomic units (OTUs), used to measure bacterial community diversity and richness. OTUs were classified using a 16S rRNA reference database at the species-level. AMOVA and LEfSe analyses were used to measure differences between patients and controls at the community- and species-level, respectively.
Results. Sequence analysis identified a total of 908 OTUs present across all samples. Patients had a microbial community structure that is significantly different and less diverse compared to healthy controls. The most overabundant species in BD patients compared to controls was Haemophilus parainfluenzae, while the most depleted included Alloprevotella rava and species in the genus Leptotrichia. Patients receiving periodontal treatment showed improvements in oral health indices, but no short-term differences in bacterial community structure. Neither the BD-associated genetic risk locus within the HLA-B/MICA region nor being on immunosuppressive medications explained the differences between patients and controls.
Conclusion. This is the first high-throughput sequencing-based evaluation of the salivary microbiome in BD. These findings demonstrate that the salivary microbiome of BD patients has a specific signature characterized by changes at the community and species level.

P5.

INCREASED EXPRESSION OF ARYL HYDROCARBON RECEPTOR IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF PATIENTS WITH ACTIVE BEHÇET'S DISEASE

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Behçet's disease (BD) is characterized by multi-systemic vasculitis. Although the pathogenesis of BD remains elusive, low frequency of regulatory T cells (Treg) and high frequency of T helper 17 cells (Th17) have been suggested to contribute to BD pathogenesis. Given that aryl hydrocarbon receptor (Ahr) is involved in the induction of Treg and Th17 cells, we analyzed the expression of Ahr and indoleamine-2,3-dioxygenase 1 (IDO1) producing endogenous Ahr ligand in the peripheral blood mononuclear cells (PBMCs) of patients with BD. Both protein

and mRNA expression of Ahr was elevated in the ex-vivo PBMCs of patients with active BD compared to healthy controls, but protein levels of IDO1 were not. Notably, IDO1 expression was significantly increased in patients with recurrent aphtous ulcer compared to healthy contols. Stimulation of PBMCs with lipopolysaccharides (LPS) and/or 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) did not alter the expression level of Ahr and IDO1 in patients with BD. Further study is warranted to evaluate the role of Ahr in the pathophysiology of BD and as a biomarker for monitoring BD patients.

P6.

TRIM21 IN MONOCYTE ENHANCES TH1/TH17 INFLAMMATION IN BEHÇET'S DISEASE

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Background. Behçet's disease (BD) is a chronic, multisystem vasculitis and autoinflammatory disorder, characterized by oral ulcers, genital ulcers, various inflammatory skin lesions, and uveitis. The exact cause of BD is still not known, many study suggest that this disease triggered by environmental factor including infectious agents such as herpes simplex virus (HSV) and streptococcus sanguinis. Tripartite motif containing 21 (TRIM21), an E3 ligase protein, regulates the production of cytokine by ubiquitination of transcriptional factors such as interferon regulatory factor (IRF) family and NF-kB. Moreover TRIM21 can present antiviral properties, mediating antiviral defense mechanisms to DNA/RNA viruses.
Objective. The purpose of this study was to elucidate TRIM21 proteins expression in monocyte of BD patient, and to identify the role of TRIM21 on immune dysregulation in BD.
Methods. Monocytes and T cells were isolated from peripheral blood using Ficoll-Hypaque density-gradient centrifugation and relevant immunomagnetic negative selection method. Protein levels were measured using western blot, ELISA, and flow cytometry. Co-cultures between monocyte and responder T cells (1:1 to 1:2 ratio) were maintained in media for 7~14 days. Knock-down of TRIM21 was performed using siRNA technique on THP-1 or freshly isolated monocytes.
Results. TRIM21 expression was increased in peripheral blood monocytes from BD patients compared to healthy control. The expression of IRF8, a representative ubiquitination target of TRIM21, was also decreased in BD monocyte. BD monocyte promoted secretion of pro- inflammatory cytokines including Th17 promoting cytokine such as IL-6, IL-1β and IL-23 following NF-kB activation. BD monocytes promoted Th17 polarization after co-culture with responder T cells from healthy donors, and IL-17A production from these co-cultured T cells was also increased. Known-down of TRIM21 in monocyte using siRNA prevents NF-kB activation and decreased Th1 and Th17 polarization of responder T cell in co-culture system.
Conclusion. From our results suggest that BD monocytes facilitate Th/1Th17 differentiation of naive T cells and TRIM21 may regulate the secretion of pro-inflammatory cytokine from monocytes.

P7.

THE ROLE OF CD206 IN PATIENTS AND MOUSE MODEL OF BEHÇET'S DISEASE

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Although the exact etiology of Behçet's disease (BD) remains unclear, a complex interaction of T cells and antigen presenting cells is known to be important in the immunopathogenesis of BD. This study was aimed to identify the role of CD206, one of pattern recognition receptors, in BD. CD206 positive cell frequencies were analyzed by flow cytometry in patients and mouse model, and several serum cytokine levels were detected by ELISA in mice. The ligand of CD206 treatment down-regulated the frequencies of CD206 in vitro culture of PBMC and in vivo treatment of normal mice. The treatment with a ligand of CD206 also decreased disease severity score and induced improvement of symptoms accompanied with regulation of cytokines in mice. CD206 positive cell frequencies were different between ligand responsive BD mice and non-responsive BD mice. All these findings showed that expression of CD206 was correlated to the BD symptoms.

P8.

SERUM LIPOPOLYSACCHARIDE LEVELS ARE ASSOCIATED WITH DISEASE ACTIVITY OF THE ORAL MUCOUS MEMBRANE IN BEHÇET'S DISEASE.

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Purpose. Gut microbial dybiosis is capable of inducing systemic, extra-intestinal and ocular inflammation in murine models. We hypothesise that the translocation of gut microbial endotoxins through the dysfunctional mucous membrane drives disease. We investigated the link between serum lipopolysaccharide (LPS) levels, as a surrogate marker of increased gut permeability, and disease activity in Behçet's Disease (BD).
Methods. BD patients attending the multidisciplinary Behçet's clinic at the Birmingham and Midland Eye Centre, UK, underwent complete clinical assessment for evidence of disease activity using the validated BD Current Activity Form. Active ocular inflammation was defined as at least a 2+ increase in intraocular cells between clinic visits or the presence of a hypopyon as assessed by slit lamp, whilst active oral lesions were defined as the appearance of new ulceration of the oral mucous membrane. Serum LPS levels were quantified by ELISA with Limulus Amebocyte Lysate chromogenic endpoint assay. Serum LPS levels in patients with BD (n=23) were compared with serum samples from healthy volunteers (n=10) and disease controls (ocular mucous membrane pemphigoid (OcMMP; n=15)). We obtained longitudinal serum samples from BD patients (n=7) to monitor changes in serum LPS with disease phenotype and progression. Non-parametric statistical analyses were analysed by Mann-Whitney U test and Kruskal-Wallis test.
Results. There was no statistically significant difference in the LPS levels between patients with BD [median: 0.244 EU/ml; interquartile range (IQR): 0.108-0.778], OcMMP [0.175; 0.140-0.202], and healthy controls [0.200; 0.164-0.251] (p=0.504). BD patients with inactive oral lesions had significantly higher levels of LPS (0.462; 0.168-0.856) compared to those with active oral lesions (0.119; 0.057-0.148) and healthy controls (0.200; 0.164-0.251) (p=0.012). There was no difference in the LPS levels of BD patients with active vs. inactive ocular inflammation (p=0.142).
Conclusions. Serum LPS levels are associated with oral mucous membrane disease activity and indicates a potential role for microbial translocation in the inflammatory pathophysiology of BD.

P9.

CXCL1, CXCR1 AND IL-17A

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Purpose. Behçet's disease (BD) is a chronic inflammatory disease that is characterized by the recurrent involvement of oral and genital ulceration, cutaneous, ocular, and vascular lesions. The pathogenesis of BD is unknown,however, genetic and environmental factors participate in the inflammatory processes. IL-8, IL-12 and IL-17 participates in the pathogenesis of BD. Dysregulation of cytokines such as TNF- IL-8/ CXCL1 is a leukocyte chemoattractant factor and accumulates neutrophils into the lesional skin. CXCL1 is produced by macrophage, endothelial cells, neutrophils and keratinocytes. Susceptibility of single nucleotide polymorphism of CXCL1 in BD has been mentioned. IL-17 protein secretion by peripheral blood mononuclear cells was influenced by different allele of the IL-17A gene. However, little is known about the association of IL-17A with each of the clinical phenotypes of BD.
Materials and methods. Genomic DNA was analyzed by PCR with specific primers. The PCR products were sequenced using an ABI Big Dye cycle sequencing termination kit (Applied Biosystems, Foster City, CA). Fisher's test was performed to examine the statistical correlations. P-values of <0.05 were considered to be statistically significant.
Results. Genotype frequency of CXCL1 (-353T/A) SNP in BD and healthy controls was TT:62.0%, TA:32.2%, AA:5.7% in healthy donor (n=87), and TT:50%, TA:44.3%, AA:4% in BD patients (n=70). The frequency of TA genotype of BD patients did not accept significant difference with healthy donor. There were no significant difference of allele frequencies of CXCR-1 (+2607G/C), CXCR2 (+785C/T, +1208T/C) SNP in BD patients and healthy controls.
There were no significant difference in the genotype and allele frequency of IL-17A gene SNP between BD patients and controls. No significant differences in the genotype frequency of IL-17 gene SNP were identified between populations with or without clinical signs, such as skin involvement, ocular involvement, vascular involvement, arthropathy, epiditimitis and central nervous involvement. However there was a higher tendency of IL-17 A genotype A frequency in BD group concerning interstinal involvement. Thus, these results suggest the possibility that there may be some association between IL-17A gene mutaion and gastrointestinal tract formation in BD. The biological function of IL-17 towards ulcer formation in the gastrointestinal tract will be required in the future experiments.
Conclusion. Our result suggests the possibility that there may be an association between the IL-17A gene polymorphism and gastrointestinal symptoms in patients with BD, although there was not a significant difference.

P10.

SERUM AMYLOID A STIMULATED PRODUCTION OF PRO-INFLAMMATORY CYTOKINES BY PERIPHERAL BLOOD MONOCYTES IN PATIENTS WITH BEHÇET'S DISEASE

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Background. Behçet's disease (BD) is a systemic inflammatory disorder characterised by an abnormal innate and adaptive immune response with consequent hyper-activation of pro-inflammatory mediators. The main clinical features of BD are represented by recurrent oral aphthosis, genital ulcers and chronic relapsing bilateral uveitis configuring the wide known "triple symptom complex". Serum amyloid-A (SAA) is an inflammatory biomarker recently associated to BD, whose production is influenced by mediators of inflammation such as IL-6, IL-1 and TNF-α. Moreover, it has been shown that several innate immune cells including neutrophils produce pro-inflammatory cytokines through inflammasome activation after SAA stimulation.
Objectives. The aim of this study was to assess the putative role of SAA in the pathogenesis of Behçet's disease.
Methods. Monocytes obtained from heparinised venous blood of Behçet's disease patients (BD, n=14) and healthy controls (HC, n=7) have been stimulated or not with SAA, and serum cytokine levels of IL-1β, IL-18, IL-6 and TNF-α have been consequently assessed using a multiplex bead analysis. Statistical approaches including two-tailed Mann-Whitney test (for two non-parametric groups) and Student's t-test (for two parametric groups) have been used for statistical comparisons between groups. Correlations have been demonstrated using Spearman's correlation (two-tailed p-value) analysis.
Results. We noticed an increased production of IL-1β (p=0.0017), TNF-α (p=0.0003) and IL-6 (p=0.0003) in BD monocytes after SAA stimulation. The amount of pro-inflammatory cytokines production did not differ between HC group and BD group. We also found that IL-1β levels were positively correlated with IL-6 (r=0.842, p<0.001), and TNF-α (r=0.889, p<0.001), whilst a positive correlation between TNF-α levels and IL-6 levels (r=0.894, p<0.001) was shown. Also IL-18 showed a positive trend with no significant differences between the two groups.
Conclusions. SAA might trigger peripheral blood monocytes of BD patients to overproduce pro-inflammatory mediators, thus contributing to the inflammatory manifestations typically observed in this disorder.

References

1. HATEMI G, YAZICI Y, YAZICI H: Behçet's syndrome. *Rheum Dis Clin North Am* 2013; 39: 245-611.
2. VITALE A, RIGANTE D, LOPALCO G, BRIZI MG, CASO F, FRANCESCHINI R, DENARO R, GALEAZZI M, PUNZI L, Iannone F, Lapadula G, Simpatico A, Marrani E, Costa L, Cimaz R, Cantarini L: Serum amyloid-A in Behçet's disease. *Clin Rheumatol* 2014.
3. LOPALCO G, LUCHERINI OM, VITALE A, TALARICO R, LOPALCO A, GALEAZZI M, LAPADULA G, CANTARINI L, IANNONE F: Putative Role of Serum Amyloid-A and Proinflammatory Cytokines as Biomarkers for Behçet's Disease. *Medicine* (Baltimore). 2015 Oct; 94(42): e1858.

P11.

INCREASED SENESCENT CD8+ T CELLS IN THE PERIPHERAL BLOOD MONONUCLEAR CELLS OF BEHÇET'S DISEASE PATIENT

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Background. Behçet's disease (BD) is a chronic inflammatory disease characterized by recurrent mucocutaneous ulceration and complications such as blindness and large vessel inflammation. Immunosenescence, aging of immune system, is related to increased susceptibility to infectious diseases, vaccine failure, and chronic low grade systemic inflammation. The role of immunosenescence in BD is not well understood.
Objective. We investigated the differences in the frequencies of immunosenescent cells in peripheral blood mononuclear cells in BD patients and controls.
Methods: Peripheral blood mononuclear cells were extracted from age-matched active BD patients (n=19), inactive BD patients (n=20), disease controls (n=15) and healthy controls (n=15). Using flow cytometry, the frequencies of senescent CD4+ T cells (CD3+ CD4+ CD27- CD28- cells), CD8+ T cells (CD3+ CD8+ CD27- CD28- cells), and B cells (CD19+ CD27- IgD- cells) were analyzed. The differences among the groups, the correlation with age in normal controls, and whether the steroid treatment or specific organ involvement affected the frequencies of senescent immune cells were investigated. In addition, senescent-associated β galactosidase (SA-β-Gal) activity was investigated in CD8+ T cells, using flow cytometry with 5-Dodecanoylaminofluorescein Di-β-D-Galactopyranoside (C12FDG).
Results. In active BD patients, the frequency of CD3+ CD8+ CD27- CD28- cells was significantly higher than in disease controls and in healthy controls, respectively. Also, the frequency of CD3+ CD8+ CD27- CD28- cells increased significantly with the age in normal controls, in accordance with the previous literature. Other senescent immune cells did not show significant differences. Neither the steroid treatment nor specific organ involvement had significant influence on frequencies of senescent immune cells. Frequencies of SA-β-Gal+ cells among CD8+ T cells were significantly higher in active BD and in inactive BD compared to those in disease controls and healthy controls HC, respectively.
Conclusion. CD8+CD28- T cells, or senescent CD8+ T cells, are increased in peripheral blood mononuclear cells of patients with BD.

P12.

IL-17 EXPRESSION BY LYMPHOCYTES IS HIGHER IN BEHÇET'S DISEASE COMPARED TO TAKAYASU'S ARTERITIS

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Objectives. Interleukin-17 (IL-17) has been associated with the pathogenesis of various autoimmune/inflammatory diseases. The aim of this study was to investigate the expression of Th17-related immunity in two phenotypically different disorders: Behçet's disease (BD) with innate and Takayasu's arteritis (TAK) with adaptive immune responses.
Methods. Peripheral blood mononuclear cells (PBMC) from 37 patients (age: 38.5±9.8 years) with BD, 25 patients (age: 42.7 ±15.5 years) with TAK and 25 HC (age: 39.1±9.3 years) were cultured in Th17 inducing conditions (IL-6, PHA, IL-1β and IL-23) for 6 days. Cultured cells were stained with CD4, CD8, CD3, TCRgamma/delta, CD19, IFN-γ and IL-17 antibodies to determine the intracellular cytokine secretion by flow cytometry.
Results. In BD patients, IL-17 expression by CD4+ T cells was observed to be higher than TAK patients (p=0.02). IL-17 expression by CD8+ and γδ+ T cells was also higher in BD compared to HC (p=0.004, p=0.003 respectively). No differences were observed between the groups in the IL-17 production by B cells. Under Th17 inducing conditions, production of IFN-γ by CD4+, CD8+, and γδ+ T cells were also higher in BD compared to TAK patients and HC (p<0.05 in all).
Conclusion. Our results suggest that under Th17 stimulating conditions, T cells express higher IL-17 levels in BD. More prominent IL-17 and IFN-γ production by all lymphocyte subsets in BD might be associated with the increased innate responses and early tissue neutrophil infiltrations in BD, which is not observed in TAK.

Key words. Behçet's disease, Takayasu's arteritis, interleukin-17, Th17 cells

P13.

A SERUM METABOLOMIC ANALYSIS IN BEHÇET'S DISEASE: A PRELIMINARY STUDY

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Background. Behçet's disease (BD) is a chronic inflammatory disorder of unknown etiology. The diagnosis of BD is mainly based on clinical manifestations and remains a challenge in clinical practice, due to the fact that there are no diagnostic biomarkers available currently. Recently metabolomics has been applied in discovering and validating biomarkers of inflammatory diseases. This study aims to identify serum metabolites associated with BD diseases and to search for the metabolites responsive to treatment using metabolomics approach.
Methods. Medical records and serum samples of 24 pre-treated BD patients and 12 post-treated patients at Peking Union Medical College Hospital were collected. 25 gender and age matched healthy volunteers serums were also collected. Metabolomics and lipidomics profiling were carried out by using UPLC-QTOFMS and UPLC-QTOFMSE respectively. Raw mass spectrometric data were processed using Progenesis QI software. Statistical analysis and putative ion identification on the post-processed data were conducted utilizing MetaboLyzer.
Results. 24 BD patients (15 men and 9 women) were all Han Chinese population. Their mean age was 35.83±11.96 years old. Their disease duration of BD was 120 months (range 13–379). Unsupervised principal component analysis (PCA) plots of the lipidomics and metabolomics data showed separation of profiles

from BD patients and healthy controls. Statistical analysis of the data revealed statistically differential metabolites between BD patients and healthy controls. Identification of selected metabolites was confirmed by comparing MS/MS fragmentation pattern with authentic standards. It is of interest to note that treatment recovered some but not all of these differential metabolites.
Conclusions. Our study suggests that the altered levels of the metabolomics profile may be indicative in the diagnosis of BD. Some of the metabolites may provide insights for therapeutic effects.

P14.

BEHÇET'S DISEASE UNDER MICROBIOTIC SURVEILLANCE?

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Background. Behçet's disease (BD) is an idiopathic systemic disease driven by excessive T-cell response, possibly triggered by infectious antigens in genetically susceptible hosts. Crohn's Disease (CD) resembles BD in symptoms and intestinal inflammation, and recent studies demonstrated intestinal dysbiosis in CD patients. We, therefore, hypothesized that intestinal dysbiosis affects the immune system and BD.
Methods. Fecal and oral samples of 22 patients and 24 age, sex and ethnicity matched controls were collected and analyzed using 16S RNA sequencing
Results. Principle covariant analysis did not reveal distinction of different clusters of fecal samples and oral swabs from patients and healthy controls. We identified enrichment of fecal samples with Ruminococcus and of oral samples with Porphyromonas gingivalis in patients compared to controls. From subgroup analysis of patient samples we identified enrichment of fecal samples with Rikenellaceae and loss of Prevotella copri associated with uveitis. In addition, Enrichment of oral samples with Streptococcus sp and Neisseriaceae was associated with uveitis.
Conclusion. We show distinct deviations in both oral and fecal microbiota of patients with BD compared to healthy controls, and between BD patients with and without uveitis. Although these results suggest a possible role for dysbiosis in the pathogenesis of BD and could implicit new treatment strategies, these results should be confirmed in a separate BD cohort, and validation of causal relations of microbial shifts and BD need subsequent investigation in for instance eye models.

P15.

CD16+VΔ2 T CELLS AND THEIR FUNCTIONAL POTENTIAL IN BEHÇET'S DISEASE

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Background. Behçet's disease (BD) is a multisystem inflammatory disorder characterized by oral and genital ulcerations, ocular, joint and skin lesions with episodes of exacerbation and remissions. The pathogenesis remains inconclusive but immuno-dysregulation involving γδ T cells (Vδ2 subsets) have been reported. Vδ2 T cells are the major subset of γδ T cells which is a prototype of atypical T cells responsible for bridging the innate and adaptive immunity. CD16 (FcgammaRIII) differentiates these Vδ2 T cells into distinct functional subsets which are less studied in BD. This study investigated the proportion of CD16+Vδ2 T cells in BD and their potential roles on the induction and/or maintenance of pro-inflammatory characteristics of the disease.
Methods. PBMCs from BD patients and healthy controls (HC) were analysed by flow cytometry for the expression of Vδ2, CD16 and CD56. Intracellular IFNγ, IL17, Perforin and TNFα expression and the effect of phosphoantigen (HMB-PP) stimulation on CD16+Vδ2 T cells was also investigated.
Results. CD16+Vδ2 T cells were significantly increased in BD compared to HC. CD16 expression was higher in CD56+ rather than CD56-Vδ2 T cells and CD56+CD16+Vδ2 T cells were significantly increased in BD. CD16+Vδ2 T cells showed greater potential to express TNF-α and IL17 whereas CD16-Vδ2 T cells expressed greater IFNγ. When compared with HC, CD16+Vδ2 T cells showed significantly increased IL17 whilst IFNγ expression was significantly decreased in BD with no significant differences in Perforin and TNF-α expression. Finally, CD16+Vδ2 T cells were up-regulated following phosphoantigen stimulation.
Conclusion. Increased CD16+Vδ2 subset found in BD in association with altered cytokine expression underpins a potential role of these cells in the disease pathogenesis which might be responsible for inducing and/or maintaining the pro-inflammatory characteristic of BD.

P16.

DIFFERENTIAL DIAGNOSTIC PROBLEMS IN PATIENTS WITH ADAMANTIADES-BEHÇET'S DISEASE

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The 48 year-old female patient presented in our emergency department with aching mucosal erosions in the mouth and lip area, itchy lesions on hands and knees and in a bad general condition. In addition, she reported a recurrent herpes labialis (approximately every 2 months) over several years. The patient suffers from Adamantiades-Behçet's disease with oculo/mucocutaneous manifestations: bilateral recurrent panuveitis, macular oedema, oral aphthous ulcers, recurrent genital ulcers, and arthralgia. The oral mucosa of the patient was covered with ulcers and small blisters on an erythematous base. The right lower lip area was covered by honey-yellow crusts. On the left forearm and elbow, both femur and tibia, gluteal and genital area multiple small vesicles on erythematous base or erythematous papules and plaques were detectable. The patient has acutely being treated with oral prednisolone because of the history of recurrent uveitis and the suspicion of a disease recurrence. Because of the untypical clinical picture of the ulcers biopsies were performed. The histology of the papules on the left elbow and femur detected an erythema exsudativum multiforme. The laboratory examination showed an active Coxsackie infection. This case is a good example of how misleading the history of a patient may be and the importance to know and recognise the special features of Adamantiades-Behçet's disease

P17.

OSTEOPONTIN LEVELS AND OTHER IN OCULAR BEHÇET'S DISEASE: A CONTROLLED STUDY

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Aim. Osteopontin (OPN) is a cytokine involved in inflammatory and autoimmune mechanisms. In this study, we aimed to investigate OPN in active and inactive Behçet's uveitis
Patients and methods. Twenty-two patients with Behçet Disease (BD) were assessed by the same ophthalmologist for eye involvement. Blood samples from each patients were taken twice: first during an eye attack and after about three months, after the attack subsided. OPN, Interleukin 12 (IL-12) and interleukin 10 (IL-10) levels were measured. Eighteen patients with active systemic lupus erythematosus (SLE) along with 18 age and sex-matched healty subjects were also studied.
Results. OPN levels in patients with active Behçet's uveitis (96.79 ± 34.09 ng/mL) and SLE group (119.88±66.55 ng/mL) were higher than in healthy controls (67.29±24.29 ng/mL) ($p<0.05$, $p<0.01$, respectively) while there was no significant differences in OPN levels between patients with active Behçet's uveitis and SLE. No significant difference in the levels of OPN was found between active and inactive periods of patients with Behçet's uveitis. OPN showed positive correlation with C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels in SLE patients ($p<0.05$, $p<0.05$, respectively). No significant differences were found in the levels of IL-10 and IL-12 between patients with active Behçet's uveitis and healthy controls. In SLE patients, IL-10 and IL-12 levels were significantly higher compared with healthy controls ($p<0.001$, $p<0.001$, respectively), and active uveitis group ($p<0.01$, $p<0.001$, respectively). There were no significant differences in IL-10 and IL-12 levels between patients with active Behçet's uveitis and those with inactive Behçet's uveitis.
Conclusions. No differences in OPN levels were observed not only between active and inactive Behçet's uveitis, but also between active Behçet's uveitis and SLE. These results suggest that OPN might not be an important cytokine at least in eye disease in BD.

P124.

IMMUNOLOGICAL PROFILING OF AQUEOUS HUMOR IN BEHÇET'S DISEASE PATIENTS WITH ACTIVE OCULAR INVOLVEMENT

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Background. Behçet's disease (BD) is a systemic inflammatory disorder whose clinical hallmark are recurrent oral and genital ulcers, variably associated with various organ involvement. Uveitis and retinal vasculitis are among the most common manifestations, occurring in 60-80% of patients during the disease course. The pathogenesis of BD is still unclear. Some HLA-I residues have recently been shown to influence antigen binding and regulate the activation of both Natural Killer (NK) cells and CD8+ cytotoxic T lymphocytes. Higher levels of Natural Killer T (NKT) cells (CD3+ CD56+) have previously been found in the aqueous humor (AH) of patients with BD-related uveitis as compared to other types of uveitis. The aim of our study was to perform an immunological profiling of AH in BD patients with active uveitis, comparing it to that of AH from patients with active Vogt-Koyanagi-Harada (VKH) disease and subjects with cataract undergoing surgery.
Patients and Methods. AH of 8 adult patients with BD (according to 1990 ISGB criteria) and active uveitis, and of 8 patients with active VKH were analyzed. Patients were defined as having active uveitis when ≥ 2 cells in the anterior chamber (Hogan scale, 1950), and/or 2+ vitritis (Nussenblatt scale, 1990), papillitis, macular edema supported by optical coherence tomography and retinal vasculitis with active 'photo fundus', were found. AH from 5 subjects undergoing cataract surgery were included as controls. Cytokines' concentrations were determined with the Bio-Plex Pro Human cytokine 27-plex assay (Bio-Rad®). Frequency of NK and NKT cells was determined by flow cytometry using anti-CD3, -CD56, -CD16 antibodies.
Preliminary Results. Levels of IL-1β, IL-1RA, IL-5, IL-7, IL-6, G-CSF, IFN-γ, IP-10, TNF-α were higher in AH from patients with BD and VKH compared to controls. In particular, we found a 3000-fold increase in IL-6 levels; G-CSF and IFN-γ were detected in AH from BD and VKH patients, but not in the control group. Lower levels of GM-CSF were found in BD and VKH patients as compared to controls. No differences were detected between BD and VKH patients regarding cytokine levels. However, HA from 4 BD patients showed a peculiar distinct pattern in terms of cytokine levels, when analyzed by unsupervised cluster analysis. The frequency of NKT (CD3+ CD56+) cells was higher in BD patients as compared to VKH, while that of NK (CD56+ CD3neg) and T cells (CD56neg CD3+) was similar. Finally, no difference was found between NKT and NK subsets in terms of proportion of CD16+ cells in both BD and VKH groups.
Discussion. Our preliminary results confirm the previous observation of increased NKT cells levels in BD uveitis as compared to VKH. In addition, AH of both BD and VKH groups showed increased levels of IL-6, G-CSF and IFN-γ, which might suggest their potential role in the immune-pathogenesis of those types of uveitis. A distinct cytokine profile able to distinguish the two conditions remains to be identified.

Epidemiology and Genetics

P18.

HLA REVISITED IN EGYPTIAN PATIENTS WITH BEHÇET'S SYNDROME: NEW ASSOCIATIONS OF HLA ALLELES WITH SUSCEPTIBILITY, PROTECTION, PRESENTATION AND SEVERITY OF THE DISEASE

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Background. Behçet's syndrome is a multisystem autoimmune syndrome. Its manifestations usually start in the young adulthood affecting mainly the skin, eyes, Brain and blood vessels (1)
Objectives. The aim of the study was to perform HLA class I genotyping in a cohort of Egyptian patients with Behçet's syndrome and comparing them with HLA genotyping in healthy population (control group) to estimate the syndrome susceptibility and possible association between HLA and syndrome presentations.
Methods. Fifty-seven Egyptian patients with Behçet's syndrome fulfilling the International study group criteria for Behçet's syndrome (2) were recruited from the Rheumatology department, Cairo University teaching hospitals. HLA class I genotyping was done for all patients via sequence specific oligonucleotides probes at the National Cancer Institute. HLA class I genotyping data of normal control group was obtained from case control studies done on Egyptian population with a total of 221 individual (3-4).
Results. The studied 57 patients were divided into 50 males and 7 females. The mean age of patients was 35.28 ± 9.73 years with mean disease duration of 9.26 ± 7.36 years. The main clinical features were oral ulcers (100%), genital ulcers (100%), eye involvement (54%) neurological involvement (29%) and vascular involvement (36%) furthermore (33%) had bilateral visual acuity ≤6/60 fulfilling the diagnosis of legal blindness. Certain HLA genotypes were significantly associated with susceptibility for Behçet's syndrome, the odds ratio (OR) for HLA-A68 was 8.4 (CI=2.9-25.9) , HLA-B15 was 6.7 (CI=2.9-15.6) , HLA-B51 was 6.6 (CI=3.4-13.0), HLA-A24 was 4.0 (CI=1.5-10.2) and HLA-A2 was 2.1 (CI=1.1-3.8). On the other hand HLA A3 genotype was found to be significantly protective with odds ratio of 0.003(CI=0.01-0.6). HLA B51 was significantly associated with ocular disease with odds ratio of 3.47. Furthermore HLA B51 was associated with legal blindness with a significant odds ratio of 5.21.
Conclusions. HLA A68, B15, B51, A24 and A2 are associated with Behçet's syndrome susceptibility in the present cohort of Egyptian patients and A3 was found to be protective. HLA B51 is associated with ocular involvement and more important the blinding eye disease and can be considered as a poor prognostic marker for ocular disease.

References

1. YAZICI H, SEYAHI E, YURDAKUL S: Behçet's syndrome is not so rare: why do we need to know?. *Arthritis & Rheumatism* 2008; 58 (12): 3640-3643.
2. WEICHSLER B, DAVATCHI F, MIZUSHIMA Y, HAMZA M, DILSEN N, KANSU E, LEHNER T *et al*.: Criteria for diagnosis of Behçet's disease. *Lancet* 1990; 335 (8697), 1078-1080.
3. EL-HAGRASSY N, EL-CHENNAWI F, ZAKI MES, FAWZY H, ZAKI A, JOSEPH N: HLA class I and class II HLA DRB profiles in Egyptian children with rheumatic valvular disease. *Pediatric cardiology* 2010; 31(5): 650-656.
4. MOSAAD YM, FARAG RE, ARAFA MM, ELETREBY S, ELALFY HA, ELDEEK BS, TAWHID ZM: Association of Human Leucocyte Antigen Class I (HLA-A and HLA-B) With Chronic Hepatitis C Virus Infection in Egyptian Patients 2010.

P20.

HLA-B5/51 GENOTYPE: AN ASSOCIATION WITH THE CLINICAL MANIFESTATIONS OF BEHÇET'S DISEASE

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Objective. To estimate the contribution of HLA-B5/51 genotype to the clinical manifestations and risk of Behçet's disease (BD) in two ethnic groups.
Subjects and methods. 146 BD patients fulfilling the International Criteria for BD (ICBD) were divided into two ethnic groups: 1) 86 patients from Dagestan (representatives of 8 ethnic nationalities in this region) with mean age30.7±9.6 years; disease duration – 8.8±10.1 years; 2) 60 ethnic Russian patients, nonresidents of Dagestan with mean age 32.9±11.1 years; disease duration – 11.2±10.1 years. All patients were examined at the V.A. Nasonova Research Institute of

Rheumatology in 1990 to 2014. HLA class I antigens were typed by a microlymphocytotoxic technique using a Gisans anti-leukocyte sera kit (SaintPetersburg).
Results. HLA-B5/51 was detected in 87 (59.6%) patients, much more often in men than in women (70 and 38%, respectively; $p<0.01$). Genital ulcers and erythema nodosum were significantly more common in HLA-B5/51-positive Dagestani (87.3 and 57%) than in HLA-B5/51-negative ones (56.5 and 26%; $p=0.0019$ and $p=0.01$;respectively). There were no significant differences in these signs in the Russian group of patients with BD depending on the presence of this allele. In HLA-B5/51-positive male Dagestani patients with BD, the risk of erythema nodosum was twice as high as that in HLA-B5/51-negative patients ($p=0.054$). In HLA-B5/51 female Dagestani carriers, the risk of genital ulcers and generalized uveitis proved to be 3.5 ($p=0.057$) and 2.7 times higher than that in HLA-B5/51 noncarriers. Frequency of HLA-B5/51 was 73.2% among the Dagestanis and 40% among the Russians. Furthermore, this investigation revealed HLA-B5/51 carriage mainly in the male BD patients. Therefore, in addition to ethnicity, gender should be borne in mind when analyzing the clinical associations with HLA-B5/51.

P21.

DETERMINATION OF METHYLATION AND EXPRESSION OF IL-10 GENE IN PATIENTS WITH BEHÇET'S DISEASE

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Behçet's disease (BD) is an autoimmune disease which is described by recurrent aphthous stomatitis, uveitis, genital ulcers, and skin lesions. Variation in the methylation of Interleukin -10 (IL-10) gene have been proven in the pathogenesis of inflammatory diseases but it was not studied in Behçet's disease. Therefore the goal of this study was to measure the methylation level of IL-10 in patients with BD compared with the control group and to determine the expression of this gene in the two groups. In this study, blood samples from 40 patients and 40 healthy control were taken, with the mononuclear cells isolated with ficoll protocol. The DNA and RNA were then subsequently extracted. Following this, the extracted RNA was converted to cDNA using the RT-PCR method, with the expression of IL-10 later evaluated by Real-time PCR. As we expected, the expression level of this gene was significantly decreased in the patient group compared to the control. Also in this study, the methylation of IL-10 was measured by MeDIP (Methylation DNA Immunoprecipitation) technique and since methylation of promoter regions have inhibitory effects on gene expression, the rate of methylation increased in this gene and hypermethylated. According to these results, we suggest that hypermethylation of promoter regions of IL-10 can affect the regulatory regions and eventually it plays a role in the pathogenesis of Behçet's disease.

P22.

TRANSITION OF CLINICAL MANIFESTATION IN JAPANESE BEHÇET'S DISEASE: A RETROSPECTIVE STUDY OF 578 PATIENTS

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Objective. To evaluate phenotype transition of Behçet's disease after the publication of retrospective study of 412 patients by Ideguchi et al in 2007.
Methods. We retrospectively analyzed 578 patients, who fulfilled 1987 Diagnostic Criteria of the Behçet's Disease Research Committee of Japan. Presence of clinical manifestations as oral ulcer, genital ulcer, etc, HLA-B51 positivity,observation period, date of diagnosis, and rate of complete type (patients having all eye, oral ulcer, skin rash, and genital ulcer) were selected as variables. We further divided the patients into three groups based on the year of diagnosis (before 2000, 2000-2007, and after 2008) and analyzed their phenotypes.
Results. The patients' characteristics of the study were as follows: female n=331, male n=247, average of disease onset, 36.8±12.4 y.o, frequency of oral ulcer 99.0%, genital ulcer 72.3%, uveitis 61.6%, skin involvement 88.8%. As previously shown, rate of uveitis and neuro type were significantly higher in male, whereas rate of genital ulcer, arthritis were higher in female. After the adjustment of observation period, we performed Cochran–Armitage test to evaluate the transition of disease phenotypes. The result showed significant decease of complete type, genital ulcer, and HLA-B*51 positivity, whereas increase of gastrointestinal disease.
Conclusions. We found continuous transition of Behçet's disease phenotypes in Japanese patients.

P23.

ASSOCIATION OF GENETIC POLYMORPHISMS IN INTERFERON-Γ, INTERLEUKIN-6 AND TRANSFORMING GROWTH FACTOR-B1 GENE WITH BEHÇET'S DISEASE SUSCEPTIBILITY

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Behçet's disease (BD) is a chronic relapsing, multisystem inflammatory disease characterized by recurrent oral and genital mucous ulcers, and ocular and skin lesions. Cytokines play an important role in the pathogenesis and disease progression of BD. The aim of this study was to investigate the impact of gene polymorphisms of T helper cell subtype Th1 and Th2 cytokines, interferon-gamma (IFN-γ), interleukin-6 (IL-6) and transforming growth factor (TGF)-β1 on BD susceptibility in a Saudi cohort. Sixty-seven unrelated patients with BD and 195 healthy controls were genotyped for IFN-γ (874A/T), IL-6 (174G/C) and TGF-β1 (509C/T) polymorphisms. Genomic DNA was extracted from the peripheral blood of BD patients and controls using QIAamp R DNA mini kit (Qiagen Hilden, Germany). IFN-γ gene was amplified using amplification refractory mutation systems (ARMS)-PCR methodology to detect polymorphisms at position 874 of IFN-γ. The TGF-β1 (509C/T) and IL-6 (174 G/C) polymorphisms were detected by PCR- restriction fragment length polymorphism (PCR-RFLP) technique. The frequency of genotype AT of IFN-γ (874A/T) was significantly higher while genotype AA was lower in BD patients as compared to controls ($p<0.05$). The frequency of T containing genotypes (AT+TT) was also higher in BD patients as compared to that in controls ($p=0.02$). The frequencies of allele T and A were not statistically different in patients and controls ($p=0.31$). There was no significant difference in the frequencies of alleles and genotypes of IL-6 (174G/C) and TGF-β1 (509C/T) polymorphisms between patient and control groups. These results indicated that genotype AT of IFN-γ (874A/T) polymorphism is associated with BD risk and genotype AA is protective to BD. On the other hand the polymorphisms IL-6 (174G/C) and TGF-β1 (509C/T) may not be associated with BD risk in our population. It is concluded that IFN-γ (874 polymorphism is associated with the susceptibility of BD, however further studies with large sample size involving different ethnic populations should be conducted to strengthen these results.

P24.

THE PREVALENCE OF BEHÇET'S DISEASE IN NORTH JORDAN

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Introduction. The prevalence of Behçet's disease (BD) is much higher in countries along the ancient Silk Route than in north Europe and the USA. Here we report the first epidemiological study of BD from another mid-eastern country, Jordan.
Purpose. To estimate the prevalence of BD among hospital workers in Jordan, with the additional aim of comparing this prevalence among hospital workers in other geographies.
Materials and methods. In the first stage of our survey, 2569 Jordanian hospital workers from 6 hospitals in the north of Jordan were interviewed by trained residents, using a screening questionnaire to identify individuals with recurrent oral ulcers (ROU), previous diagnosis of and/or any major symptom related to BD. In the second stage all individuals with ROU or previous diagnosis of BD identified at stage one, who agreed to a further investigation, were examined by two rheumatologists for the presence/ confirmation of BD according to the

International Study Group (ISG) classification/diagnostic criteria. Pathergy test was performed at 4 sites according to recommendations. The study protocol was approved by ethical committees at Jordan University of Science and Technology, Irbid-Jordan, and the ministry of health.
Results. 2569 employees were interviewed representing 60% of the total number of hospital workers., all were Arabs except for one individual of Cherkasian ethnicity. There were 1245 (48.4%) males and 1324 (51.6%) females, M: F was 0.94:1, mean age: 34.28±8.4 years (range18-73). ROU were present in 210 (8.2%) and family history of ROU in 236 (9.2%) individuals. A previous diagnosis of BD was recorded in 10, family history of BD was reported in 65 (2.5%). The diagnosis of BD according to ISG classification /diagnostic criteria was confirmed in the 10 subjects with previous diagnosis and established in additional 7 hospital workers. Mean age of the 17 patients identified as BD was 38.6±10.7 (range 26-65 y). A family history of BD was noted in 3 (25.0 %) while a family history of BD was present in 62 (2.6%) in the whole group excluding the BD patients (p=0.008). M:F was 2.4:1 compared to 0.94:1 in the whole group. The prevalence rate of BD was estimated 66:10.000 (95% CI 34.8 to 97.5:10000) in the north of Jordan.
Conclusion. In this ever first survey of BD in Jordan, our results indicated that the prevalence of BD in the north of Jordan is among the highest around the world, at 66:10.000, similar to that reported from some parts in Turkey. For easy reference, the prevalence we found can now be compared with those among hospital workers in other geographies.

P25.

OCULAR BEHÇET'S DISEASE IS LESS COMPLICATED WITH ALLERGIC DISORDERS – A NATIONWIDE SURVEY IN JAPAN

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Objectives. Behçet's disease is a systemic inflammatory disorder polarized to the Th1 and Th17 immune systems. Allergic diseases are polarized to the Th2 immune system. The aim of the present study is to investigate the prevalence of allergic diseases in patients with Behçet's disease as a nationwide questionnaire survey in Japan.
Patients and methods. The study involved a large-scale interview survey of Japanese patients with Behçet' s disease at 21 institutes of ophthalmology, and 353 patients (255 males and 98 females) were recruited for this study. We analysed the history of allergic diseases such as atopic dermatitis (AD), allergic rhinitis (AR), bronchial asthma (BA), and drug and/or food allergies (FA).
Results. Oral aphthous ulcers, ocular lesions, skin lesions, genital ulcers, arthritis, neurological lesions, intestinal lesions, deep vein thrombosis and epididymitis were reported in 95.8%, 98.6%, 72.5%, 44.8%, 13.9%, 6.8%, 6.2%, 3.7% and 1.4% of the patients, respectively. It was also reported that 73 patients (20.7%) had histories of allergic diseases. This percentage was significantly lower than ina survey that Japan's Ministry of Health, Labour and Welfare conducted for healthy population (47.6%) (odds ratio = 0.29, 95% confidence interval = 0.22-0.38, $p=4.9\times10^{-22}$).AD (5 cases, 1.4%), AR (36 cases, 10.2%), and BA (19 cases, 5.4%) among the patients were significantly fewer than those of healthy population ($p=4.9\times10^{-14}$, $p=3.3\times10^{-22}$, p=0.006, respectively).
Conclusions. The prevalence of allergic diseases in patients with Behçet's disease was found to be less than in the entire Japanese population.

P26.

ASSOCIATION STUDY OF TRAF5 AND TRAF3IP2 GENE POLYMORPHISMS WITH SUSCEPTIBILITY TO BEHÇET'S DISEASE AND VOGT-KOYANAGI-HARADA DISEASE IN A JAPANESE POPULATION

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Objective. Previous study reported that the polymorphisms of TNF receptor associated factor 5 (TRAF5) and TRAF3 interacting protein 2 (TRAF3IP2) genes were associated with Behçet's disease (BD) and Vogt-Koyanagi-Harada disease (VKH) in a Han Chinese population. In this study, we investigated whether the TRAF5 and TRAF3IP2 polymorphisms are associated with BD and VKH in a Japanese population.
Materials and methods. We recruited 488 Japanese BD patients, 380 Japanese VKH patients, and 1,067 Japanese healthy controls. We genotyped four single nucleotide polymorphisms (SNPs) (rs6540679, rs10863888 and rs12569232 in TRAF5 and rs13210247 in TRAF3IP2) assessed in the previous study using TaqMan assay.
Results. Of the four SNPs, rs13210247 in TRAF3IP2 showed a significant association with BD (p=0.048), and the G allele of rs13210247 had an increased risk of BD (OR=1.53): this finding is in line with the previous study in a Han Chinese population. The other three SNPs were not significantly associated with BD risk. For VKH, rs6540679 in TRAF5 showed a significant association (p=0.0039), and the A allele of rs6540679 had an increased risk of VKH (OR=1.30), whereas the A allele served a protective role in VKH cases of previous study. The other SNPs did not show any significant association with VKH.
Conclusions. We found that rs13210247 in TRAF3IP2 contributes to the risk of BD in both the Japanese and Han Chinese populations, suggesting that TRAF3IP2 is an important risk factor for susceptibility to BD. Further genetic and functional studies are needed to clarify the contribution of TRAF3IP2 to the development of BD.

P27.

PREVALENCE OF BEHÇET'S DISEASE AND OTHER UVEITIC CONDITIONS IN SECONDARY EYE CARE: A PRELIMINARY STUDY

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Aim. The aim of this preliminary study was to document demographic and clinical features of uveitis patients in secondary care setting.
Methods. Uveitis patients who presented at Devrek State Hospital Ophthalmology Clinic between September 2015 and April 2016 were prospectively recorded. The total number of common visits was obtained from the hospital management and the number of uveitis related visits were reached through uveitis patient files.
Results. Between September 2015 and April 2016, 7.536 eye examinations were performed at the ophthalmology clinic (the only eye care center in Devrek district) and 31 of these visits were related with uveitis (0.41%). Fourteen patients (mean age: 37.8 ±18.5, 5 male, 9 female) were diagnosed with uveitis and among them only 3 cases were diagnosed with Behçet's Disease (BD). Other diagnoses included acute idiopathic anterior uveitis (n=5), ankylosing spondylitis (n=3), Fuchs uveitis (n=1), idiopathic panuveitis (n=1) and intermediate uveitis (n=1). Five patients were referred to a tertiary center ophthalmology clinic: 3 cases with BD, 1 case with idiopathic panuveitis, 1 case with intermediate uveitis. There were only two pediatric cases: 1 case with BD and 1 case with intermediate uveitis.
Conclusion. The prevalence of Behçet's disease was reported as 32.1% among uveitis patients in a previous, multicenter tertiary care center study in Turkey. This pilot study indicated a relatively lower prevalence of BD in secondary care setting (21.4%), while BD patients represented 60% of the cases referred to a tertiary center. There may be a referral bias for overrepresentation of BS cases in tertiary uveitis centers.

P28.

BEHÇET'S DISEASE: ETHNOS AND FAMILIAL AGGREGATION

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Objectivs. To study the prevalence of familial aggregation in patients in three ethnic groups: Dagestanians, Chechens and Russians.
Materials and methods. 180 BD patients (probands) who were observed as out- patients and in- patients were questioned within the period of 2011-2014. Distribution of pts according ethnic indication: 86 dagestanians, 34 chechens and 60 Russians. Diagnosis of BD was done according ICGBD criteria (1990). Average age of pts- 30,7+9,6 yrs, disease duration 8,8+10,1 yrs. Genealogical tree of probands for symptoms of BD in relatives was determines by questionnaire. Pts could definitely name only the presence of recurring stomatitis among their relatives.
Results. Cases with recurring aphtous stomatitis (RAS) were found in 54 families: among Dagestanians in 37%, Chechens in 22, Russians- 18%. Repeated cases of RAS in families: father-13, mother-11, siblings: brother-13, sister-8, son-2, daughter-7 In siblings, RAS was met more often than in other relatives. In 13 probands with BB cluster variants of familial aggregation were found- in three families RAS was found: mother-brother- uncle-; mother-son-daughter; father-brother-uncle.
Conclusion: the strong association has been confirmed in different relatives with RAS who should be included in the risk group on BD.

P29.

THE CORRELATION OF PREFECTURAL PREVALENCE OF BEHÇET'S DISEASE WITH CIGARETTE SMOKING RATE IN JAPAN

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Introduction. It is not well known that whether cigarette smoking is associated with pathogenesis of Behçet's disease. Smoking was previously shown to be associated with chronic progressive neurological manifestations of Behçet's disease. On the contrary, smoking was reported to have a favorable effect on mucocutaneous symptoms of Behçet's disease.
Patients and methods. The prevalence of Behçet's or other systemic autoimmune diseases in each of 47 prefectures of Japan is obtained by the registration system of The Ministry of Health, Labour and Welfare (MHLW) Research Project for the Treatment of Intractable Diseases from 1974 to 2014. The smoking rate of adults in each prefecture is obtained by the Comprehensive Survey of Living Conditions by MHLW.
Results. Total number of the registered Behçet's patients in Japan of 2014 was 20,035 (female 11,449) and the point prevalence was 158 patients per million. The prevalence of each prefecture varies from 101 to 240 patients per million. The prefectural prevalence of Behçet's disease is correlated with the smoking rate of adults (p=0.0021). The smoking rate does not correlate with the prefectural prevalence of other systemic autoimmune diseases including SLE, MCTD, GPA, MPA (+PN), Takayasu arteritis or RA with vasculitis. The annual incidence of Behçet's disease in Japan did not show a clear trend from 1974 to 2014; on the other hand, smoking rate has been continuously dropping during this period.
Discussion. The cross sectional data indicated that the prefectural rate of cigarette smoking is associated with prevalence of Behçet's disease in Japan. Of note, the data are not enough to support the cause and effect relationship of smoking and Behçet's disease. The shown relationship can be casual, or be mediated by unknown confounding factors.

P30.

BRITISH PAEDIATRIC SURVEILLANCE UNIT (BPSU) STUDY OF BEHÇET'S SYNDROME IN CHILDREN AND YOUNG PEOPLE IN THE UNITED KINGDOM

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Behçet's syndrome is a rare multi-system inflammatory condition. The disease burden of Behçet's syndrome in patients under 16 years of age in the UK is not well described. The British Paediatric Surveillance Unit (BPSU; www.rcpch.ac.uk/bpsu) has a long history of rare disease epidemiological research. Paediatricians in the UK receive monthly alerts to notify any cases they have seen during the previous month. Return rates for BPSU alerts are high at above 90% providing a robust method of identifying incidence and prevalence of rare paediatric disease.
Aims. 1) To identify the incidence and prevalence of Behçet's syndrome in children under 16 years of age in the UK; 2) To describe clinical manifestations, demographics and patterns of clinical care
Methods. From 1st May 2015, paediatricians in the UK via the BPSU and members of the British Society of Paediatric Dermatologists received monthly email notification forms. Clinicians were asked to report any child up to the age of 16 who had 2 or more of the following features not explained by an alternative diagnosis:

1) Recurrent oral aphthous ulceration
2) Skin involvement
3) Positive pathergy test
4) Eye involvement
5) Genital ulceration
6) Family history of Behçet's syndrome in a biological parent or sibling
7) Vascular involvement
8) Neurological involvement

Reporting clinicians were sent a questionnaire which was completed from case notes and returned to the study team for analysis.
Results. Over the first 11 months, 90 cases have been notified and 28 completed questionnaires analysed (16 cases have been excluded; 8 errors and 8 duplications). Seven of the reporting cases are incident and 21 are prevalent cases. 21 out of 28 cases fulfil the criteria for definite Behçet's syndrome defined in this study as an ICBD score of four or more 1. Children have a wide array of clinical manifestations with recurrent oral ulceration being the most common then genital ulceration (67%) and skin involvement (46%). Eye involvement, neurological and vascular involvement were less common (see Table 1). Most children were followed up in tertiary care by a number of different specialties. According to the reporting clinician, over half the patients had their disease controlled on treatment whilst 29% still had active disease despite treatment.

Table I. Showing demographics, clinical features, management and outcomes of analysed cases (n=28). Numbers in brackets indicate percentages.

SEX	Female	16 (57.1)
	Male	12 (42.9)
ETHNICITY	Any white background	22 (78.6)
	White and Black African	1 (3.6)
	Indian	1 (3.6)
	Pakistani	1 (3.6)
	Turkish	1 (3.6)
	African	1 (3.6)
	Not known	1 (3.6)
MEAN AGE	At Presentation	8.75 years
	At Diagnosis	9.35 years
DISEASE FEATURES	Oral ulceration	27 (96.4)
	Genital ulceration	19 (67.8)
	Skin involvement	13 (46.4)
	- Erythema nodosum	5 (17.8)
	- Skin ulcers	4 (14.2)
	- Pseudofolliculitis	3 (10.7)
	Eye involvement	6 (21.4)
	- Anterior uveitis	1 (3.6)
	- Intermediate uveitis	2 (7.2)
	- Retinal vasculitis	1 (3.6)
	Vascular involvement	2 (7.2)
	Neurological involvement	3 (10.7)
	Other manifestations	
	- Abdominal pain	3 (10.7)
	- Diarrhoea	1 (3.6)
	- Arthralgia	4 (14.2)
FAMILY HISTORY	Sibling/Parent	7 (25.0)
	Non-first degree relative	3 (10.7)
CLINICAL TEAMS INVOLVED	Paediatric Rheumatologist	27 (96.4)
	Adult Rheumatologist	11 (39.3)
	Paediatric Dermatologist	8 (28.6)
	General Paediatrician	16 (57.1)
	Ophthalmologist	23 (82.1)
	Oral Medicine/Paediatric Dentist	14 (50.0)
	Clinical Psychologist	2 (7.2)
	Support Worker	3 (10.7)
	Gynaecologist	3 (10.7
	Special Nurse	12 (42.9)
	Paediatric Immunologist	5 (17.8)
OUTCOMES	Outcome not known	1 (3.6)
	Stable off medication	2 (7.2)
	Recovered with sequelae	1 (3.6)
	Controlled on medication*	16 (57.1)
	Active disease despite medication	8 (28.6)

**Of those children controlled on medication, 2 were on topical therapy only and 14 required systemic treatment which included azathioprine and anti-TNF therapies most commonly*

Discussion. Study findings are limited at this stage related to the small number of completed cases which have been analysed. Incidence and prevalence rates will be calculated once completed 12 month's data is obtained. However, case reporting highlights the extreme rareness of Behçet's syndrome in children within the UK. Comparison of frequency of disease manifestations with non-UK cohorts will be important in future analysis as there may be differences in our UK population, for example a low frequency of ocular involvement. This is important when considering the design of healthcare services that address the needs of children.
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P31.

ARTICULAR MANIFESTATION OF BEHÇET DISEASE IN NORTHERN ITALY

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Purpose. Behçet disease (BD) is a chronic relapsing inflammatory disorder of unknown etiology. We aim to analyze articular involvement in patients with Behçet's disease (BD) of a regional hospital of Northern Italy.
Methods. We retrospectively collected all patients diagnosed with BD following ISG criteria between 1990 and 2016 and followed at the regional hospital S. Chiara, Trento. Data analysis was done by using descriptive statistical indices such as mean and confidence interval. The comparisons were done by hisquare test.
Results. Fifty-nine consecutive patients (45.7% men and 54.3% women) were enrolled. Mean age at disease onset was 39 (range, 22-65) years old, and the observed frequency of HLA-B51 was 73.0% (43/59).
Ethnic backgrounds of the patients were reported as follows: 81.4% (48 cases) from Trentino province (TP), 8.5% (5 cases) from other Italian regions different from TP, 6.8% (4 cases) from Northern Africa, 3.4% (2 cases) from the Middle East.
Musculo-skeletal involvement (MSI; namely arthritis, arthralgia or inflammatory spondylitis) was reported as a presenting symptoms in 23.5% (14/59) of patients, following oral aphthous ulcers (50.0%), genital aphthous ulcers and uveitis (both 32.3%). If not present at onset, MSI developed during the course of disease in other 24 patient, for a total of 50.8% (38/59). Among these, 47.4% received a diagnosis of arthritis (18/38), whereas 89.5% (34/38) reported at least one episode of arthralgia during the disease course, mainly complained as diffused/polyarticular (44% of cases).
Oligo-arthritis was the most frequently reported among patterns of arthritis (42%), followed by monoarthritis (33%) and polyarthritis (25%). Knees was most frequently involved (33%), wrist and ankle followed with 17% of cases; hand, foot and lumbar involvement accounted for 11% of cases each. Mean CRP was 32.0 (range, 0.2 - 266.3) mg/L and ESR 41 mm/h (range, 12 - 89). There was no association between HLA-B51 or HLA-B27 and any type of musculoskeletal involvements ($p>0.05$). It was not possible to analyze extraarticular manifestation associated to MSI flares given the retrospective nature of our study and the low statistical power.
Conclusions. MSI is frequently seen in BD, in more than a half of patients. Despite the data reported in literature for Southern Europe and Middle East, oligoarticular involvement was the most represented arthritis pattern in our cohort, perhaps reflecting a different genetic background of these patients from Northern Italy.

P32.

A DARWINIAN VIEW OF BEHÇET'S DISEASE

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Behçet's Disease (BD) is a multisystem autoinflammatory disease that is prevalent with a specific global distribution between 30° and 45° north across Asia and Europe. The strongest genetic association in BD is the major histocompatibility complex on chromosome 6, specifically HLA-B*51. MHC class I molecules can present peptides to CD8 cytotoxic T cells and control Natural killer cell activity. However ,what is not clear is the function of HLA-B*51 in BD. A recent review supports the concept that MHC class I facilitates immune reactions in a tissue-specific manner that may explain BD pathogenesis.
Recently the Neanderthal genome has been sequenced and analysis has shown a group of HLA molecules that have passed through admixture from Neanderthals to modern humans. Prominent among these is HLA-B*51. The fact that a specific gene has been maintained at high prevalence over such a long period of time suggests a protective effect, probably against pathogens. We will speculate as why the functional characteristics of HLA-B*51 are related to its maintenance in the genome and how this is relevant to BD. Several other SNP in genes including, TNF IL10, PTPN22 and GIMAP, have been reported as associated with BD but only in certain ethnic groups. We will present how these genes may influence HLA-B*51 responses and play a role in the pathogenesis of BD.

P33.

IMPORTANCE OF LESS SENSITIVE FEATURES TO INCREASE PROBABILITIES OF BEHÇET'S DISEASE DIAGNOSIS

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Introduction. The new International Criteria for Behçet's Disease (ICBD) introduced the concept of a plausibility scale for BD. Scoring points >1 and <4 in ICBD suggests very unlikely to possible but not probable diagnosis of Behçet's Disease (BD). To increase the plausibility of BD-diagnosis in those patients who don't fulfill the criteria combinations of less sensitive and specific BD-features can be useful. The aim of this study was to design BD-specific probability tables to be used in patients not yet diagnosed as BD according to ICBD criteria.
Methods. Complete international data-set of the ITR-ICBD study, include 2556 BD patients and 1163 controls from 27 countries was used as a sample. Separate calculations were performed for the Silk-Road, Far-East Asian, African and Western clusters. Positive Likelihood Ratios (LRs) of different features were performed for each cluster. Combinations the LRs for 1- and 0-point features in ICBD were assessed. The results of the combinations were called LR products. Regarding the low prevalence of BD in different populations, the calculations performed based on the prevalence of BD in population who suffer Recurrent Aphthous Stomatitis (RAS) because RAS is a common lesion in normal population and a sine qua non feature for BD. The prevalence of BD in RAS+ population was called pretest probability of BD in this study. The pre-test odds of BD increased by more than 700-fold in the RAS+ population. Post-test probabilities were then calculated as (pre-test odds x LRs) / ((pre-test odds x LRs) + 1).
Results. To use LRs from less sensitive BD-features, LR-products were calculated for the BD-features with only 1 or 0 scoring point in ICBD (skin, neurological, vascular and positive Pathergy test, each one score; joint, cardiac, gastrointestinal manifestations, as well as epididymitis, positive HLA-B51 and family history with score 0). The highest LRs for these clinical features were 4.8 for neurological manifestations in Silk-Road, 13 for HLA-B51 in Far-East Asian cluster, 7.3 and 12.1 for epididymitis in African and Western clusters respectively. The highest LR products obtained by combination of Epididymitis + gastrointestinal + joint manifestations (LR product = 33) in Silk-Road, positive Pathergy test + HLA-B51 + FH (LR product = 332) in Far-Eastern Asian countries, positive Pathergy test + HLA-B51 + FH (LR product = 284) in Africa and Neurologic manifestation + epididymitis (LR product = 91.7) in Western cluster. The higher LRs leaded to the higher posttest probabilities because the increase of numerator contributed to increase in the quotient of the posttest probability calculation.
Conclusion. Combination of LRs for BD-features increased the post-test probability of BD. This study shows the importance of all BD features to diagnose BD and shows the differences of this impact in different areas of the world. Further validation studies may reveal the weakness of current method and improve the estimated probabilities.

P34.

BEHÇET'S SYNDROME ASSOCIATED WITH TAKAYASU'S ARTERITIS: A CASE SERIES OF 10 PATIENTS

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Background. Behçet's syndrome (BS) and Takayasu's arteritis (TA) are both systemic vasculitis of an unknown etiology, each with unique involvement pattern. BS is characterized mainly by recurrent skin –mucosa lesions and uveitis. Arterial involvement is rare in BS and manifests usually as aneurysms or in situ thrombosis. TA affects aorta and its main branches causing narrowing or occlusions. We describe here 10 BS patients with concomitant TA with demographic and clinical characteristics, treatment strategies and outcome.
Methods. We reviewed the charts of patients diagnosed with BS and TA for information regarding patients' gender, age at diagnosis of BS and TA, BS manifestations, symptoms prior to TA diagnosis, type of aortic involvement, and the drugs that were used. All BS patients fulfilled the international study group criteria. The diagnosis of TA was based on the finding of typical homogenous arterial wall thickening.
Results. We identified 10 (0.1%) patients among 9000 BS patients. Their mean age at the time of diagnosis of BS was 31.6±11.5 years, and at the time of diag-

nosis of TA was 37.5±10.8. F/M ratio was 7/3. TA preceded BS in 4 cases (6, 6, 12 and 15 years) and occurred simultaneously in the remaining 6. Skin-mucosa lesions were the most common finding, followed by uveitis (6/10), and arthritis (3/10). Initial symptoms of TA were fatigue and fever in 2 patients, absent pulse in 2, fatigue in 2, arm claudication in 1. The remaining 3 patients were diagnosed as TA while being evaluated for the extent of vascular disease for BS. Subclavian (6/10) and carotid arteries (7/10) were the most commonly involved arteries. In addition to prednisolone, the initial agent was methotrexate in 4 patients, azathioprine in 4, and cyclophosphamide in 1. At the end follow-up (1,2, 2, 3, 7, 7, 9, 18, 21, 23 years), 6 patients had a stable disease following the first treatment, 3 had to switch to infliximab and 1 had to switch to azathioprine after methotrexate. By the end of the follow-up, BS manifestations have resolved in 8 patients, while recurrent arthritis persisted in 2. Seven patients were still on immunosuppressive therapy due to TA, while the remaining 3 were off treatment. None had died.
Conclusions. BS may be associated with TA. Similar associations of TA have been reported with ulcerative colitis, Crohn's disease, and ankylosing spondylitis (1-3). Whether it is a true association or mere co-existence is always debated. Interestingly, in this hybrid setting, both TA and BS followed their own course: while BS abated in time, TA continued its persistent activity.

References

1. TADDIO A *et al*.: World J Gastroenterol. 2013;19: 5933-5.
2. TERAO C *et al*.: Arthritis Rheumatol. 2015.
3. GAN FY *et al*.: Clin Rheumatol. 2014; 33: 355-8.

P35.

AN ITALIAN FAMILIAL CASE OF BEHÇET DISEASE AFTER VARICELLA ZOSTER VIRUS INFECTION

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Behçet's disease (BD) is a multisystem vasculitic syndrome that is characterized by recurrent oral and genital ulcerations, ocular manifestations and additional clinical manifestations in multiple organ systems. The etiology of BD is unknown; environmental and genetic factors may contribute to the development of the disease. A genetic contribution to BD etiology has been suspected for several years on the basis of HLA association, a higher prevalence of BD in some ethnic groups, and the existence of familial cases. Although, the majority of patients with BD are sporadic cases with no family history, a familial aggregation of BD patients has long been noted mainly from Japan and Turkey. A possible role of viruses, particularly the Herpes group of viruses, has also been postulated. In this specific case we present an Italian family in which two of the family members, daughter and father, had BD. The proband, a 25-year-old woman, was admitted to the hospital complaining of recurrent fever and pain genital apthous ulcers. She was diagnosed three years prior to this with BD based on the clinical manifestations of recurrent oral and genital aphthous ulcers, and skin manifestations. On admission, the daughter had painful and multiple ulcerations of the oral mucosa and papulo-pustular lesions; the physical examination was otherwise unremarkable. Laboratory findings for complete blood cell count, ESR, CRP, blood biochemistry analysis and urinalysis were normal. Tests for ANA, anti ds-DNA, c-ANCA and p-ANCA were negative. HLA B51 antigen and the pathergy skin test were negative. The chest radiography and abdominal ultrasonography were normal. Ophthalmological and neurological examinations were also normal. After unsuccessful treatment with colchicine, azathioprine, and methotrexate, in an attempt to reduce the dose of systemic corticosteroids, Adalimumab (40mg every other week) was administered and the clinical condition improved dramatically. The proband's father, a 51 year-old man, was diagnosed with BD two years prior with oral and genital aphthous ulcers and skin manifestations. The HLA analysis revealed B51 antigen positivity. He was undergoing treatment with colchicine and intermittent prednisone. Both subjects were white Caucasians and Italians by descendent. In both cases, the first symptom connected to BD was oral aphthous ulcer which had occurred after chickenpox. After 18 years from the oral apthae onset, the daughter developed recurrent pain genital aphthous ulcers associated with fever and cutaneous papulo-pustular lesions. The father, after 19 years from the oral ulcers onset, developed recurrent genital aphthous ulcers and skin manifestations with papulo-pustular lesions. In both cases, laboratory test for varicella-zoster-virus (VZV) revealed a VZV-IgG positivity and VZV-IgM negativity. To the best of our knowledge, this study provides the first report documenting familial distribution in Italian BD patients. Although the occurrence of BD in consaguineous subjects suggests a genetic etiology, the occurrence of the first symptom after a VZV infection may indicate a possible role of this virus in BD development.

P36.

MEAN PLATELET VOLUME AS A BIOMARKER REPRESENTING CLINICAL ACTIVITY AND TREATMENT RESPONSE IN BEHÇET'S DISEASE

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Background. Chronic inflammation is known to be associated with increased cardiovascular (CV) event rate in autoimmune diseases. Platelet activation may be a link in the pathophysiology of diseases leading to thrombosis and inflammation. Mean platelet volume (MPV), a platelet index, is an indicator of platelet activation. Several studies have shown increased MPV in Behçet's disease (BD) patients with higher disease activity. But, the others failed to find the relation between clinical activity and MPV in BD. Moreover, it is still not clear whether MPV increases or decreases with BD clinical activities and over the duration of treatment.
Objectives. The current study was conducted to evaluate platelet function by measuring MPV in a selected population of newly diagnosed BD subjects. We also aimed to assess associations between MPV and various symptoms. Finally we investigate the changes of MPV in response to treatment.
Methods. We excluded those with established CV diseases or any conventional CV risk factors such as diabetes, hypertension, hyperlipidemia and smoking. Finally 86 BD patients (62 females, age: 49.2±11.3 years) and 160 age- & sex-matched healthy subjects (120 females, age: 49.1±11.6 years) as controls were enrolled for analysis. All patients started to receive treatmet according to the spectrum of symptoms (corticosteroid: 65;75.6%, colchicine: 63;73.3%, DMARDs: 28;33.3%). They underwent laboratory evaluation including HLA-B51, MPV, platelet count, ESR, and CRP at baseline, 1 month, 3 months, 6 months and 12 months. Clinical findings such as oral aphthae, genital ulcer, erythema nodosum, acne, enteritis, uveitis, arthritis and vascular events were all recorded.
Results. At baseline, MPV was higher in BD patients as compared to healthy controls (9.053±0.916 vs. 7.988±0.538 fL, p=0.002). Baseline MPV was higher in patients with oral aphthae, skin manifestation, and vascular event (p<0.05). Initiation of treatment resulted in a significant decrease in MPV (6.952±1.700, 7.250±1.676, and 7.321±1.688 fL at 1 month*, 3 months* and 6 months, respectively; *p<0.001).
Conclusions. The result of this study provides additional evidence supporting the previous reports that MPV is higher in active BD. We also found the correlation of MPV with active symptoms and long-term treatment response in BD patients. A increased MPV seems to be a mirror activity of BD.

P37.

GENOTYPING A PANEL OF GENE VARIATIONS RELATED TO BEHÇET'S DISEASE: A PRELIMINARY ITALIAN STUDY

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Background and aim. Behçet's disease (BD) is a multisystem vasculitis with several manifestations, including recurrent oral and genital ulcers, ocular inflammation, gastrointestinal ulceration and skin lesions. About BD pathogenesis, there is growing evidence that genetics factors contribute to the disease susceptibility and clinical phenotype (1-4). The present study aims to evaluate the mutational state of several BD-related genes in order to investigate their frequency in a cohort of Italian patients.
Materials and methods. We genotyped 15 tag single nucleotide polymorphisms (SNPs) in 11 BD-related genes. Genomic DNA was isolated from whole blood of 50 consecutive BD patients (mean age: 45.5 years; range: 26-67 years; sex ratio: 30M/20F) recruited from Southern Italy. We studied *ERAP1* rs27044 and rs17482078, *HLAB-51:01* rs76546355, *HLAF-AS1* rs4713242, *IL10* rs1518111 and rs1800872, *IL12A* rs17810546, *IL23R* rs17375018, *IL23R-IL12RB2* rs924080, *CCR1* rs7616215, *STAT4* rs7574070 and rs7572482, *KLRC4* rs2617170, *UBAC2* rs9517668 and rs3825427 by applying PCR amplification. PCR amplicons were visualized by agarose gel electrophoresis, direct sequenced and bioinformatically analysed.
Results. Genotypes for all SNPs underlined a high frequency of *IL10*, *CCR1*, *STAT4* and *ERAP1* SNPs. In detail, *IL10* rs1800872 and rs1518111 were identified respectively 40 (80% of cases) and 26 times (52% of cases). We identified *CCR1* rs7616215 in 39/50 patients (78%), *STAT4* rs7574070 in 35/50 patients (70%), while *ERAP1* rs27044 in 32/50 patients (64%).

Conclusions. The results of our investigation showed a high frequency of targeted SNPs in Italian patients. This finding supports the correlation between tagSNPs and BD previously reported in literature by several research groups for different populations. Our preliminary results need to be further confirmed in a larger cohort of patients and controls.

References
1. TAKEUCHI M *et al*.: *Ann Rheum Dis* 2016; doi: 10.1136.
2. GUL A. *Current Opinion in Rheumatology* 2014; 26: 56-63.
3. CONDE-JALDON M *et al*.: *PLoS One* 2014; 9: 1-6.
4. MENTHON DE M *et al*.: *Arthritis Rheum* 2009; 61: 287-1296.

P38.

INVESTIGATING THE MUTATIONAL STATE OF *ERAP1* GENE: THE IDENTIFICATION OF KNOWN AND NOVEL SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) IN A COHORT OF ITALIAN BEHÇET'S DISEASE PATIENTS

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Background and aim. Endoplasmic reticulum aminopeptidase 1 (*ERAP1*) is a key component of the pathway that processes the peptides to optimize their length for MHC-I binding. Single nucleotide polymorphisms (SNPs) in this enzyme have been associated with the susceptibility to several diseases, including Behçet's disease (BD) (1-6). We aim to perform a replication study for *ERAP1* tagSNPs rs2287987 (p.Met349Val), rs30187 (p.Lys528Arg), rs17482078 (p.Arg725Gln) and rs27044 (p.Arg730Glu) previously reported in Turkish (5) and Spanish (6) populations in a Southern Italian cohort. Additionally, in order to discover new BD-susceptibility markers, we also intend to genotype all *ERAP1* exons and exon-intron boundaries.
Patients and methods. We studied a total of 50 BD patients (mean age: 45.5 years; range: 26-67 years; sex ratio: 30M/20F). Genomic DNA was isolated from patient whole blood by means of standard procedures. A preliminary bioinformatics step of primer design, based on gene Reference Sequence (NG_027839.1), was performed by using NCBI Primer-Blast tool. *In vitro* PCR amplification and direct sequencing were carried out for molecularly studying *ERAP1* whole structure. Downstream *in silico* analysis was also conducted for DNA variant analysis. PolyPhen-2 tool was also queried for predicting SNP functional effects.
Results. About known tagSNPs detection, rs2287987 was found in 13/50 patients (26% of cases); rs30187 in 29/50 patients (58%); rs17482078 and rs27044 respectively in 19/50 patients (38%) and 32/50 patients (64%). In addition, seven novel variations were found within *ERAP1* exons. Two *de novo* SNPs resided within *ERAP1* exon 2, rather than p.Arg53Pro and p.Glu56Leu: the first SNP was predicted to be damaging (maximum pathogenicity PolyPhen-2 score) and was found in 9/50 patients (18%). No pathogenic effect was recognized for the second change (p.Glu56Leu), whose frequency was equal to 26% of cases. Exon 3 p.Glu183Val and p.Phe199Ser were identified respectively in 8/50 patients (16%) and in 3/50 patients (6%); both showed a predicted pathogenic effect. Exon 4 p.Lys259Leu was a benign SNP with poor frequency (3/50 patients, 6% of patients). The variation p.Glu337Gln of exon 6 was found in 5/50 patients (10% of cases); no functional impact was predicted for this change. The last SNP was located within the exon 7 of 6/50 patients (12%) and showed high predicted pathogenicity.
Conclusions. Here we reported known and novel *ERAP1* variations in a cohort of Italian BD patients. Our preliminary data were consistent with an association between *ERAP1* and BD. However, future genetic and functional studies, including a larger number of patients and controls, are required to validate our preliminary finding.

References
1. TAKEUCHI M *et al*.: *Ann Rheum Dis* 2016; doi: 10.1136 .
2. OMBRELLO M *et al*.: *Curr Opin Rheumatol* 2015; 27(4): 349-56.
3. STAMOGIANNOS A *et al*.: *Mol Immunol* 2015; 67: 426-35.
4. ZHANG L *et al*.: *Invest Ophthalmol Vis Sci* 2015; 56(10): 6029-35.
5. GUL A: *Curr Opin Rheumatol* 2014; 26(1): 56-63.
6. CONDE-JALDON M *et al*.: *PLoS One* 2014; 9: 1-6.

Clinical and Outcome Measures

P39.

ELEVATED SERUM PROLACTIN IN EGYPTIAN PATIENTS WITH BEHÇET'S SYNDROME

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Background. Behçet's syndrome is an autoimmune disease that is more prevalent among the countries of the ancient Silk Road. (1) Altered levels of prolactin in autoimmune diseases was reported but contradicting data support the role of prolactin in Behçet's syndrome and none was reported among Egyptian patients (2-3).
Objectives. The aim of the study was to investigate the prolactin level in a cohort of Egyptian patients with Behçet's syndrome. Furthermore to associate the prolactin level with patient characteristics, genetic background and disease patterns.
Methods. Patients were enrolled from the Rheumatology department at Kasr Alainy Hospital. Patients fulfilled the International study group criteria for Behçet's syndrome. Serum prolactin level was assayed for patients using electro-Chemiluminescence immunoassay. Normal References were obtained from a reference study validating the used immunoassay platform (4).
Results. Fifty-four patients were studied, among them (88%) were males the rest were females. The patients' mean age was 35.24±9.85 years with mean disease duration of 9.33±7.5 years. The main clinical features were oral ulcers (100%), genital ulcers (100%), eye involvement (55.5%) neurological involvement (27.7%) and vascular involvement (37%). Erythema Nodosum was noted in 48% of the patients. Consanguinity was found in 22% of patients. HLA B51 was positive in 48%. Serum prolactin was significantly higher in the Behçet's patients compared to normal reference (p-value=0.04). (mean serum prolactin was 10.9±6.86 ng/mL in patients compared to 8.86± 2.87ng/mL in normal reference). Serum prolactin was significantly lower in HLA B51 positive patients than in HLA B51 negative patients (p-value=0.03). Similarly consanguineous patients had statistically significant lower serum prolactin level (p-value=0.007). Patients with Erythema Nodosum had higher serum prolactin level however it did not achieve statistical significance (p-value=0.08). No other associations with disease presentation as ocular, vascular and neurological involvement were found.
Conclusions. Serum prolactin is elevated in Egyptian patients with Behçet's syndrome. Genetic Backgrounds as HLA and consanguinity may affect serum prolactin in Behçet's patients.

References
1. DIRESKENELI H: Behçet's disease: infectious aetiology, new autoantigens, and HLA-B51. *Annals of the rheumatic diseases* 2001; 60(11): 996-1002.
2. KESER G, OKSEL F, ÖZGEN G, AKSU K, DOĞANAVŞARGIL E: Serum prolactin levels in Behçet's Syndrome. *Clinical rheumatology* 1999; 18(4): 351-352.

P40.

ALLERGIC REACTION TO ORAL BACTERIA IN PATIENTS WITH BEHÇET'S DISEASE AND THE RELATED DISEASES

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Most of patients with Behçet's disease (BD) tend to have hypersensitivity against streptococci (1) which might be acquired through the innate immune mechanism in the oral cavity, as previously described (2). Following recurrent aphthous stomatitis (RAS), BD patients generally have the systemic symptoms by immune reactions to streptococci and other related bacteria which are reported to be increased in number in the oral cavity (3). Then, we tried to prick with self-saliva to the forearm skin of the patients. It is of interest to find whether BD patients, non-BD patients with similar symptoms, herpes simlex virus (HSV) infection and healthy controls respond to streptococci included in self-saliva and whether the methodology could be used for a diagnosis of BD, although previously demonstrated about the reactivity in some patients with BD and non-BD RAS (4).
Methods. The skin test was done on the forearm of the patients and controls using Lancetter (Sweden) with self-saliva, as follows, 1) Crude self- saliva (S), 2) sterilized saliva by syringe filter (SS), and 3) control saline (CS) were used and 4) pathergy test by 25G syringe needle was also done after surgical sterilized forearm skin of the patients and controls. The cutaneous reactions were observed 24-48 hours after prick.

The patients and controls were 22 BD patients classified by Japanese Classification, and non-BD diseases including RAS, erythema nodosum (EN), Lipschutz genital ulceration (GU) and herpes simplex viral infection and 10 healthy controls. The cutaneous responses were also compared among BD patients with or without HLA-B51. This study has been approved by the local ethics committee.
Results. The skin prick with self-saliva was more sensitive than "pathergy test" conventionally used for BD diagnosis. More than 90% of BD patients showed erythematous reactions of more than 5 mm in diameter by S and also smaller reaction to SS in some active BD patients, though no reaction was seen to CS. Only one case exhibited pathergy positive (5%). The relatively stronger cutaneous responds by prick with self-saliva were found in patients with HLA-B51, but the reactions seemed to be due to the disease severity, because the clinically active patients without HLA-B51 also showed stronger response to self-saliva prick.
Regarding the BD relative diseases, 4 of 6 patients with RAS including a child patient (67%) showed weak response exhibiting erythema spot around 4mm in diameter, though non-BD EN patients were no response. However, a patient with GU showed a weaker cutaneous reaction to self-saliva. In a GU case, the sign of Epstein-Barr virus (EBV) was not detected, though it is reported to be due to EBV infection (5).
Patients with oral and labial herpes simplex virus infection and healthy controls were no response to their own saliva prick.
Conclusion. Although the pathogenesis of BD is still unclear, they had hypersensitivity to their self-saliva including oral streptococci, which they may have so-called "oral bacterial allergy". It might be considered that BD patients were initially immunized by oral bacteria including S. sanguinis, because their systemic symptoms sta

P41.

THE ASSESSMENT OF WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN BEHÇET'S DISEASE

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Aim. The aim of the study was to assess the relationship between the course of Behçet's disease and work productivity and activity impairment.
Materials and methods. In this cross-sectional study, 110 consecutive BD patients were included. The Work Productivity and Activity Impairment questionnaire that is a 6-item instrument to measure impairment in both paid and unpaid work was used in the study.
Results. In the working group, 30.41% had missed work during the previous week. The mean percentages of daily activity impairment were higher in patients with musculoskeletal involvement (39.81±33.61) compared to those without (23.48±32.45) (p=0.008). A greater decrease in working hours was observed in patients with eye involvement (45.52±15.29) compared to those without (54.15±15.29) (p=0.007). In the study, most of the male patients (67.8%) were afraid of losing their job compared to females (30%) (p=0.000).
Conclusion. The highest levels of lost productivity and the most severe effects on daily life are consequences of eye and musculoskeletal involvement in the study population. More effective therapeutic approaches are required to improve the working lives of patients with BD. Moreover, male patients were afraid of losing their job, suggesting a match between the expected clinical course and the predictions of BD patients.

P42.

ILLNESS PERCEPTION IN PATIENTS WITH BEHÇET DISEASE: EMOTIONAL REACTIONS TO DISEASE SYMPTOMS

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Aim. This study aimed to assess the relationship between illness perception and disease pattern with regard to gender, disease course and symptoms in BD.
Materials and methods. One hundred ten consecutive BD patients were included in this cross-sectional study. A revised version of the Illness Perception Questionnaire (IPQ-R) was used for the present study. The questionnaire consisted of 3 main sections regarding, identity, beliefs about the illness and cause. The questionnaire was completed by patients at the BD outpatient clinic before their visits.
Results. The identity score regarding the number of disease related symptoms was higher in patients with both cutaneous involvement (cutaneous (+):6.13±3.28 vs cutaneous(-):3.5±2.44) and musculoskeletal involvement (musculoskeletal involvement(+):6.77±3.08 vs musculoskeletal involvement(-): 5.08±3.3) compared to the other patients (p=0.029 and p=0.011, respectively). In Beliefs about illness section, the timeline score represented chronic duration for eye involvement was poor compared to other cases (eye involvement (+):26.17±5.47 vs eye involvement(-): 22.14±8.57) (p=0.005). In the Cause section, increases in the scores of stress, family problems, emotional state and personality within the psychological attribution subscale and altered immunity within the immunity subscale were found to be higher in females compared to males (p<0.05).
Conclusion. Patients with BD perceived more symptoms and negative opinions about cutaneous involvement, musculoskeletal symptoms and eye involvement. In their causal model, female patients revealed a high level of emotional distress due to their symptoms.

P43.

PATHERGY TEST IN BEHÇET'S DISEASE: DIAGNOSTIC OR PROGNOSTIC?

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Background. Behçet's disease (BD) is a multi-systemic disorder which is classified as a systemic vasculitides. The disease features serious and debilitating sequelae such as blindness. While no specific laboratory test for BD diagnosis exists, pathergy test is a useful diagnostic measure. Pathergy test is a feasible and cost-effective initial step in diagnosis of BD. The early diagnosis and timely management of high risk cases can pre-empt the BD-related morbidities.
Objectives. We investigated the prognostic value of pathergy test in defining the risk of major manifestations in the course of BD.
Methods. The data of 7299 BD cases were extracted from our Behçet's disease database. The research was conducted by the Behçet's Disease Unit of Rheumatology Research Center (RRC), located in Shariati Hospital, Tehran University of Medical Sciences (TUMS). Our center acts as a referral tertiary center for BD patients nationwide. Suspicious cases are referred from across the country to establish the BD diagnosis. BD patients were examined in a multidisciplinary clinic. Pathergy test is performed for all BD patients prior to the first visit and is read by a dermatologist after 24 hours. Thereafter we divided the confirmed BD cases into two subsets: patients with positive pathergy test [P(+)]and negative pathergy test [(P(-)]. The comparisons were performed by the Chi-square and Fischer's exact test.
Results. P (+) subgroup consisted of 3648 (50.0%) and P(-) subgroup included 3651 cases. Ocular lesions (including anterior/posterior uveitis and retinal vasculitis) were more commonly developed in P (-) subset (p-value<0.0001). On the contrary mucosal lesions were more common in P (+) subset (p-value<0.0001). Skin manifestations were more common in P (+) subset (p-value<0.0001). Furthermore P (+) patients were more prone to gastrointestinal (p-value=0.038) and neurological lesions (p-value=0.038). No significant difference in cardiac, pulmonary and large vessel involvements between two subsets was noted.
Conclusions. This study underlined the prognostic significance of pathergy test. Our results divulged a positive association between positive pathergy and a cluster of BD manifestations (mucosal, skin, gastrointestinal and neurological manifestations). This notion may help the clinician in prediction of BD course and providing optimum care.

P44.

SUBFOVEAL CHOROIDAL THICKNESS AS AN INDICATOR OF SUBCLINICAL OCULAR AND SYSTEMIC INFLAMMATION IN EYES WITH BEHÇET'S DISEASE WITHOUT ACTIVE OCULAR INFLAMMATION

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Background. To investigate whether subfoveal choroidal thickness, measured using enhanced depth imaging optical coherence tomography (EDI-OCT), is an indicator of subclinical ocular inflammation and systemic inflammation in eyes with Behçet's disease (BD) without active ocular inflammation.
Methods. Ocular findings and clinical features of non-uveitic patients with BD (NUBD group), patients with a previous history of Behçet's uveitis in an inactive state (IUBD group), and healthy controls evaluated from October 2014 to September 2015 were analyzed retrospectively. Subfoveal choroidal thickness was measured using EDI-OCT.
Results. The NUBD group included 46 eyes in 24 patients; the IUBD group included 18 eyes in 12 patients; and the control group included 35 eyes in 23 individuals. Mean subfoveal choroidal thicknesses differed significantly among these groups (p=0.048). Choroidal thickness was significantly greater in the NUBD (297.4±81.0 μm) than in the IUBD (253.0±77.2 μm, p=0.042) and control (261.2±78.6 μm, p=0.047) groups. Disease activity score was significantly higher in the NUBD than in the IUBD group (p<0.001), while the use of cyclosporine was significantly associated with choroidal thickness in eyes with NUBD (p=0.021).
Conclusion. Subfoveal choroidal thickness, as measured by EDI-OCT, may be a clinical indicator of subclinical ocular inflammation and systemic inflammation in BD patients without active ocular inflammation.

P45.

THE COMPARISON OF MENTAL DISORDERS IN BEHÇET'S DISEASE AND RHEUMATOID ARTHRITIS PATIENTS

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Background. Mental disorders (MD), especially depressive, have high rates in rheumatic disorders (RD) – Behçet's Disease (BD) and Rheumatoid Arthritis (RA). Depressive disorders have close pathogenesis interrelations with RD and are usually related to cognitive disorders.
Objective. to compare the variants of MD in BD and RA-patients.
Methods. the investigation has been realized in accordance with the interdisciplinary program "Stress factors and mental disorders in immune-mediated inflammatory rheumatic diseases".
225 (100 BD and 125 RA) patients were enrolled in the study. In BD patients prevailed men (70%), in RA – women (77%). Mean age (M±m) of BD patients was 32,5±0,88 years, RA – 47,4±1,01 years. All the patients met the criteria of the International Study Group for BD (1990) and ACR criteria for RA classification. The disease activity was assessed by scoring system BDCAF for BD, DAS28 for RA. The parenchymal and nonparenchymal CNS lesions had 15,6% BD patients. RA patients hadn't CNS involvements but had polyneuropathy as extra-articular manifestation in 22,4%. MD were diagnosed by psychiatrist in accordance with the ICD-10 in semi-structured interview. For evaluation of severity and the variants of cognitive disorders psychology and neuropsychology methods were used.
Results: MD were diagnosed in the majority of patients (86%), significantly more often (p<0,001) in RA (94%) versus (vs) BD (79%) patients. The depressive disorders dominated (BD – 100%, RA – 93%). The chronic and recurrent depressive disorders prevailed in both groups: in RA more often than in BD patients (58,4% vs 39,2%, p=0,003). Cognitive disorders of different severity were diagnosed in most patients with BD and RA (73% vs 66,4%, n/s). The mechanical memory (63%) and attention deficit (72%) in BD and impairment of associative memory (90%) and logical thinking (71%) in RA were the most frequent manifestations of cognitive disorders. The patients with MD did not differ significantly on age, gender, RD duration and clinical features from the patients without MD in both groups. The diagnosis of major depressive disorder was associated with high disease activity in RA and was not in BD. MD were not related to neurologic manifestations neither in BD (19,4% vs 10,5, p=0,29), nor in RA (23% vs 12,5%, p=0,36). In linear regression analysis cognitive disorders were associated with disease duration, BDCAF score, fibrinogen level, chronic psychosocial stress factors and depression severity in BD patients. In RA patients cognitive disorders were associated with apathetic affectivity, current depressive episode, extra-articular manifestations, non steroid anti-inflammatory drugs treatment and older age. The diagnoses and severity of MD didn't have relation to the prednisone and immunosuppressive treatment in both groups.
Conclusion. the results have shown high rates of MD, especially chronic depression and cognitive disorders in BD and RA patients. The necessity of interdisciplinary strategy implementation for the improvement of individualized treatment approaches in RD has been confirmed.

P46.

EFFICACY AND SAFETY OF INFLIXIMAB AND CYCLOSPORINE COMBINATION THERAPY FOR UVEORETINITIS IN BEHÇET'S DISEASE

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Aim. To evaluate the long-term efficacy and safety of infliximab and cyclosporine combination therapy (ICCT) for uveoretinitis in Behçet's disease (BD).
Methods. We retrospectively reviewed the medical records of 11 patients with uveoretinitis secondary to BD who received ICCT and followed-up for more than 1 year. Frequency of ocular inflammatory attacks and BD ocular attack score 24(BOS24) were used as the indices for evaluation of efficacy during each 6-month period before and after initiation of ICCT. In the assessment of safety, severe adverse events (AEs) and any AEs possibly related to the therapy were collected throughout the treatment period.
Results. The mean (± standard deviation [SD]) follow-up after initiating ICCT was 5.6±2.3 years. The mean (±SD) number of ocular attacks were 2.9±1.6 times during the 6 months before initiating ICCT (baseline period), 0.6±0.9 times during months 1-6, and 0.5±0.9 times during months 7-12 (p<0.01, Friedman test). The mean (±SD) BOS24 was 5.2±2.4 during baseline period, 1.5±2.1 during months 1-6, and 1.7±3.1 during months 7-12 (p=0.013, Friedman test). No severe AEs were observed except for urinary tract infection in one patient. Two patients exhibited transient elevation of serum creatinine level which was normalized after a dose reduction of cyclosporine.
Conclusion. ICCT for uveoretinitis due to BD is well tolerated and effective in terms of decreasing both the number and severity of ocular inflammatory attacks.

P47.

SERUM LIPOPOLYSACCHARIDE LEVELS ARE ASSOCIATED WITH DISEASE ACTIVITY OF THE ORAL MUCOUS MEMBRANE IN BEHÇET'S DISEASE.

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Purpose. Gut microbial dybiosis is capable of inducing systemic, extra-intestinal and ocular inflammation in murine models. We hypothesise that the translocation of gut microbial endotoxins through the dysfunctional mucous membrane drives disease. We investigated the link between serum lipopolysaccharide (LPS) levels, as a surrogate marker of increased gut permeability, and disease activity in Behçet's Disease (BD).
Methods. BD patients attending the multidisciplinary Behçet's clinic at the Birmingham and Midland Eye Centre, UK, underwent complete clinical assessment for evidence of disease activity using the validated BD Current Activity Form. Active ocular inflammation was defined as at least a 2+ increase in intraocular cells between clinic visits or the presence of a hypopyon as assessed by slit lamp, whilst active oral lesions were defined as the appearance of new ulceration of the oral mucous membrane. Serum LPS levels were quantified by ELISA with Limulus Amebocyte Lysate chromogenic endpoint assay. Serum LPS levels in patients with BD (n=23) were compared with serum samples from healthy volunteers (n=10) and disease controls (ocular mucous membrane pemphigoid (OcMMP; n=15)). We obtained longitudinal serum samples from BD patients (n=7) to monitor changes in serum LPS with disease phenotype and progression. Non-parametric statistical analyses were analysed by Mann-Whitney U test and Kruskal-Wallis test.

Results. There was no statistically significant difference in the LPS levels between patients with BD [median: 0.244 EU/ml; interquartile range (IQR): 0.108-0.778], OcMMP [0.175; 0.140-0.202], and healthy controls [0.200; 0.164-0.251] (p=0.504). BD patients with inactive oral lesions had significantly higher levels of LPS (0.462; 0.168-0.856) compared to those with active oral lesions (0.119; 0.057-0.148) and healthy controls (0.200; 0.164-0.251) (p=0.012). There was no difference in the LPS levels of BD patients with active vs. inactive ocular inflammation (p=0.142).
Conclusions. Serum LPS levels are associated with oral mucous membrane disease activity and indicates a potentialrole for microbial translocation in the inflammatory pathophysiology of BD.

P48.

COMPARISON OF SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY (SD-OCT) FINDINGS AND LASER FLARE PHOTOMETRY (LFP) LEVELS IN BEHÇET UVEITIS

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Purpose. This study aims to compare the Spectral Domain Optical Coherence Tomography (SD-OCT) findings and laser flare photometry (LFP) measurements in Behçet uveitis.
Methods. This study included 17 patients with active posterior/panuveitis associated with Behçet disease (BD) (Group 1), 18 patients with quiescent uveitis with BD (Group 2), 31 Behçet patients without ocular involvement (Group 3) and 12 healthy volunteers (Group 4).
Central Macular Thickness (CMT) was assessed with SD-OCT and Subfoveal Choroidal Thickness (SCT) was evaluated with the Enhanced Depth Imaging (EDI) software of the same device. Anterior chamber flare measurements were obtained with KOWA FM-600 LFP.
Results. Mean age of the groups were 29.7±9.3, 37.3±13.2, 35.1±15.5, 34.2±16.5 and male/female ratios were 13/4, 11/7, 11/20, 6/6 respectively. CMT was not significantly different among the groups. SCT of the groups were; 425 (177.0) in Group 1, 380(147.0) in Group 2, 310(231.5) in Group 3 and 300 (156.2) in Group 4. SCT of Group 1 was significantly higher than the other groups (p:0.002). Flare values were 10.6(12.8) ph/ms in Group 1, 4.8(3.7) ph/ms in Group 2, 3.6(1.9) ph/ms in Group 3 and 3.3(0.85) in Group 4. Anterior chamber flare value of Group 1 was significantly higher than the other groups (p<0.001). BCVA and anterior chamber flare values showed negative correlation (rho:-0.573, p<0.001) while CMT and flare values were positively correlated (rho:0.267, p:0.006).
Conclusion. Flare is a reliable indicator of the inflammation in Behçet uveitis. Its concurrent use with OCT to evaluate choroid and macula, enables the assessment of inflammation and severity of complications.

P49.

ESTABLISHING A NATIONAL SERVICE FOR BEHÇET'S SYNDROME IN THE UK – EXPERIENCE OF THE FIRST FOUR YEARS

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Behçet's disease (BD) is very rare in the UK and there is considerable diagnostic delay and variation in practice (1). Reliably delivering a diagnosis and holistic management for a complex multi-system disease across the UK is challenging and access to high cost therapies such as biologics, is often subject to regional variation. Between 2008 and 2012 with guidance from the UK National specialised commissioning team a new partnership project including clinicians, managers and the Behçet'sSyndrome Society (BSS) developed the concept for a National Service. 3 National Centres of Excellence for Behçet's Disease were commissioned in 2012 (Birmingham, Liverpool and London). The centres were based on key design principles including a 'one stop' multidisciplinary approach to diagnosis and problem solving (2-5), agreement on core metrics for process and outcomes (EQ-5D, Behçets Disease Activity Form, visual acuity, ocular disease activity, standardized oral medicine assessment, disease flares, psychological assessment and patient satisfaction) together with a drug pathway for systemic therapy enabling funding to follow the patient. The service, founded on principles based on improvement science and system wide patient and practitioner education. A patient-centred, holistic philosophy for chronic disease management was adopted (6). Clinical nurse specialist, clinical psychology and patient support were delivered in partnership with the BSS. The service, accountable to the national commissioners is appraised annually. Overall satisfaction with the service was high (>95% would recommend a friend or family). By December 2015 there were 1,221 patients under active follow up (London 640, Birmingham 319, Liverpool 262). A total of 1102 new patients were seen and 5528 follow ups. At the three centres between 2013 and December 2015 there were a total of 387 new biologic prescriptions (321 London, 94 Liverpool, 66 Birmingham) 205 of them authorised at satellite centres. 355 were for anti TNF, 15 interferon alpha 13 for rituximab and 1 each of ustekinumab, anakinra, tocilizumab and abatacept.

P50.

PULMONARY EMBOLISM IN BEHÇET: PARTICULARITIES

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Objectives. Pulmonary embolism is an unusual complication of Behçet's disease but could be life threatening. The purpose of this study is to determine demographic and clinical features of patients with Behçet presenting pulmonary embolism and their clinical course.
Methods. We analyzed retrospectively the medical records of 1572 patients fulfilling the international diagnostic criteria of Behçet's disease. This study was conducted between 1980 and 2015 in internal medicine department of university hospital of Casablanca (Morocco). We included those with pulmonary embolism, and determined their demographic and clinical characteristics, and outcomes.
Results. Among 1572 patients with Behçet's disease, fourteen (12 men and 2 women mean aged at 31.5 ± 3 years) were diagnosed as having pulmonary embolism. This was inaugural in 2 cases. The discovery of pulmonary embolism was fortuitous in one case. Hemoptysis and recent dyspnea were the most relevant clinical signs. Inflammatory parameters were elevated in 4 patients. It was associated to Cardiac thrombosis in 3 cases (43% of intra cardiac thrombosis in our cohort were complicated by pulmonary embolism), it was associated to pulmonary aneurism in one case. Vena cava thrombosis were asoosiated in 5 patients, that were isolated in 2 cases. Venous thrombosis of lower limbs were noticed in 8 patients (only 8% of venous thrombosis of lower limbs were complicated by pulmonary embolism). Venous thrombosis of lower limbs were isolated in 2 cases, associated to vena cava thrombosis in 3 cases and to pulmonary aneurysms in 3 cases with carotid and vertebral stenosis in one case. Pulmonary embolism was noticed in a case with isolated pulmonary aneurysm. Pulmonary infarction has been found in 4 cases. One patient was positive for lupus anticoagulant antibody. All our patients were treated by anticoagulation therapy combined with mild to high dose of corticosteroids. Immunosuppressive therapy was used in 8 patients (cyclophosphamide or azathioprine). Three patients died; 2 patients with aneurysm rupture and one with a neurological involvement.
Conclusion. Pulmonary embolism is a severe and rare event in Behçet disease. But, it should be considered in some conditions like hemoptysis or recent dyspnea. What is specific to Behçet disease is that pulmonary embolism is a rare complication of venous thrombosis of lower limbs, it is explained by the presence of vasculitis which make the migration of emboli difficult. On the other side, it is more associated to cardiac thrombosis. When associated to pulmonary aneurism it remains difficult to treat, hence the use of immunosuppressive therapy which has transformed the prognosis in angio-Behçet in general.

P51.

ATYPICAL NEUROLOGICAL MANIFESTATIONS IN BEHÇET'S DISEASE: 40 CASES

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Objectives. Neurological involvement is one of the most severe manifestations in Behçet's disease. Its prevalence is nearly 15%. Most commonly, parenchymal and non-parenchymal involvement are described. However, atypical presentations of neuro-Behçet can occur and should be known to be treated adequately. The aim of this study is to recognize those atypical manifestations and to describe their clinical and radiological features.
Methods. One thousand five hundred and seventy seven Behçet's disease patients were retrospectively studied. This study was conducted between 1980 and 2015 in internal medicine department in university hospital of Casablanca (Morocco).These patients fulfilled the international study group for Behçet's disease criteria. Patients with atypical neurological findings were studied according to clinical examination, laboratory tests and neuro-radiological investigations. We excluded patients with common parenchymal, non-parenchymal and mixt neurological involvement.
Results. Among 252 cases of neuro-Behçet, 40 patients (15,87%) presented with atypical neurological manifestations. Male to female ratio was 3.03. Neurological involvement was inaugural in one case. Average disease duration of Behçet's Disease before neurological manifestations onset was 4 years. Isolated meningitis was noted in 16 cases. Twelve cases had isolated cranial nerve involvement: Optic nerve (5 cases) presenting with a clinical picture of retrobulbar optic neuritis. Abducens nerve (4 cases). Facial nerve (2 cases). Auditory nerve (one case) presenting with right hearing impairment and left hear loss. Peripheral neurological involvement was noted in 7 cases: chronic polyradiculoneuritis (4cases), acute polyradiculoneuritis (one case), sensitive mononeuritis (one case) and a motor neurone disorder (one case). Papillitis were reported in 2 cases, chorea in 1 case, Inflammatory pseudotumor of the spinal cervical cord: 1 case, Sd Brown Sequard: 1 case.
Conclusion. Neurological spectrum in Behçet's disease is very large and varied; every neurological condition can be met, but atypical manifestations remain rare. The diagnosis of these conditions and their association to Behçet's disease can be easy when the underlying disease is already known, especially when it occurs in flare period. But most of the time the diagnosis remain difficult, particularly when it is inaugural.

P52.

ORAL HEALTH RELATED OUTCOME MEASURES, MUCOCUTANEOUS INDEX AND OHIP-14, CORRELATE WELL WITH THE CLINICAL ASSESSMENT OF ORAL ULCERS IN BD

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Aim. The aim of this study was to assess the roles of oral health-related outcome measures in planning of management for oral ulcer activity in Behçet's disease (BD).
Materials and method. Eighty-nine BD patients (F/M:43/46, mean age:34.6±15.3 years) were included in the study. They were treated with colchicine (1.5 mg/day; n=50 at baseline and n=53 at follow-up) or immunosuppresive medications (n=39 and n=36, respectively). The mean disease duration and follow-up periods were 10.8±7.8 years and 14.7±9.9 months. The disease severity score reflecting organ involvement was 5.02±1.5 at baseline and 5.7±1.9 at follow-up. Two validated patient-reported outcome measures were used for assessing oral ulcer activity (Mumcu 2009; Mumcu 2014). Mucocutaneous index (MI) was composed of a genital ulcer activity index, an erythema nodosum activity index and the Composite index (CI) for oral ulcers. Pain and functional disability were subscales of the each part of the indexes. Score of MI could be between 0 and 30 (0-10 points for each involvement). Oral health-related quality of life was assessed by Oral Health Impact Profile-14 (OHIP-14). Responses were coded from 0 to 4. Total OHIP-14 scores ranged from 0 to 56. High scores indicated a poor oral health related quality of life. Multidimensional properties of OHIP-14 were examined by factor analysis (Mumcu 2007). The threshold levels generated from the ROC analyses in OHIP-14 score best associated with clinically important improvement was -38.1% (sensitivity: 86.7%, specificity: 97.1% respectively, Hayran 2009).
Results. Oral ulcer activity was observed in 64.04 % (n=57) at baseline and 61.8 % (n=55) during follow-up periods. Scores of CI and OHIP-14 were "0" in inactive BD patients. The mean number and healing time of oral ulcers during the last month were similar at baseline (2.8±2.5 and 6.7±4.4 days) and follow-up periods (3.2±2.4 and 6.1±4.5 days) in active patients (p>0.05). Score of CI and subscale scores of OHIP-14 were also similar at baseline (5.9±2.5; 23.9±16.1) and follow-up periods (5.3±2.1; 22.3±18.3) in active patients (p>0.05). A significant correlation was present between CI and OHIP-14 scores as patient-reported outcome measures in active patients during both follow-up periods (r: 0.7, p=0.000). According to treatment protocols, the mean number and healing time of oral ulcer were not different in patients treated with either colchicine (3,03±2,6; 6.3±3.4 days at baseline vs 3,4±2,5; 6.5±4.8 days) or immunosuppresive medications (2.6±2,6; 6.9±5.5 days vs 3.01±2.2; 5.6±4.2 days, respectively) in both periods (p>0.05).
Conclusion. MI and OHIP-14 indices as patient-reported outcome measures were observed to be well correlate with clinical parameters in patients with active oral ulcers in our study. Both, therefore, can be used as oral health-related outcome measures in prospective controlled clinical studies and clinical management of BD patients.

Key words. Behçet's disease, patient-reported outcome measures and oral ulcer activity.

P53.

CLINICAL SIGNIFICANCE OF SERUM YKL-40 IN BEHÇET'S DISEASE

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Background. Serum YKL-40, secreted by activated macrophages and neutrophils, is a potential biomarker of inflammation and endothelial dysfunction. Behçet's disease (BD) is a chronic multisystemic inflammatory disease involving hyperactivity of neutrophils, activation of macrophages, and impaired function of vascular cells with endothelial injury. Because serum YKL-40 levels appear to be regulated by cytokines involved with BD, such as IL-6 or IL-17, it may represent a marker for inflammation seen with BD.
Objectives. The aim of this study was to evaluate the serum YKL-40 level in patients with BD and to analyse its association with other inflammatory cytokines. Serum YKL-40 levels were also compared against the clinical features and disease activity of BD.
Methods. This study included 112 patients with BD (mean age 42.25±11.53 yr; M/F 30/82) and 45 age- and gender-matched healthy volunteers (mean age 41.74±10.73 yr; M/F 12/33). Disease activity was evaluated with BD Current Activity Form (BDCAF) score and electronic medical record-based activity index (EMRAI) score. Serum values of YKL-40, IL-6, and IL-17 were established by enzyme-linked immunosorbent assay (ELISA).
Results. The patients with BD had significantly higher serum levels of YKL-40 (median 41.88; range 12.52-171.30 ng/mL) than those of healthy controls (median 20.92; range 5.01-64.20 ng/mL) (p<0.001). Using receiver operating characteristic (ROC) analysis, the cut-off value for YKL-40 of 30.005 ng/mL was determined. BD patients were categorised into two groups according to the serum YKL-40 level (≥30.005 ng/mL and <30.005 ng/mL): the EMRAI scores and the proportion of patients in the active phase of BD presenting with ≥2 major criteria were significantly higher in patients with elevated YKL-40 levels (p=0.044 and p=0.045, respectively). Further analysis categorised the 112 BD patients as having active or inactive disease: a statistically significant elevation in YKL-40 levels was observed in patients with active BD (median 45.92; range 13.09-171.3 ng/mL), as compared to patients with inactive BD (median 34.17; range 12.52-137.6 ng/mL; p=0.046). Serum YKL-40 values were positively correlated to IL-6 and the EMRAI scores (p=0.039 for each comparison). This finding indicated that serum YKL-40 levels are increased in BD patients and positively correlate with disease activity.
Conclusion. The circulating YKL-40 may play a pivotal role in inflammation seen with BD and may be used to monitor BD patients.

P54.

APPLICATION ICBD CRITERIA IN TUNISIAN POPULATION

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Objective. to evaluate the performance of new criteria of Behçet disease (BD) in Tunisian population
Methods. We compared two groups of patients: group 1 (G1) including patients with BD diagnosed according to ISG criteria, and group 2 (G2) including patients with differential diagnosis of BD or with at least one major criteria of BD. We applied original (ICBD) and revised (ICBDr) ICBD criteria in the two groups, and we calculated sensitivity, specificity, positive and negative predictive values, accuracy, optimization, Youden index and area under the ROC curve.
Results. We collected 430 patients in G1 (average of age: 34 years, sex-ratio: 2.2) and 571 patients in G2 (average of age : 41 years, sex-ratio : 0.23) with significant differences. Frequencies of the main clinical features were significantly different between the 2 groups: buccal aphtosis (100 vs 3.5 %), genital aphtosis (79.3 vs 0.7%), cutaneous involvement (85 vs 9%), positive pathergy test (41.9 vs 0.4%), ocular involvement (46.5 vs 16%), vascular involvement (35 vs 4%), neurological involvement (28 vs 11%), articular invovlement (45.3 vs 53.4%) and intestinal involvement (1.6 vs 13%). Different statistic results of application of ICBD and ICBDr are shown in Table I:

Statistic result	ICBD	ICBDr
Sensitivity (%)	100	99.3
Specificity (%)	97.5	98.6
Postive predictive value (%)	96.8	98.4
Negative predicitve value (%)	100	99.4
Accuracy (%)	98.6	99
Optimization rate (%)	0.7	2.5
Youden index	0.97	0.98
Area under the ROC curve	1	0.99

Comparing ICBD and ICBDr criteria to ISG criteria, we noted a gain of sensitivity of 8 and 7.3% respectively, and a gain of sepcificity of 0.5 and 1.6% respectively.

Conclusion. Our study showed a better performance of new criteria (in the 2 versions), in diagnosis and classification of BD compared to ISG criteria commonly used.

P55.

COMPARISON OF DEEP VENOUS THROMBOSIS ASSOCIATED WITH BEHÇET'S DISEASE TO IDIOPATHIC DEEP VENOUS THROMBOSIS

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Objective. to compare epidemiological, clinical and evolutive characteristics of patients with deep venous thrombosis related to Behçet's disease (DVT-BD) to patients with idiopathic deep venous thrombosis (Id-DVT)
Methods. We compared two groups of patients hospitalized for management of deep venous thrombosis (DVT) : the first group included patients with DVT-BD (G1) and a second group (G2) patients with Id-DVT. Epidemiological, clinical and evolutive characteristics were analyzed and compared in the two groups using Chi square test for qualitative variables and ANOVA test for quantitative variables.
Results. 712 patients were included in this study : 105 patients in G1 and 607 patients in G2 with a mean age of 34.83 and 56.32 years respectively (p<0.05). The sex-ratio M/F was 6.5 in G1 and 1.05 in G2 (p<0.05).
The diagnostic delay was similar in 2 groups (19.96 days in G1 vs 13.32 days in G2). On the other hand, patients of G1 were significantly hospitalized for more longer period (12.46 days) than those of G2 (10.8 days, p=0.028). Unusual location was significantly less frequent in G2 (4.61%) than in G1 (18.09%), p<0.05. Comparison of frequencies of thrombotic risk factors and evolutive characteristics between the two groups is presented in Table I.

Table I. Compraison of frequencies of thrombotic risk factors and evolutive characteristics between the 2 groups.

	G1	G2	*p*
Number	105	607	
Tobacco (%)	52.38	34.59	<0.05
Veinous failure (%)	1.9	37.89	NS
Varicose veins (%)	7.61	16.14	0.023
Obesity (%)	8.57	28	<0.05
Bed rest (%)	3.8	24.38	<0.05
Plaster (%)	0	1.64	NS
Traumatism (%)	1.9	88.96	0.014
Surgery (%)	2.85	13.34	0.002
Drug taking (%)	2.85	7.9	NS
Follow-up period (months)	78.04	24.42	<0.05
Post-phlebitic syndrom (%)	30.47	11.86	<0.05
Recurrence (%)	31.42	6.75	<0.05

Conclusions. Behçet'disease typically affects young male patients, which explains the young age of the G1 than in G2 and the largest male predominance in G1. This disease is characterized by frequent unusual location of thrombosis as shown by results of our study. Almost thrombotic risk factors were more frequent in G2, which demontrates difference of physiopathologic mechanism of thrombosis between the 2 groups.

P56.

EVOLUTION OF DEMOGRAPHIC AND CLINICAL FEATURES OF BEHÇET'S DISEASE IN TUNISIA

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Background. The demographic and clinical characteristics of Behçet's disease (BD) in Tunisian patients was determined on 2006 (1).
Objective. To study evolution of these characteristics before and after 2006.
Methods. patients with BD (ISG criteria) and seen in the Department of Internal Medicine of the University Hospital La Rabta in Tunisia, from 2006 to 2015 (group 1), were retrospectively enrolled. Demographic and clinical data were recorded, analyzed and compared to those found for 260 patients seen from 1990 to 2006 (group 2).
Results. Two hundred and sixty six patients were recorded after 2006. They were 164 men and 102 women (sex-ratio was 1.6). The mean age at the onset of the disease was 29.45 years.
Comparison of demographic and clinical characteristics between 2 groups is shown in Table I.

	Group 1 (N=266)	Group 2 (N=260)	*p*
Sex-ratio (M/F)	1.6	2.61	0.003
Age of onset of BD (years)	29.45	28.9	NS
Oral aphtosis (%)	95.84	100	0.001
Genital aphtosis (%)	62.64	83.4	<0.005
Pseudofolliculitis (%)	63.53	73.46	0.017
Ocular involvement (%)	39.09	49	0.001
Articular involvement (%)	33.46	39	0.015
Venous thrombosis (%)	23.68	32.83	<0.005
Neuropsychiatric symptoms (%)	35.09	24	0.043
Gastrointestinal involvement (%)	2.65	1.5	NS

All clinical features, but neuropsychiatric ones, were significaltly more frequent in group 1.

Conclusion. In our series, BD seems less severe during the last 10 years.

P57.

ARTERIAL ANEURYSMS COMPLICATING BEHÇET'S DISEASE

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Introduction. Behçet's disease is a systemic vasculitis with a tropism for the venous system. Arterial involvement is uncommon (1%) and mainly represented by aneurysms that can be life-threatening.
Material and methods. This retrospective study was conduced in the internal medicine department of the University Hospital Ibn Rochd of Casablanca, over a period of thirty-five years between 1980 and 2015. Where included all the cases of Behçet's disease diagnosed in our service (1572 case). We aimed to determine the epidemiological profile, the different possible clinical manifestations and to discuss both prognosis and treatment in such cases.
Results. 37 patients – 32 men and 5 women – presented arterial involvement in type of arterial aneurysm, which represents a rate of 2.35%. Mean age at diagnosis was 32 years old (ranges 17-54). This complication was the revealing event for Behçet's disease in 2 cases, concomitant in 3 cases and occurring after an average of 6-year-period evolution of the disease in 32 cases. The aneurysm affected: the pulmonary artery (22 cases), the abdominal aorta (5 cases), the femoral artery (5 cases), the internal carotid artery (2 cases), the iliac artery (2 cases) and the middle cerebral artery (1 case). The aneurysm was associated with venous disease (18 cases), pulmonary embolism (2 cases) and intracardiac thrombus (1 case). The medical treatment has relying on anticoagulants (6 cases), anti-aggregating agents (9 cases), corticosteroids (36 cases), immunosuppressive drugs – cyclophosphamide (23 cases) and azathioprine (12 cases), while 7 patients underwent surgical intervention. Evolution was favorable in 23 patients and with negative outcome in 14 patients (9 relapses and 5 deaths).
Conclusions. Arterial aneurysms are the most common arterial complications in the context of Behçet's disease, while the prognosis remains poor in the absence of early and appropriate management (corticosteroids, immunosuppressive agents, surgery).

P58.

A PSEUDOTUMOR REVEALING BLADDER VASCULITIS

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Introduction. Behçet's disease is a systemic vasculitis that often presents with mucocutaneous, articular, vascular and ocular manifestations, however any other visceral organs might be affected. Though, urological problems remain a rare condition in the course of this disease.
We report a case of Behçet's disease with bladder involvement, compiled in the internal medicine department of the University Hospital of Casablanca in a series of 1572 patients with Behçet's disease over a period going from 1981 to 2015.
Case presentation. We report the case of a 35-year-old man for whom the diagnosis of Behçet's disease was retained regarding the international criterias and presenting with neurological and vascular complications.
The patient is followed up since 2011 for Behçet's disease with vascular involvement – Budd-Chiari syndrome – treated with immunosuppressive therapy, corticosteroids and anticoagulants. A one year later, he develops urological complications, revealed by hematuria, VKA overdose being ruled out by an INR into the normal ranges. Cystoscopy exploration showed the presence of a pseudotumor with malignancy suspicion but the biopsy revealed vasculitis in the context of Behçet's disease, so the patient was put back under high-doses corticosteroids and azathioprine treatment. Control cystoscopy has shown complete regression of the tumor.
Conclusion. Urogenital manifestations in the context of Behçet's disease are rare and poorly studied, bladder vasculitis being exceptional and often with misleading aspects. Treatment relies only on anti-inflammatory drugs: corticosteroids and immunosuppressive agents. Evolution is rapid and favorable, the only complication being recurrence.

P59.

CLINICAL CHARACTERISTICS OF LATE ONSET BEHÇET'S DISEASE

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Objectives. To determine clinical characteristics of late onset Behçet's disease (BD).
Methods. Five hundred and seventy eight patients fulfilling the international criteria of Behçet disease were retrospectively included. Patients were divided in two groups according to their age at BD onset. Group 1 included patients in whom onset of BD occured after age 40; Group 2 those in whom disease began before age 40. Frequencies of clinical features were analyzed and compared in the two groups using the chi square test for qualitative variables and ANOVA test for quantitative variables.
Results. BD onset occured after age 40 in 121 patients (20.9%), they were 72 men and 49 women with mean age at the disease beginning of 42.21 years. Comparison of the two groups is presented in Table I.

Table I. Comparison of patients with onset BD after (group 1) and before (group 2) age 40.

	Group 1 (n=121)	Group 2 (n=457)	*p*
Sex-ratio (M/F)	1.46	2.19	0.05
Age at BD onset (years)	42.21	26.29	<0.05
Delay of diagnostic (years)	4.49	4.62	NS
Oral aphtosis (%)	97.5	98.2	NS
Genital aphtosis (%)	71	74.5	NS
Pseudofolliculitis (%)	71.27	57.8	0.005
Erythema nodosum (%)	15.78	14.8	NS
Positive pathergy test (%)	54.7	48.9	NS
Ocular involvement (%)	46.6	35.5	0.02
Articular involvement (%)	37.7	47.1	NS
Neurological involvement (%)	28.9	28	NS
Involvement of cerebral vessels (%)	6.34	6.61	NS
Vascular involvement (%)	32.1	32.2	NS
Intestinal involvement (%)	1.76	2.47	NS

Conclusions. Male predominance was significantly lower in late onset BD. In our series, uncommonly, ocular involvement was significantly more frequent in late onset BD group because typically it is the opposite.

P60.

EFFECTS OF GENDER ON THE CLINICAL FEATURES OF BEHÇET'S DISEASE

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Objectives. To define the effect of gender on the clinical features of Behçet's disease (BD).
Methods. Five hundred and seventy eight patients fulfilling the international criteria of Behçet disease were retrospectively included. Patients were divided in two groups according to their gender. Group 1 included male patients and Group 2 female patients. When the age was over 40, begin of onset was considered as a late onset. Age of begin onset is defined by of the age of the occurrence of the first symptom attributed to BD. Frequencies of clinical features were analyzed and compared in the two groups using the chi square test for qualitative variables and ANOVA test for quantitative variables.
Results. Three hundred and eighty sex patients were male (66.8%) and 192 were female (33.2%). The mean age of diagnostic was 33.52 years in group 1 and 35.43 years in group 2 (p=0.035). Comparison of the two groups is presented in Table I.

Table I. Comparison of male patients (group 1) and female patients (group 2).

	Group 1 (n=386)	Group 2 (n=192)	*p*
Age at BD onset (years)	29.54	29.78	NS
Delay of diagnostic (years)	4.07	5.64	0.001
Late onset BD (%)	18.65	25.52	0.05
Oral aphtosis (%)	97.6	98.9	NS
Genital aphtosis (%)	77.6	66.1	0.003
Pseudofolliculitis (%)	74	55.2	<0.05
Erythema nodosum (%)	10.9	25	<0.05
Positive pathergy test (%)	53.8	52.9	NS
Ocular involvement (%)	46.6	39.5	NS
Articular involvement (%)	34.2	50.7	<0.05
Neurological involvement (%)	27	32.2	NS
Involvement of cerebral vessels (%)	6.9	5.2	NS
Vascular involvement (%)	39.1	18.2	<0.05
Intestinal involvement (%)	2	1.5	NS

Conclusions. Delay of diagnosis of BD, mean age of diagnosis and late onset of BD were higher in women than men. Genital aphtosis, pseudofolliculits and vascular involvement were more frequent in group 1 than in group 2; testifying more severe forms in men. On the other hand, erythema nodosum and articular involvement were more frequent in women.

P61.

BUDD-CHIARI SYNDROME IN BEHÇET DISEASE: MOROCCAN EXPERIENCE

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Purpose. Budd-Chiari syndrome (BCS) due to occlusion of the major hepatic veins, the adjacent inferior vena cava, or both. It is considered as a rare but serious complication of Behçet's disease (BD). This study was performed to define the prevalence, clinical features and laboratory findings, treatment and clinical course of BCS associated with BD.
Methods. We analyzed retrospectively the medical records of 1572 patients fulfilling the international diagnostic criteria of Behçet's disease. We included those with Budd-Chiari syndrome, and determined their demographic, clinical and biological characteristics and outcomes.
Results. Thirteen male patients and two women, mean age 34 years had Budd-Chiari syndrome associated to Behçet's disease. BCS was indicative of the disease in 20 %. Inferior vena cava was involved in 80% of the cases, Hepatic veins thrombosis was found in 20%. All forms of Budd- Chiari were noted: Chronic form in 67%, subacute form in 27% and fulminant form in one case. According to Child Pugh score, 60% of our patients were staged Class A, 27% Class B and 13% Class C. Ascites was the main clinical sign; present in 60% of the cases. Alanine aminotransferaselevels were elevated in 40% with low albumin in 47%. Other venous thrombosis (superior vena cava and lower limbs) were associated to Budd Chiari syndrome in 40%. Arterial involvement was associated in 30% (Pulmonary embolism and pulmonary artery's aneurysm). Cardiac manifestations were also present in 20% (Intracardiac thrombosis and coronary aneurysm). Two patients were positive for antiphospholipid antibodies. All patients had anticoagulation therapy; which was delayed in one case after the regression of the pulmonary aneurysm, associated to high- dose corticotherapy in all cases. Cyclophosphamide or azathioprine was used in 93% of cases. We noted severe complications in 47% (Digestive bleeding, confusion, infections and liver failure). Four patients have died.
Conclusion. Budd-Chiari syndrome in patients with Behçet's disease is rare but can be life threatening. It is frequently associated to other sever vascular manifestations that can be tricky to treat like in the presence of pulmonary artery aneurysm. The prognosis was improved with the use of immunosuppressive therapy in addition to anticoagulation in BCS associated to BD.

P62.

BASELINE ENDOTHELIAL DYSFUNCTION MIGHT PREDICT IMMUNOSUPPRESSIVE NEED IN YOUNG, MALE BEHÇET'S PATIENTS WITH EARLY DISEASE: A PROSPECTIVE FOLLOW-UP

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Objectives. Major organ involvement such as vascular or ocular disease, especially in young males, is one of the main causes of mortality and morbidity in Behçet's Disease (BD). However, the prognosis and predictors of vascular involvement is unsufficiently studied. In this study, we aimed to follow young, male BD patients which have the highest risk for new major organ involvement, prospectively. Subclinical vascular involvement and endothelial dysfunction were also investigated.
Methods. Thirty-six male patients with BD consecutively consulted in the Outpatient Clinics of Marmara University, 35 males with ankylosing spondylitis and 36 healthy males were included into the study. Bilateral upper and lower extremity venous doppler ultrasonography (US), brachial and carotid arterial US (for assessing endothelial dysfunction) were performed in baseline visit for all study groups and in the first year follow-up visit for BD patients. Patients with BD were assessed prospectively with 3-6 months intervals and in any urgent visit.
Results. At baseline, the mean disease duration was 3.3 years in patients with BD. The rate of venous insufficiency was significantly higher in male BD patients without vascular events, compared to healthy controls (BD vs HC; 30.5% vs 0%) and similar to patients with AS (BD vs AS; 30.5% vs 32%). Markers of endothelial dysfunction (FMD and NID) were similar between BD patients and healthy controls, however CIMT (Carotid intima media thickness) was significantly higher in BD (0.54 mm vs 0.47 mm). The mean follow-up duration was 44.6 months. Major organ involvement developed in 4 (11%, 3 vascular and 1 ocular involvement) patients during follow-up. All of them were in first 2 years of follow-up. Immunsuppresive (IS) therapy was required in 22% (n=8) of patients, due to major organ involvement in 4 (11%) and refractory mucocutaneous symptoms in other four (11%) patients. In the first year follow-up visit, endothelial functions and CIMT were observed to be significantly improved compared to baseline (Baseline vs Follow-up; 6.8±4 vs 10.9±4.5, p=0.003 for FMD, 0.55±0.13 vs 0.47±0.1, p=0.004). The patients requiring IS treatment in the follow-up had significantly lower FMD at baseline compared to the rest of the group (4.4 vs 8.5, p=0.005).
Conclusion. Preliminary results of our study (which will be a long-term cohort) demonstrated a lower incidence of major vascular events in male BD patients during prospective follow-up compared to historic controls in the literature. However, our results confirmed a more severe disease course in the first year of disease follow-up. The decreased rate of baseline FMD in patients with later IS requirement suggest that FMD can be a predictor for major organ involvement in BD.

P63.

RELATIONSHIP BETWEEN MENSTRUATION AND SYMPTOMS OF BEHÇET'S SYNDROME

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Background. It is well known that menstruation triggers several conditions such as migraine, recurrent aphtous stomatitis and acne vulgaris in otherwise healthy individuals (1). It may exacerbate chronic autoimmune diseases and familial Mediterranean fever (FMF) (2-4). There is also one study that briefly mentions menstruation causes activation in Behçet's syndrome (BS) (4).
Objectives. We investigated the relationship between menstruation and specifically the skin-mucosa lesions of BS. As controls, we studied FMF patients.
Methods. Premenopausal women with BS and FMF seen consecutively at the outpatient clinic of Cerrahpasa Medical Faculty at Istanbul, were interviewed. BS patients were asked whether they experienced increased skin-mucosa lesions during the menstrual period. A similar questionnaire assessing this time the frequency of serositis and fever attacks was given to the patients with FMF. As a control the participants were also asked whether they experienced headaches during the same period as well.
Results. A total of 140 BS patients with a mean age of 36±8 and mean disease duration of 9±6 years were studied. While 21 (15 %) were off treatment, 103 (74 %) were using colchicine and the remaining were using other immunosuppressive agents. As shown in the Table, among BS patients, 78 (56%) associated at

least one symptom with menstruation. The most commonly reported symptom related with menstruation was the papulopustular involvement (50%), followed by oral (30%) and genital ulcers (21%) and nodular lesions (21%). We also studied 185 patients with FMF. Their mean age was 32±8 and mean disease duration was 12±8 years. All patients were using colchicine for a mean duration of 8±7 years. A total of 138 patients (75%) reported that their attacks overlapped with menstruation. These attacks included mostly peritonitis in 126 patients (68%), pleuritis in 102 (55%), and fever in 73 (40%). Among both BS and FMF patients, similar number of patients (41% and 41%, respectively) reported that menstruation triggered headaches.

Table.

	Yes	No	Do not remember
Behçet syndrome (n= 140)			
Oral ulcer, n (%)	42 (30)	45 (32)	53 (38)
Genital ulcer, n (%)	30 (21)	94 (67)	16 (11)
Papulopustular lesions, n (%)	70 (50)	56 (40)	14 (10)
Nodular lesions, n (%)	30 (21)	90 (64)	20 (14)
At least one BS symptom, n (%)	78 (55)	-	-
Headache, n (%)	58 (41)	45 (33)	37 (26)
Familial Mediterranean Fever (n=185)			
Peritonitis, n (%)	126 (68)	51 (28)	8 (4)
Pleuritis, n (%)	102 (55)	74 (40)	9 (5)
Fever, n (%)	73 (39)	100 (54)	12 (6)
At least one FMF symptom, n (%)	138 (75)	-	-
Headache, n (%)	76 (41)	77 (42)	32 (17)

Conclusions. This survey showed that, in about half of the patients with BS at least one skin mucosa lesion is exacerbated with menstruation. Most commonly reported were the papulopustular lesions. Menstruation had a stronger effect on FMF, triggering at least one symptom in about ¾ patients. The main limitation of the study was the self-reported assessment methodology, rather than a prospective diary assessment. Our findings provide further evidence that papulopustular lesions of BS and acne vulgaris are pathologically related (5).

References

1. KHANNA N *et al*.: *Indian J Dermatol Venereol Leprol* 1991.
2. AKAR S *et al*.: *Rheumatol Int* 2006.
3. COLANGELO K *et al*.: *Rheumatology* (Oxford) 2011.
4. KARADAG O *et al*.: *Rheumatol Int* 2013.
5. KUTLUBAY Z *et al*.: C*lin Exp Rheumatol* 2015.

P64.

THE DIFFERENCE BETWEEN INTERNATIONAL CRITERIA FOR BD (ICBD) AND THE BD CRITERIA OF INTERNATIONAL STUDY GROUP (ISG) IN OUR BEHÇET'S DISEASE (BD) PATIENTS WHO FULFILLED JAPANESE BD CRITERIA

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Background. In Japan, we have a criteria for BD since 1988 (1). In Japanese patients diagnosed according to this Japanese BD criteria, the recent number of patients with the ocular lesions decreased compared with those with of the passed time; however, those the intestinal lesions increased. Moreover, a new international criteria for Behçet's disease (ICBD) was proposed in 2006 (2, 3). In ICBD the intestinal lesions were excluded as well as the criteria of international study group (ISG) in 1990. Purpose: To analyze the clinical features of BD with comparison among four 5-year-patient groups. Thereafter, to search which criteria was useful for Japanese BD patients between ISG and ICBD.
Methods. We enrolled our 264 (67.2%) BD patients out of 393. We diagnosed the patients having BD with Japanese BD criteria. We divided our patients to four groups with ones arriving period of 5 years: 49 BD patients were arrived at our clinic and started following until 2000, 70 patients from 2001 to 2005, 77 from 2006 to 2010, and 69 from 2011 to 2015, and compared symptoms of BD among four groups. We then analyzed the escape rate of our Japanese BD patients when we evaluated between ISG and ICBD. Moreover, we compared each rate, which criteria will be more usefull for Japanese BD patients comparing escape rate with chi square test.
Results. The characteristics of our 264 BD patients were as described below: 264 recurrent oral aphtous ulcers (100.0%), 206 genital ulcers (78.0%), 103 ocular manifestations (39.0%), 246 skin manifestations (93.2%), 161 arthritis (61.0%), 7 pathergy tests (2.7%), 71 intestinal lesions (26.9%), 23 neural lesions (8.7%), 22 vascular (8.3%), 11 epidemititis (4.2%), 75 male (28.4%), 136 HLA-B5 (51.5%), 86 HLA-B51 (32.6%), 16 HLA-A26 (6.1%). There was no significant differentiations among periods. The escape rate of our BD patients using ISG was 12.9% (n=34) and that using ICBD was 23.4% (n=15), and statistical analyses showed that ICBD may be useful criteria for Japanese BD patient (chi's $p<0.005$: $p=0.0044$).
Conclusions. The clinical features of our BD patients did not change among four 5-year periods. In our BD patients diagnosed with Japanese BD criteria, the diagnosing criteria for BD called ICBD was better item than ISG.

References

1. Y. MIZUSHIMA: Recent research into Behçet's disease in Japan. *International Journal of Tissue Reactions* 1988: 10; 59-65.
2. INTERNATIONAL TEAM FOR THE REVISION OF THE INTERNATIONAL CRITERIA FOR BEHÇET'S DISEASE: Evaluation of the International Criteria for Behçet's disease (ICBD). *Clinical Experimental Rheumatology* 2006: 24; S13.
3. INTERNATIONAL TEAM FOR THE REVISION OF THE INTERNATIONAL CRITERIA FOR BEHÇET'S DISEASE: Revision of the International Criteria for Behçet's Disease (ICBD). *Clinical and Experimental Rheumatology* 2006: 24; S14-5.
4. INTERNATIONAL STUDY GROUP FOR BEHÇET'S DISEASE: Criteria for diagnosis of Behçet's disease. *Lancet* 1990: 335; 1078-80.

P65.

OUTER PLEXIFORM LAYER ELEVATION AS A SURROGATE MARKER FOR HISTORY OF POSTERIOR OCULAR ATTACKS IN BEHÇET'S DISEASE

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Background. In Behçet's disease, ocular attacks, posterior inflammations in particular, cause irreversible loss of vision or blindness. Continuous follow-up is important to prevent ocular attacks and the history of posterior attacks should be considered when deciding on the observation period. In this study, the relationship between previous ocular attacks (vitreous opacity and retinal vasculitis) and optical coherence tomography findings were analyzed.
Methods. Fifty-nine eyes of 31 consecutive patients (Median age of 47.3±10.8 years) with Behçet's disease, who visited the Department of Ophthalmology of Kyoto University Hospital between February 2013 and October 2015, were included in the current retrospective study. Patients with signs of active inflammation were excluded. Eyes were examined using spectral domain optical coherence tomography (Spectralis; Heidelberg Engineering, Heidelberg, Germany). For the evaluation of the integrity of the photoreceptor layers, the status of the ellipsoid zone (EZ) and external limiting membrane (ELM) within a 1 mm area centered at the fovea, were assessed for each eye, by using horizontal and vertical scans through the fovea. The results were classified into three groups: complete, discontinuous, and absent.
Results. There were significant differences among the three EZ line groups and ELM line groups in logMAR VA (both $p<0.0001$), retinal thickness (both $p<0.0001$), and the number of ocular attacks ($p=0.0060$ and $p=0.0030$, respectively). Elevation of the outer plexiform layer (OPL), accompanied by the collapse of the inner nuclear layer (INL) (OPL elevation), was observed in 20 of the 59 eyes (35.7%). Eyes with OPL elevation had significantly poor VA ($p=0.0027$), thinner retinal thickness ($p=0.0167$), longer disease duration ($p=0.0313$), and a greater number of ocular attacks ($p<0.0001$), than did eyes without OPL elevations. In 53 eyes with preserved outer retina alone, the number of OPL elevations showed a strong positive correlation with the number of past ocular attacks ($r=0.7030$, $p<0.0001$).
Conclusions. The status of the outer retinal layers showed significant associations with VA, while OPL elevation showed significant association with a history of posterior ocular attacks in patients with Behçet's disease without current active inflammation.

P66.

ACUTE- AND CHRONIC PROGRESSIVE-TYPE NEURO-BEHÇET'S DISEASE: INVESTIGATION OF 2 CASES

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Neuro-Behçet's disease (NBD) is classified into acute- and chronic progressive-types based on differences in the responsiveness to treatment and prognosis. We encountered 2 patients with acute-type neuro-Behçet's disease (ANBD) and chronic progressive-type neuro-Behçet's disease (CPNBD), respectively. Case 1 was a 61-year-old male with a medical history of recurrent oral aphtha and uveitis, who had been diagnosed with BD. Dysarthria, trunkal ataxia, and left facial palsy developed up to 4 months prior to admission to the department of neurology. Brain MRI showed swelling of the pons, and high intensity was noted on T2-weighted imaging. High-intensity regions were also noted in the middle cerebellar peduncle, midbrain tegmentum, posterior limb of the internal capsule, and the thalamus. On examination of the cerebrospinal fluid (CSF), the cell count was 78/μl, and the CSF IL-6 level was 37.6 pg/ml, showing an increase. Based on these findings, the patient was diagnosed with acute-phase NBD. After the steroid pulse therapy, the patient was transferred to our department. No after-treatment was performed following the steroid pulse therapy, but the neurologic manifestations and brain MRI findings improved. When CSF IL-6 level was measured one month after the final steroid pulse therapy, no increase was observed. After all, the patient was diagnosed with ANBD. The patient is now being treated with colchicine alone, with no aggravation of the neurologic manifestation. Case 2 was a 43-year-old male with systemic malaise, loss of motivation, and writing disturbance from 6 months prior to visiting the department of neurology. Bladder and rectal disturbances had developed 2 months earlier, and ataxic gait had appeared one month earlier. On T2-weighted and FLAIR MRI, high-intensity regions were noted in the basilar part of the pons, bilateral cerebral peduncles, thalamus, and internal capsule. On CSF examination, the cell count was 165/μl, and the CSF IL-6 level was 224 pg/ml, showing an increase. Based on the presence of recurrent oral aphtha, genital ulcer, folliculitis-like skin eruption, and neurologic manifestation, the patient was diagnosed with acute-phase NBD. Methotrexate (MTX) treatment was initiated after the steroid pulse therapy. Brain MRI performed after one-month treatment noted atrophy centering the brainstem, for which the MTX dose was increased, but the aphasia and trunkal ataxia remained aggravated, and atrophy of the brainstem and cerebellum progressed. Thus, the patient was transferred to our department. Elevated CSF IL-6 levels persisted upon re-examination. In combination with the MRI findings, the patient was diagnosed with CPNBD. Since dose escalation of MTX led to liver disorder, concomitant treatment with infliximab (IFX) was initiated. We report 2 patients with ANBD and CPNBD, respectively. CSF IL-6 measurements were useful for differentiation and judgment of the disease state. Both patients were cigarette smokers, and the latter was HLA-B51-positive. IFX for treatment of NBD became covered by national health insurance in Japan, but increased accumulation of cases is necessary to confirm the efficacy and safety.

P67.

DEVELOPMENT OF A MULTI-DISCIPLINARY SERVICE FOR CHILDREN AND YOUNG PEOPLE WITH BEHÇET'S SYNDROME

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Behçet's syndrome is a rare multi-system inflammatory condition, which can have an onset in childhood in between 4-26% of cases1. Recent UK National Commissioning in 2012 has led to the development of three National Centre's of Excellence for Behçet's syndrome in Liverpool, Birmingham and London. The aims of the centres were to ensure that patients can access timely diagnosis and receive optimal treatment including high cost biologic therapies, while providing a 'one-stop shop' for patients who previously had to visit numerous specialists.
Aims. To develop a multi-disciplinary service for children and young people up to 18 years to reflect the health needs of paediatric patients.
Service Development. Since 2012, a 3 monthly multi-disciplinary clinic has been run at Alder Hey Children's NHS Foundation Trust. Previous to this, children and young people up to the age of 18 years were seen by a number of different specialties in separate clinics. Table 1 shows the healthcare professionals actively involved in this service. Those highlighted in grey are the core members of the clinic and were identified by a service evaluation prior to the set up of the clinic as most likely to be needed to deliver the needs of the majority of children with Behçet's syndrome. Review of previous and current cases both at our centre and another tertiary centre highlighted frequent muco-cutaneous and gastrointestinal involvement with minimal eye or neurological involvement. Joint clinics between colleagues in other specialties and paediatric rheumatology were already established (*on Table 1) allowing cross-speciality management in the few children presenting with other manifestations. This also ensured that children and their families were not overwhelmed by the number of professionals present in the clinic.

Table I. Members of the multi-speciality clinic and supporting teams.

Speciality	Role
Paediatric Rheumatologist	Diagnosis and management, coordination with other teams
Adult Rheumatologist	Diagnosis and management, transition lead and link to adult service
Oral Medicine	Diagnosis and management including arrangement of oral biopsy if deemed appropriate
Paediatric Dentist	Diagnosis, management and advice regarding dental hygiene
Paediatric Gastroenterologist	Diagnosis (including ruling out inflammatory bowel disease) and management including GI investigations as appropriate
Clinical Nurse Specialist	Support families, disease and drug education, school liaison. Telephone clinic helpline
Support Coordinator	Support patient and families with non medical aspects of condition, school/college liaison, welfare rights, signposting to other agencies
Paediatric Neurologist*	Diagnosis and management of neurological involvement
Paediatric Ophthalmologist*	Eye screening, diagnosis and management of ocular involvement
Paediatric Gynaecologist	Diagnosis and management of genital ulceration
Paediatric Dermatologist*	Diagnosis and management of skin involvement
Paediatric Immunologist/Infectious Disease Consultant*	Diagnosis and aiding identification of differential diagnoses such as periodic fevers and immunodeficiency
Paediatric Rheumatology Occupational Therapist & Physiotherapist	Management of musculoskeletal involvement, fatigue and pain
Paediatric Rheumatology Clinical psychologist	Addressing impact of chronic disease on emotional well-being, including pain/fatigue management, support around medications/procedures/transition, disease acceptance and patient resilience.

Professionals highlighted in grey are those core members that routinely attend the MDT clinic. *specialists who do not routinely attend the Behçet's MDT clinic but with whom joint clinics with Paediatric Rheumatology exist where patients can be reviewed simultaneously by both specialities.

Links with the adult service are facilitated through the input of both the adult rheumatologist and support coordinator who support both the adult and paediatric clinics. This had led to a better patient experience in transition to adult care as the patient is already well known to these professionals and is familiar with them. Input from oral medicine and paediatric dentistry has aided diagnosis and topical management of children with recurrent oral ulceration, together with improving dental hygiene which can be poor in this patient group. When indicated, oral biopsy can be arranged in an age-appropriate manner, for example under general anaesthetic or with Entonox and local anaesthetic.
Gastroenterology input into the service allows a joint assessment and rapid access to endoscopy and other gastrointestinal investigations with the dual purpose of ruling out IBD and establishing whether there is any GI involvement related to Behçet's syndrome
Discussion. Behçet's syndrome is a very rare disease in the UK and the spectrum of disease may differ to Silk Route countries. Development of this service will generate crucial data for UK and Northern European practice. Collaborative working across specialties is vital for a correct diagnosis particularly in incomplete cases. However, it is also important in the holistic management of children and young people.

P68.

SUPERIOR AND INFERIOR VENA CAVA THROMBOSIS: OUTCOME AFTER INTRODUCTION BY IMMUNOSUPPRESSIVE AGENT IN MOROCCO

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Introduction. Behçet's disease (BD) is a systemic disorder with a vascular tropism where the vessels might be affected. Venous thrombosis is the most common vascular complication. Among its locations, vena cava thrombosis (VCT) are rare but can be life-threatening.
The purpose of this work is to specify the frequency of VCT in the course of Behçet's disease in morocco and to analyse epidemiological, clinical and therapeutic modalities.
Patients and methods. This retrospective study was conduced in the internal medicine department of the University Hospital IbnRochd of Casablanca, over a period of thirty-five years between 1980 and 2015.
Where included 1572 cases of Behçet's disease, all diagnosed in our service and meeting the diagnosis criteria as defined by the international study group (ISG) for Behçet's disease.
Results. 52 patients with VCT – 47 men and 4 women – were gathered during this period, representing a rate of 3.30 % of 1572 cases, with a mean age of 35 years (ranges 17-54).
The diagnosis of VCT and BD was concomitant in 10 cases and occurred during the course of the disease in 42 cases after an average of 6 years of evolution. Among the localization. inferior VCT is the most frequent localization (32 patients, including 15 cases of Budd- Chiari syndrome). The superior VCT was reported in 24 patients, whereas 5 patients had both a superior and inferior VCT. Vena cava thrombosis was associated with deep venous thrombosis (DVT) of the lower limbs in 24 cases and with an aneurysm in 7 cases (pulmonary artery: 4 cases, femoral artery: 2 cases, abdominal aorta; 1 case).
Regarding the therapeutic modalities, 41 patients were under anti-coagulant treatment, 45 patients received corticosteroids and 51 of the patients were under immunosuppressive agents (cyclophosphamide, azathioprine). The evolution was significantly improved after the introduction of the immunosuppressive therapy, which were firstly initiated in 2006(76°/° the favorable evolution after 2006 vs 41°/°).
Discussion/Conclusion. Vena cava thrombosis in the context of Behçet's disease is a very serious pathology threatening the patient's vital and functional prognosis. Preventive measures, early diagnosis and effective treatment are the keys to a successful management of such complications' risks.

P69.

ACUTE MYOCARDITIS REVEALING BEHÇET DISEASE

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Introduction. Cardiac involvement in Behçet disease (BD) is rare, accounting for 6% of patients. We report an exceptional case of acute myocarditis revealing this disease.
Case report. A 32 year-old man with a history of recurrent oral ulcerations was admitted for a prolonged fever evolving since 3 weeks. The patient has reported a mild chest pain since one day. No respiratory, gastrointestinal or urinary signs were noted. At examination he was febrile at 40°C with 3 oral ulcers associated with 2 genital ulcers and multiple pseufolliculitis on the back. There were no lymph nodes, no crackles or heart murmur. A full blood count showed leukocytosis (WBC= 16 400 elt/mm3) with neutrophils at 15 500 elt/mm3. C reactive protein was 83 mg/l with a negative procalcitonin. Urine and blood culture were normal. Chest X rays and electrocardiogram were normal as well. Transthoracic echocardiography showed no vegetation. Cardiac MRI revealed myocarditis of inferior and lateral left ventricular wall. Echovirus, adenovirus, coxackie virus and syphilis serologies were negative. Acute myocarditis revealing a BD was diagnosed and the patient was initially started with pulses of methylprednisolone than cyclophosphamide, oral steroids and colchicine with resolution of fever and ulcerations.
Conclusion. To the best of our knowledge, this is the third case of myocarditis complicating BD in the literature. Increased awareness of such association is necessary as it can be associated with increased mortality.

P70.

ASSOCIATED MALIGNANCY IN BEHÇET DISEASE

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Introduction. Behçet disease (BD) is rarely reported to be associated with malignancies in the literature. Our aim is to identify clinical characteristics of BD patients associated with malignancies
Material and methods. A retrospective chart review was performed on 211 Behçet patients diagnosed in the Internal Medicine Department of Fattouma Bourguiba Hospital between 2000 and 2016. All patients were diagnosed according to the International Study Group of Behçet Disease Criteria. Patients with malignancies were identified and studied with regards to their clinical characteristics.
Results. Three patients were diagnosed with BD and associated malignancy. All of them were males with cutaneomucous manifestations. Vascular involvement was identified in one case. We identified one case of basal cell carcinoma at the age of 38, one case of bronchial carcinoma diagnosed at the age of 47 and one case of caecum adenocarcinoma at the age of 41. BD has been diagnosed since the age of 12, 18 and 13 respectively. Only the patient with bronchial carcinoma has had a fatal outcome. No patient has been treated with immunosuppressive drugs. No risk factors have been identified except a familiar polyposis in the case of caecum adenocarcinoma.
Conclusion. Unlike the other studies we did not find hematologic malignancies in our cohort. BD associated malignancies seem to be more frequent in males with a younger age at diagnosis. Whether BD is or not a promoting factor of malignancies is still uncertain and need further investigations.

P71.

VASCULAR INVOLVEMENT IN BEHÇET DISEASE IN THE TUNISIAN CONTEXT

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Introduction. Behçet disease (BD) is a systemic vasculitides characterized by recurrent oral genital aphthosis and ophthalmic manifestations. Vascular involvement can affect up to 40% of Behçet patients. We aimed to describe clinical characteristics and management of vascular involvement in BD in the Tunisian context.
Patients and methods. We retrospectively reviewed medical records of BD patients diagnosed according to the International Study Group of Behçet Disease Criteria admitted in the Internal Medicine Department of Fattouma Bourguiba Hospital between January 2005 and February 2016. Clinical characteristics and management of vascular involvement were described then a comparative study between patients with (group 1) and without vascular involvement (group 2) was performed
Results. Among 211 patients with BD, 56 (28%) were diagnosed as having vascular involvement. Their mean age was 31.5 years with a sex ratio of 4.2. Deep venous thrombosis were diagnosed in 63.5% of them as following: upper limb in 12.7%, lower limb 25.4%, bilateral lower limb in 4.8%, inferior vena cava in 11%, and more than one site in 4.8%. Superficial venous thrombosis was diagnosed in 23.6%. Arterial involvement was found in 25.4% with pulmonary embolism in 14.3%, pulmonary arterial aneurysm in 11.4% and myocardial infarction and coronary aneurysm in 1.6%. An associated thrombophilia abnormality was found in 9.6% of the cases. Treatment consisted in colchicine in all cases with anticoagulants in 73.3%, corticotherapy in 45.2% and immunosuppressive drugs in 25.4%. Embolisation was performed in 2 cases. Patients of group 2 were aged 30 years old on average with a sex ratio M/F= 1.5. Comparative study between group 1 and group 2 revealed a significant prevalence of males, erythema nodosum history and positive pathergy test in group 1 (p=0.08; p=0.017; p=0.034 respectively). There were no differences concerning ocular, neurological, gastro intestinal and genital involvement.
Conclusion. According to our results, vascular involvement in Behçet disease is frequent in the Tunisian context. Males, patients with positive pathergy test and those with erythema nodosum history are at a higher risk to develop vascular complications requiring then close monitoring.

P72.

HUGHES STOVIN SYNDROME REVEALING BEHÇET DISEASE

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Introduction. Hughes-Stovin Syndrome (HSS) is a very rare clinical disorder characterized by deep venous thrombosis and multiple pulmonary and/or bronchial aneurysms. Aneurysms in the systemic circulation can also be seen. It is supposed to be a clinical variant manifestation of Behçet disease. We report the first case of HSS with aortic aneurysm.
Case report. A 55 year old man presented to the emergency room with pain and swelling of his left leg. Physical examination was unremarkable except edema of left leg and few folliculitis on the back. A color Doppler examination showed deep vein thrombosis. A chest x-rays revealed widening of the superior mediastinum. Contrast Enchanced Computed Tomography (CT) showed a non complicated ascending thoracic aorta aneurysm of 48 mm. Echocardiography was normal. He gave no history of fever, hemoptysis or chest pain, but reported a history of recurrent oral and genital ulcers. Complete blood count, serum creatinine, erythrocyte sedimentation rate and urine analysis were within normal limits. Laboratory testing of associated thrombophilia abnormalities revealed protein S deficiency. Human leukocyte antigen (HLA B 51) was negative. The diagnosis of HSS revealing a Behçet disease associated with protein S deficiency was made. Ophthalmic investigation revealed no uveitis or vasculitis. Treatment consisted in Methylprednisolone (3 days pulse, 1g daily) followed by oral prednisone (1mg/kg/j daily) and Cyclophosphamide (6 pulses monthly). Oral anticoagulation was held.
Conclusion. Hughes Stovin syndrome is often considered as a form of Behçet disease. It is typically treated with corticosteroids and immunosuppressors. Anticoagulants might be problematic as they can be associated with hemorrhagic complications.

P73.

VENOUS QUALITY OF LIFE DOES NOT CHANGE IN FOLLOW UP IN PATIENTS WITH VASCULAR BEHÇET'S DISEASE

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Introduction. Vascular involvement is one of the major causes of mortality and morbidity in Behçet's disease and lower extremity deep vein thrombosis is the most frequent manifestation of it. The post-thrombotic syndrome (PTS) is the most common complication of deep vein thrombosis (DVT) with evident impairment of quality of life, occurring in 20%–80% of patients within the first 1–2 years after deep venous thrombosis (DVT) of the lower limb.
Objectives. There is no data about post-thrombotic syndrome and the course of the quality of life in time in deep venous thrombosis associated with Behçet's Disease. We prospectively measured change in quality of life during approximately 1 year, and evaluated determinants of quality of life, including development of post-thrombotic syndrome.
Materials and methods. In this study, 94 patients with VBD, who were regularly followed in Marmara University Behçet clinic, 29 patients with DVT associated with non-BD reasons, who were followed in Vascular Surgery Department, were assessed. During the follow-up patients are evaluated with Villalta scale, CEAP (Clinical, Etiologic, Anatomic, Pathophysiologic) classification, VCSS (Venous Clinical Severity Score) and VDS (Venous Disability Score at every visit. Venous disease-specific quality of life (the primary outcome) was measured using the Turkish validated form of Venous Insufficiency Epidemiological and Economic Study Quality of Life/Symptom questionnaire (VEINES- QoL/Sym).
Results. Baseline VEINES-QoL and VEINES-Sym scores of the BD group were better than the non-BD group. Physical component of SF-36 was similar between the groups. Mental component of SF-36 was better in BD group compared to non-BD group. During follow-up, PTS frequency did not change and venous disease specific and generic QOL scores (VEINES QoL/Sym, PCS, MCS scores) of the patients tend to improve over time but there is no statistical significance except the mental component of SF-36.
Conclusion. Effective control of vascular inflammation with immunsuppressive therapy in VBD might explain lower CPTS and better venous QoL in VBD. In the follow of Behçet patients the insignificant change in the venous disease spesific quality of life can be explained by the long periof of time (mean±SD:74,23±59,5) post DVT.

Table I. Change in quality of life from baseline to last assesment.

	Baseline	Last visit	change	P value
	mean±SD	mean±SD	mean±SD	
VEINES-QoL	89,73±16,93	91,25±16,18	1,52±12,07	^{h}0,499
VEINES-Sym	39,23±9,32	40,20±9,28	0,98±6,44	^{h}0,285
PCS-1	43,22±10,56	45,55±10,24	2,33±8,36	^{h}0,111
MCS-1	46,43±9,03	51,38±8,81	4,95±10,96	^{h}0,006**
BSAS	21,36±15,24	19,86±14,82	-1,50±13,54	^{h}0,231

P74.

VITAMIN D STATUS AND BEHÇET'S DISEASE IN THE MIDWEST REGION IN IRELAND

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Introduction. Current literature shows that vitamin D plays a significant role in immune system modulation and functioning. Plethora of studies has revealed higher rate of vitamin D deficiency among patients with autoimmune diseases.
Aim. The aim of the study was to evaluate the serum 25-hydroxyvitamin D (25(OH) D) levels of Behçet's disease (BD) patients in the Midwest of Ireland, and to correlate with its disease activity.
Methods. All BD patients attending our rheumatology service were matched with healthy controls and included in the study. Any subjects who were on vitamin D supplement were excluded from the study. The serum was measured by enzyme-linked immunosorbent assay (ELISA) method; vitamin D levels lower than 20ng/ml were defined as vitamin D deficient, and between 20-40ng/ml as vitamin D insufficient.
Results. A total of 19 BD were included in the study (4 male, 15 female, median age of 41.26 years, range, 19-82 years). The mean serum 25(OH)D levels of BD patients were 47.68ng/ml (range, 21-76ng/ml). The mean 25(OH)D levels were relatively lower when compared between active BD patients against inactive patients 51.07ng/ml (range, 26-76ng/ml) and 35ng/ml (range, 21-49ng/ml) respectively. Overall, none of the patients had vitamin d deficiency, however 6 patients had vitamin d insufficiency.
Conclusion. In contrast to many previous studies in other BD cohorts and other autoimmune diseases, our study suggests that the mean 25(OH)D levels are higher in the BD group. In active patients however, the serum levels are relatively lower compared to the inactive BD patients, which is in concordance with the literature. Our findings suggest vitamin D as a potential suppressor of inflammatory response in BD, however higher quality studies are needed to support this and conclusively understand its role in the inflammatory pathway.

P75.

A SUBGROUP ANALYSIS OF COMORBIDITIES IN BEHÇET'S DISEASE; RESULTS FROM A PROSPECTIVE CASE-CONTROLLED STUDY

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Objectives. Behçet's Disease is a complex multisystem disease and accurate diagnosis is challenging due to the variety of symptoms patients may present with. Differentiating symptoms associated with disease and comorbid conditions is important for optimal management. There are currently no guidelines for the management of comorbidities in Behçet's Disease.
Methods. In this single-centre prospective study, 118 patients and 116 demographically-matched controls were offered structured interviews to document previous and current comorbidities. Comorbidities were clustered into cardiovascular, inflammatory, psychological, respiratory, gastrointestinal and cancer subgroups. Total comorbidities and each subgroup were correlated against Behçet's Disease clinical activity, oral ulcer severity scores and vitamin D levels.
Results. The Behçet's group had more cardiovascular (p=0.009), gastrointestinal (p<0.0001), psychological (p<0.0001) and respiratory (p<0.0001) comorbidi-

ties, whereas the control group reported more cancer (p=0.043) comorbidities. There was no significant difference in inflammatory diseases between the groups (p=0.13). Furthermore, patients with 3 or more comorbidities scored higher in the Behçet's Disease Clinical Activity Form compared to those with 0 or 1-2 comorbidities (p<0.0001 and p=0.006, respectively) suggesting a more severe clinical phenotype. There was no correlation between vitamin D levels and comorbidities, nor did low vitamin D (<50nmol/L) correlate with a more severe clinical phenotype.

Conclusions. This is the first case-control study to report comorbidities in Behçet's Disease. The findings suggest that patients have significantly more comorbidities than controls and that this may impact their clinical phenotype. In light of the increased number of cardiovascular diseases found in our patients, we suggest that patients with Behçet's Disease are evaluated yearly for cardiovascular risk factors in line with other inflammatory conditions such as rheumatoid arthritis.

Key words. Behçet's Disease; Behçet's Syndrome; Comorbidities; Comorbid; Cardiovascular; Psychological; Respiratory; Gastrointestinal.
The authors declare no conflicts of interest in this study.

P76.

DEVELOPMENT OF A PATIENT CONCERNS INVENTORY FOR BEHÇET'S DISEASE

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Introduction. Behçet's Disease (BD) is a complex, multi-system inflammatory disorder, which varies greatly in its clinical expression and severity from patient to patient and potentially between patients from different countries. Individual, holistic management is essential to minimise the impact of BD on patients' lives. Recognising all of a patient's concerns can be challenging; patients may have multiple, wide-ranging and sensitive problems and time for consultation with a physician can be pressured. Patient Concerns Inventories (PCIs) (1), have been shown to aid communication between patients and clinicians, enhance the medical consultation and improve patient satisfaction.
Aim. The aim of this work was to develop an initial Patient Concerns Inventory (PCI) for BD, that can be refined in subsequent phases of development for use in the clinical setting. The aim of the final PCI is to improve communication between patients with BD and clinicians, reducing potentially unmet needs of patients.
Method. This work was undertaken by a 3rd year Medical student. The PCI is developed in 4 phases. Phase 1 (presented here) underpins the development, through detailed systematic review of the literature.
Phase 1: Two literature searches, using databases Medline, Scopus and PubMed, were undertaken to develop a list of needs and concerns of patients with BD. Search 1 used parameters 'Behçet*' 'AND' 'unmet need' to identify unmet needs described in the literature. Search 2 used the parameters 'Behçet*' 'AND' 'QoL' to find quality of life (QoL) instruments used in BD research. These were then accessed and their items adapted into the initial PCI.
Phase 2: Healthcare professionals with experience of BD will refine the initial PCI based on professional experience.
Phase 3: Three facilitated patient focus groups comprising a total of 20 patients, identified by purposeful sampling, will provide qualitative feedback to finalise the amount and content of questions on the BD PCI.
Phase 4: Pilot study to evaluate the PCI in a multidisciplinary BD clinic.
Results. (Phase 1): Systematic searching of the literature produced a list of 57 items for the initial PCI. These have been organised under the headings physical well-being, life impact, psychological well-being, sleep quality, medication, and surgery and will be presented in full at the meeting
Conclusion. A set of initial PCI specific for BD has been developed from a detailed systematic review. These will be subjected to further refinement by medical and allied-health professionals and patients, to produce a final PCI for clinical use and which can be evaluated in a pilot study. The Behçet's PCI has the potential to enable better recognition of patient needs and concerns that can be addressed more effectively in clinical interactions. With differences in disease severity, general culture and approach to illness between countries, there is considerable attraction in refining the final BD PCI through a collaborative international process.

Reference

AHMED AE, LOWE D, KIRTON JA, BRUCE H, KENNEDY T, ROGERS SN, MOOTS RJ; *J Rheumatology* 2016 Feb 15 pii: jrheum.150068

P77.

CORONARY ARTERY DISEASE IN PATIENTS WITH BEHÇET'S DISEASE: A RETROSPECTIVE, SINGLE CENTER STUDY

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Objective. To investigate the clinical characteristics of Behçet's disease (BD) patients complicated with coronary artery disease (CAD), which is the most life-threatening complication of BD.
Methods. We retrospectively reviewed the medical records of all BD patients who were admitted to Peking Union Medical College Hospital from January 2001 to April 2016. CAD was defined as aneurysm, stenosis and (or) occlusion of coronary arteries documented by angiography or contrast-enhanced computer tomography. Demographic, clinical and laboratory data were systemically collected and analyzed.
Results. In total, 468 patients with BD were hospitalized, including 12 cases (2.6%) complicated with CAD. All patients with CAD were male. The mean onset age of BD and CAD were 32.3 and 36.2 year, respectively; while the mean duration from the onset of BD to diagnosis of CAD was 3.8 year. Angina pectoris (6/12) and acute myocardial infarction (6/12) were the most common cardiac symptoms, arrhythmia was rare symptoms (1/12), and one patient is asymptomatic. Traditional CAD risk factors, including hypertension, diabetes mellitus and alcohol consumption, except smoking (4/12), were absent. Seven cases were presented with coronary artery aneurysm, including two cases with two aneurysms. Eight cases were presented with coronary artery stenosis, including five cases with two to tree artery stenosis. Coronary artery occlusion was documented in three cases. Other major artery and venous involvement were presented in five and two cases, respectively. Oral ulceration (12/12) and pseudofolliculitis (5/12) were the most common BD-associated symptoms, followed by erythema nodosum (3/12) and pustule (3/12). The Median ESR and CRP was 25.5 (mm/Hr) and 16.25 mg/L. Elven cases were treated with glucocorticoid (mean dose 58.5 mg/d, prednisone or equivalent), including one case treated with methylprednisolone pluse therapy. Cyclophosphamide (10/12) was the most commonly used immunosuppressive agent.
Conclusions. CAD was a rare complication of BD, which predominately affect male patients. Absence of traditional CAD risk factors, as well as concomitant active BD symptoms, and elevated inflammatory markers, collectively suggested active inflammation of vessel walls was the major mechanism of CAD in BD.

P78.

LOW MEDICATION ADHERENCE IS ASSOCIATED WITH ORAL ULCER ACTIVITY AND QUALITY OF LIFE IN BEHÇET'S DISEASE

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Objective. The aim of this study was to evaluate the relationship among oral ulcer activity, oral health related quality of life and self-reported medication adherence in Behçet's disease (BD) patients.
Materials and methods. The study group composed of 358 BD patients (F/M:192/166, mean age: 38.3±10.4 years). The disease severity score was calculated according to organ involvement and was categorized as mild (<4) or severe (≥4). Oral health related quality of life (OHRQoL) as an outcome measure was evaluated by oral health impact profile-14 (OHIP-14). High scores were related with poor OHRQoL status. Medication adherence was evaluated through the use of 8-item Morisky Medication Adherence Scale (MMAS) having a score range between "0" to "8" with high scores indicating better adherence. Low-adherence was defined as <6 points for MMAS.
Results. The ratio of patients with low medication adherence was higher in mild disease course (57.5%) as compared to severe ones (42.5%) (p=0.03). In female

BD patients, oral ulcer activity was significantly associated with low medication adherence (72,7%) when compared to high medication adherence (50%) (p=0.018), whereas a similar relationship was not observed in males (p=0.52). In addition, OHIP-14 scores were higher in low medication adherence group (27.1±16.6 versus 20.1±17.6) in females (p=0.04).
Conclusions. This is first study measuring self-reported medication adherence in cases of BD. Low adherence levels were found to be associated with female gender, oral ulcer activity and poor OHRQoL status indicating the importance of effective disease control and oral symptoms in management of this chronic disease.

P79.

AN EXEMPLAR BEHÇET CASE, IN ALL ITS MULTISYSTEMIC FEATURES

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Introduction. Behçet's disease (BD) is a chronic, relapsing, inflammatory disorder of unknown etiology, with vasculitis underlying the pathophysiology of its multisystemic effects. Without recurrent oral or genital ulcerations, skin lesions, or a positive pathergy test, a patient does not fulfill the classification criteria of the International Study Group for BD (ISG) 1990. We present a case of BD started with articular and nervous manifestations, who expressed only in a second time aphthous oral and genital ulcers.
Case report. a 43-year-old woman visited our rheumatologic clinic with acrocianosis, arthritis of hands and feet and sacroiliac pain (at MR left iliac sclerosis). At serum exams, no ANA or ENAs were present. Owing to her psoriasis, a diagnosis of psoriatic arthritis was made and a treatment with MTX and SLZ was started, without benefit. After six months, fever, right hypoesthesia and progressive loss of sight appeared. HLA-B51 was found.
CT and angio-MRI of brain, Doppler of supra-aortic brunches, connective-vasculitic autoantibody profile and inflammatory markers were all normal. Study of the central visual field and visual evoked potentials were altered in right eye, as right optic retrobulbar neuritis. Methylprednisolone 1 g ev/die for 5 days was started, followed by 1 mg/Kg/die of prednisone, with complete recovery of sight. Therapy with adalimumab was started, with benefit. After 18 months, she developed a new arthritic flare and pseudofolliculitis on extensor surface of both legs, bipolar aphthosis, hypoesthesia on right side of the body and right hearing impairment. Moreover she started to complain epigastric pain and diarrhea (no alimentary intolerances were found; on endoscopic colon exams a neutrophilic phlebitis that leads to mucosal inflammation was found). On brain and cord MRI with contrast: tiny aspecific focal gliotic lesions in emicerebellar iuxta- and subcortical bilateral front. Cyclophosfamide treatment was started. Her next examination is planned in two months.
Conclusion. in BD specific laboratory markers are lacking, so the diagnosis is made on the basis of a minimum number of clinical signs mentioned in the international criteria. We showed the case of a woman who developed aphthosis only after more than one year form the appearance of articular and neurologic problems; and with the aphthosis also intestinal BD signs appeared.
Although neurologic manifestations of BD are now well recognized, intestinal BD manifestations (despite of particular severity as they are associated with significant morbidity and mortality) are very difficult to diagnoses and to treat. Indeed, medical treatment of intestinal BD is largely empirical, since well-controlled studies have been difficult to perform due to the heterogeneity and rarity of the disease. Other organ manifestation including vasculitis and central nervous system disease should be included by the Criteria for BD.

P80.

DISEASE CHARACTERISTICS OF BEHÇET'S DISEASE AMONG FILIPINO PATIENTS SEEN IN RHEUMATOLOGY CLINICS

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Objectives. The goal of this research is to look at the characteristics of Behçet's Disease (BD) among Filipinos to increase awareness and avoid delay in diagnosis which might pose a threat for the development of fatal and sometimes irreversible complications.
Design. Retrospective.
Setting. Multiple rheumatology clinics seen by the rheumatology consultants of the Philippine General Hospital.
Methodology. We reviewed charts of patients diagnosed with BD using the 2006 International Criteria for Behçet's Disease (ICBD) seen in several rheumatology clinics by the rheumatology staff of the Philippine General Hospital. Demographic data, clinical manifestations, ancillary procedure results and pathergy test; medications received and outcomes were extracted. Descriptive statistics were applied.
Results. Thirty-one patients were included in this study. Majority (77%) were female with mean age at diagnosis of 38.61 years and mean disease duration of 56 months. A positive family history of BD is present in 10% of patients. Among the criteria features, the most common is oral ulcers present in 94% of patients followed by ocular manifestations seen in 68% while 65% have cutaneous findings. Pathergy test is positive in 17% of patients. Majority (74%) of our patients received oral steroids, 58% received Colchicine and 48% received NSAIDs. Most of our patients noted improvement but some still had recurrences of their symptoms. Thirteen patients (42%) still had recurrent oral ulceration and 23% had recurrence of skin lesions. Two of our patients (6%) developed blindness but no mortality was recorded.
Discussion and conclusion. Behçet's disease among Filipinos poses a clinical challenge among physicians. At least a year of delay in diagnosis is seen in this cohort and appears to be the main hindrance for early initiation of treatment. Oral ulcers in combination with ocular manifestations and genital ulcers serve as major clue in the diagnosis. While majority of cases in the cohort had good outcome, it is a totally disabling disease as seen in the 2 cases that developed blindness. We recommend a bigger multispecialty study or a nationwide database to expand this cohort of patients, understand the disease as it presents locally and increase awareness of the disease to prevent disability.

P81.

INTERFERON-γ RELEASE ASSAY (T-SPOT.TB) IN THE DIAGNOSIS OF TUBERCULOSIS INFECTION IN PATIENTS WITH BEHÇET'S DISEASE: A SINGLE CENTER EXPERIENCE IN CHINA

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Objectives. To investigate the diagnostic value of the T-SPOT.TB in BD patients complicated with tuberculosis infection.
Method. The clinical, radiology and laboratory data were collected and analyzed in 175 hospitalized BD patients from the Peking Union Medical College Hospital between January 2010 and March 2015. The diagnostic test performances of T-SPOT.TB were evaluated by calculating sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios, as well as ROC. Statistical analysis was carried out using IBM SPSS version 19.
Results. Of the 175 BD patients, the positive rate of SPOT.TB in BD patients was 34.3% (60/175) including 16 patients clinically diagnosed as active TB (BD-ATB),twelve patients with old TB (BD-OTB) and 32 patients with latent TB (BD-LTB). Among BD-ATB patients, fourteen patients (87.5%) had positive SPOT.TB and the median number of spot-forming cells (SFCs) being 332 (IQR: 100-1214). Among BD-OTB patients, eleven patients (91.75%) had positive SPOT.TB with the median number of SFCs being 152(IQR: 42-758). Thirty-two patients with positive SPOT.TB but lack of clinical TB symptoms and imaging evidence of TB were classified as LTB. The median numbers of SFC in BD-LTB patients were 80 (IQR: 40-300). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the T-SPOT.TB test for the diagnosis of ATB were 87.5%, 73%, 36.8%, 98.3%, respectively. Positive likelihood ratio (PLR) and negative likelihood ratio (NLR) were 3.24 and 0.17.

The median number of SFCs in the BD-ATB group was higher than that in the BD-LTB group and BD-OTB (p<0.001 and p<0.012). It was suggested that BD patients with higher numbers of SFCs may have a higher risk of ATB. By ROC method, it was suggested that 70 SFCs act as a cutoff for diagnosing BD-ATB with the sensitivity, specificity, PPV, NPV, PLR and NLR were 87.5%, 85%, 24.6%, 98.5%, 5.79 and 0.15, respectively. The area under the curve was 0.862 (95%CI 0.757-0.968).
Conclusions. BD patients with higher numbers of SFCs may have a higher risk of ATB. SFCs numbers over 70 may serve as an efficient cutoff value for diagnosing ATB in BD patients.

P82.

IDENTIFYING CORE DOMAINS FOR BEHÇET'S SYNDROME TRIALS: AN INTERNATIONAL PHYSICIAN AND PATIENT DELPHI EXERCISE

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Background. An unmet need for reliable, validated and widely accepted outcome measures for trials in Behçet's syndrome (BS) was identified through: i) a systematic review; ii) a survey among Behçet's experts; and iii) an outcome measures interest group meeting during the 16th International Conference on Behçet's Disease (1,2). The OMERACT Behçet's Syndrome Working Group has been working to advance outcome measures in BS with the goal of creating a core set of data-driven measures for use in clinical trials for BS. To identify domains, subdomains, and outcomes to be assessed in trials of BS, a Delphi exercise among Behçet's experts and patients has been initiated. This abstract describes the results for round 1 of the Delphi.
Method. A list of possible domains, subdomains, and outcomes was prepared using the results of a systematic literature review on outcomes assessed in previous Behçet's studies (1), patient priorities identified through qualitative interviews (2), and expert opinion. A 3-round Delphi has begun among physicians from different specialties experienced in BS and among patients with BS. The patient survey was the same as the physician survey with medical terms explained. The web-based survey was formatted in both English and Turkish and emailed to 123 physicians and 130 patients. Agreement by ≥70% of either physicians or patients resulted in an item accepted.
Results. 74 physicians and 35 patients participated in Round 1. The physicians were experts in BS from 21 countries and from within a wide range of specialties, including Rheumatology (50%), Ophthalmology (12%), Internal Medicine (12%), Dermatology (16%), Gastroenterology (3%), and Neurology (1%). Among the participating patients there was good representation of each type of organ involvement. Table 1 shows the domains that received ≥70% endorsement to be measured in all trials in BS and the additional subdomains for trials for each type of involvement. In addition to these domains, ≥70% patients endorsed the assessment of pain, fatigue, sleep, sexual functioning, psychological functioning, and acute phase reactants in all trials of BS.
Conclusion. Multiple disease-related domains in BS have been identified by physicians and patients as important to address in clinical trials, suggesting that a core set for all trials will be needed and subdomains for subsets of disease will also be useful. Rating and ranking of these domains and subdomains in the next 2 rounds will enable the development of a core set of domains to be assessed in trials of BS.

P83.

FECAL CALPROTECTIN LEVEL LOOKS PROMISING IN IDENTIFYING ACTIVE DISEASE IN BEHÇET'S SYNDROME PATIENTS WITH GASTROINTESTINAL INVOLVEMENT: A CONTROLLED AND PILOT STUDY

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Background. The fecal calprotectin (FC) is widely used as a non-invasive method for identifying patients with active Crohn's disease (CD) and ulcerative colitis. Gastrointestinal involvement of Behçet's syndrome (GIBS) shows clinical and endoscopic similarities to CD. A previous study in a small number of Behçet's syndrome (BS) patients with mainly mucocutaneous lesions showed serum calprotectin levels did not differ between active and inactive patients (1). Another study suggested FC may help to diagnose GIBS patients (2). We are not aware of studies addressing whether FC helps to distinguish active GIBS patients from those in remission.
Objectives. To determine whether FC helps predict active disease in GIBS patients.
Methods. We collected fecal specimens from 23 GIBS (11 M, 12 F and mean age 44±9 yrs) patients before colonoscopy. The reasons for colonoscopy were assessing active disease in patients presenting with abdominal pain (with or without diarrhea) (n=9) or confirmation of a remission in asymptomatic patients (n=16). Four symptomatic and 3 asymptomatic patients had active ulcers by endoscopy. On the other hand, 5 symptomatic and 13 asymptomatic patients did not have ulcers. We also included 22 active and 25 inactive CD patients as controls. We used 150 μg/g as the cut-off for a positive FC level. We also looked at the correlation between FC and serum CRP levels, Crohn's disease activity index (CDAI) and disease activity index for intestinal Behçet's disease (DAIBD) scores.
Results: FC was >150 μg/g in all of the 7 GIBS patients with ulcers compared to 4/16 of GIBS patients without ulcers (OR, 95%CI: 42 to 888). The mean FC was 1125±800 μg/g (95%CI: 341 to 1908) among symptomatic patients with ulcers (n=4) and 209±213 μg/g (95%CI: 22 to 396) among symptomatic patients without ulcers (n=5). On the other hand, the mean FC was 243±73 μg/g (95%CI: 158 to 328) among asymptomatic patients with ulcers (n=3) and 95±160 μg/g (95%CI: 0.4 to 189) among asymptomatic patients without ulcers (n=11). Among CD patients, 16/25 active patients and 3/22 patients in remission had FC level >150 μg/g (OR, 95%CI: 11 to 49). There was a low correlation between FC and serum CRP levels (r=0.3, p=0.1), a moderate correlation between FC and CDAI scores (r=0.5, p=0.02) and very low correlation between FC and DAIBD scores (r=0.01, p=0.9). Among the 4 GIBS patients who had high FC levels despite being in remission for gastrointestinal (GI) involvement, 1 had active mucocutaneous lesions, 1 had concomitant macrophage activation syndrome, and 1 had polycythemia vera with trisomy 8. None of the patients were receiving NSAIDs that could increase FC levels.
Conclusions. Pending the study of more number of patients, FC may turn out to be a useful non-invasive tool for ruling out active GI lesions in asymptomatic GIBS patients. A high FC level demands caution for the presence of active ulcers especially in symptomatic patients, but whether the presence of other BS manifestations can cause false positive results remains to be studied.
References
1. OKTAYOGLU P *et al*.: *Scand J Clin Lab Invest* 2015.
2. KIM DH *et al*.: ECCO.2014.

P84.

A BEHÇET'S DISEASE PATIENT WITH PERCARDIAL TAMPONADE RELATED TO RIGHT CORONARY PSEUDOANEURYSM

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Introduction. Behçet's disease (BD) is a chronic, multisystem disorder characterized by recurrent self-limited inflammatory episodes affecting the mucocutaneous tissues, eyes, all types and sizes of blood vessels, and several other organs and tissues including the joints, lungs, and central nervous and gastrointestinal systems1. BD classified as variable vessel vasculitis that may involve both veins and arteries. Arterial involvement may present with thrombosis, occlusion or aneurysm. Coronary aneurysm and pericardial tamponade are rarely reported in the course of BD. Herein we presented a BD patient with pericardial tamponade and right coronary aneurysm that occurred after femoral artery bypass surgery.

Case report. Thirty-seven-year-old male patient diagnosed as having BD with the findings of recurrent oral ulcers, folliculitis and pathergy skin test was treated with colchicine for 10 years. The patient used colchicine irregularly and didn't show up at the outpatient clinic controls. Eight months ago, he was admitted to the outpatient clinic of cardiovascular surgery with the complaints of severe pain and a swelling on the right groin. A femoral artery aneurysm was diagnosed and thereafter femoropopliteal bypass surgery was applied. The patient discharged from the hospital and followed without any immunosuppressive therapy. Twenty days after the operation he was admitted to the emergency clinic with cardiogenic shock and cardiac tamponade along with a mass appearance in the right ventricle that was detected on chest CT. On admission, acute phase reactants were found to be elevated (ESR 27 mm/h, CRP: 84 mg/L). Emergency pericardiocentesis was performed and persevered thrombus image was demonstrated on postoperative imaging. Coronary artery pseudoaneurysm was seen on right coronary CT angiography (Figure 1). With the all findings, the patient was referred to the rheumatology department and induction treatment with pulse corticosteroid (1gr methylprednisolone for three days) and IV cyclophosphamide therapy at a dosage of 15 mg/kg/month were started. Daily high dose corticosteroid treatment (60 mg/d for 2 weeks then 40 mg/d) was continued. One month after the treatment acute phase reactants was found normal (ESR: 3 mm/h, CRP: 5 mg/L) and no thrombus or pericardial effusion was observed on echocardiography and thorax CT. Elective stenting of the right coronary artery under immunosuppressive therapy was planned.

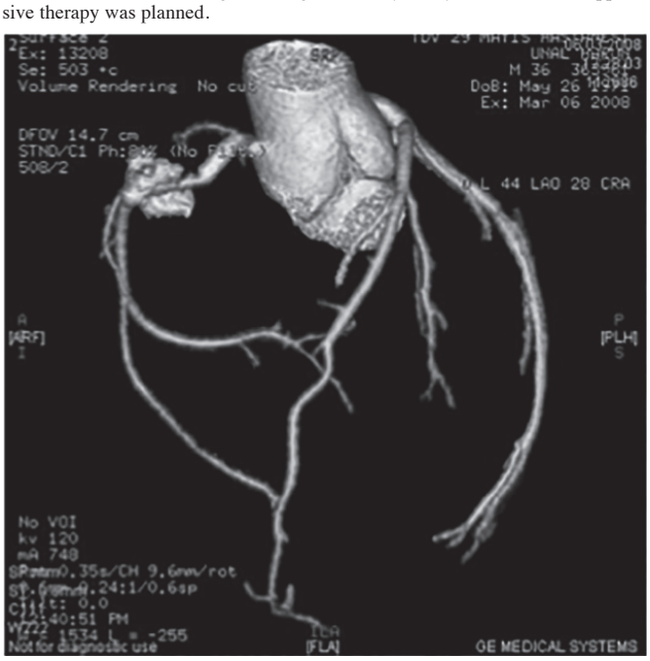

Fig. 1. Coronary artery pseudoaneurysm demonstrated on right coronary CT angiographhy.

Discussion. Pericardial tamponade related to coronary artery aneurysm is a rare vascular involvement of BD which has been reported in a very few cases. In our case, surgical treatment before effective immunosuppressive treatment is thought to have contribution to the development of pericardial tamponade. In BD patients with severe vascular disease, the extension of vessel involvement must be evaluated carefully and the control of inflammation with immunosuppressives is essential before referring these patients for any surgical intervention.

P85.

A SYSTEMATIC LITERATURE REVIEW ON THE TREATMENT OF MAJOR ORGAN INVOLVEMENT OF BEHÇET'S SYNDROME INFORMING THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF BEHÇET'S SYNDROME

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Objectives. The first EULAR recommendation for the management of Behçet's syndrome (BS) was published in 2008 and since then new data especially with biologic drugs have appeared. To review the evidence for efficacy and safety of therapeutic interventions in BS patients with eye, vascular, gastrointestinal (GI) and neurologic involvement (CNS).

Methods. We used the GRADE methodology as framework for guidelines development. For the systematic literature review, we searched The Cochrane Library, DARE, HTA; MEDLINE; EMBASE; and IPAD. Randomized controlled trials (RCT), controlled clinical trials, or open label trials comparing an active drug in patients with BS with other agents or placebo were included. If controlled trials were not available for answering a specific research question, uncontrolled evidence from prospective or retrospective cohort studies or case series about a minimum of 5 patients were also included.

Results. We reviewed the titles and abstracts of 3927 references, followed by the full texts of 397. 302 studies met our inclusion criteria. Three RCTs with cyclosporine-A (CycA) and 1 RCT with azathioprine showed beneficial results in BS patients with eye involvement. There were several observational studies with Interferon-alpha and monoclonal TNF-alpha antagonists in patients with eye involvement, including those among patients refractory to conventional treatment modalities. Decreases in the frequency of ocular attacks, complete or partial remission and improvement in visual acuity were observed in the majority of patients treated with these agents. As for vascular involvement, retrospective case control studies showed that immunosuppressives (IS) significantly decreased the frequency of recurrences in BS patients with deep vein thrombosis (RR, 95%CI: 0.17, 0.08- 0.35) (Figure 1). A similar effect was not observed with anticoagulants + IS compared with IS alone (RR, 95%CI: 1.5, 0.8 to 2.6). Observational studies showed that cyclophosphamide and high dose glucocorticoids (GCs) decreased mortality in patients with arterial aneurysms. Treatment with IS and GCs decreased postoperative complications in patients who had surgery for arterial aneurysms. Observational studies showed beneficial results with 5-ASA derivatives and azathioprine in the initial management of BS patients with GI involvement. Remission could be obtained with thalidomide and/or monoclonal TNF-alpha antagonists in the majority of patients with refractory GI involvement. Retrospective studies also showed IS decreased postoperative recurrences in patients operated for intestinal perforations or major bleeding (RR, 95%CI: 0.56, 0.33 to 0.95). Observational studies in BS patients with CNS involvement showed IS and GCs improved the outcome. CycA should be avoided in such patients since retrospective case control studies showed that CycA had increased the risk of development of CNS involvement (RR, 95%CI: 12.6, 4.7 to 33.7).

Conclusions. It's sobering to note that the majority of the studies forming the basis for the recommendations related to major organ involvement in the updated EULAR Recommendations for the management of BS have been observational.

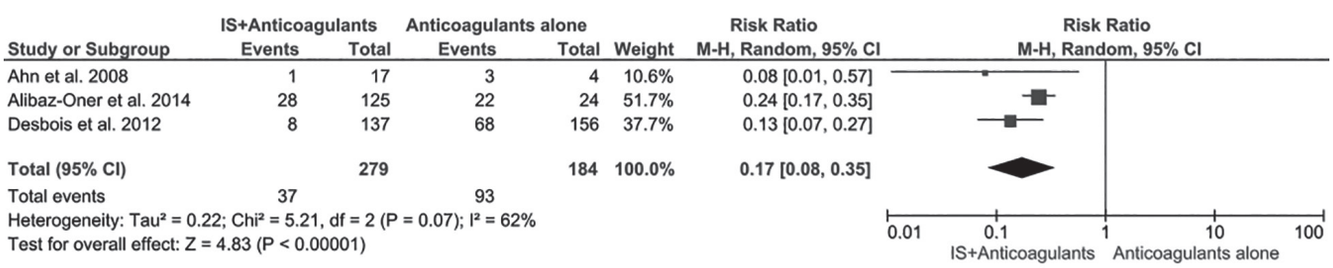

Fig. 1. (P-85)

P86.

MULTIPLE COAGULATION DISORDERS- THROMBOPHILIA AND ANTIPHOSPHOLIPID SYNDROME IN A PATIENT WITH BEHÇET'S DISEASE

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We present the case of a 26 year old, male patient with Behçet's disease, complicated with recurrent intracardiac thrombus, superior caval, left jugular vein and superficial venous thrombosis, as well as bilateral pulmonary embolism, that also associated multiple coagulation disorders: factor V deficiency, anti beta2 microglobulin antibody, and lupus anticoagulant. The debut was with high persistent fever, intense sweating, irritative cought and weight loss for over 6 months, lab results showed intense inflammatory syndrome, leukocytosis and neutrophilia, and the echocardiography revealed the presence of a floating nodular lesion inside the right atrium. Computer tomography imaging showed a right pulmonary artery thrombosis and also a left pulmonary branch thrombosis (6mm), and pulmonary nodular pleural lesions in both pulmonary bases and the patient received antibiotics, antimycotics and anticoagulants. Clinical examination also revealed edema of the anterior cervical region, dysphagia and latero cervical adenopathies so another computer tomography is performed and showed new findings: a thrombus in the left internal jugular vein that extended into the superior vena cava and the right atrium. This thrombotic phenomenon appeared under anticoagulation treatment (INR >3). During hospitalization, the patient develops oral aphthous lesions, and erythematous pustular lesions (1-4 mm diameter) at the puncture sites, sustaining the positive diagnosis of Behçet's Disease.

Treatment with high doses of cortisone, hydroxychloroquine, colchicine, and oral anticoagulants is initiated with good response initially, but one month later with a new flare and right jugular vein thrombosis, atrial thrombosis, bilateral pulmonary thromboembolism developed so the disease was classified as extremely active and immunosuppression with cyclophosphamide was initiated. Evolution was favorable, with normalization of the inflammatory syndrome, no new thrombus formations and fever and cutaneous lesions remission.

The presence of extensive thrombosis required other lab investigations, and those showed the presence of anti beta2 microglobulin antibody, and lupus anticoagulants, and also a factor V deficiency. These results sustained other two important diagnoses: Antiphospholipid syndrome and Thrombophilia.

Searching the literature, the association of the three simultaneous situs: intracardiac, superior cava and jugular venous thrombosis in a patient with Behçet's has only been reported in one case so far, this one being the second. Also, it has been reported that the factor V deficienty is more frequent encountered in patients with Behçet than the general population, more frequent in the thrombosis-group without a proven causal raport. Nevertheless, patients with vascular-Behçet's should be promptly screened for concomitant coagulation disorders.

P87.

PET/CT IMAGING IN PATIENTS WITH VASCULAR BEHÇET DISEASE

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Background. Behçet's disease (BD) is a multisystemic disease characterized by recurrent inflammatory manifestations. BD is classified as variable vessel vasculitis. While inflammatory thrombotic venous findings are dominant in patients with vascular-BD, arterial lesions manifesting as aneurysms and occlusive/stenotic lesions can also be seen. In addition to clinical findings, imaging studies with CT, MRI, and Doppler ultrasonography play an important role in the diagnosis of vascular involvement. PET/CT is a relatively new tool being used in the assessment of large-vessel vasculitis, and there are conflicting reports about using PET/CT in patients with BD. We herein aimed to investigate our records for the role of PET-CT in the diagnosis and follow-up of BD patients with vascular involvement.

Methods. We retrospectively reviewed the charts of BD patients who were investigated with PET/CT for any reason related to disease activity. Patients fulfilling the ISG criteria or with a preliminary diagnosis of BD were included for the analysis. Using a standard form, clinical findings, acute phase response including ESR and CRP, and additional imaging findings, such as CT or MRI, performed within the last 2-week of PET/CT scanning were recorded. Vascular FDG uptake was graded using a 4-point semi-quantitative scale. PET/CT scans were considered positive if vascular FDG uptake was ≥ 2 (equal to or greater than liver).

Results. We identified 12 patients investigated with PET/CT. The mean age of the patients was 43 years, the mean disease duration was 14 years, and 11 (91%) were male. Demographic and clinical findings are summarized in Table 1. Patients underwent PET-CT due to fever of unknown origin (n=6), fatigue with unexplained high acute phase response (n=3), abdominal pain (n=1), or unexplained neck pain (n=1). Five of them fulfilled the ISG criteria, and 4 had positive PET/CT findings due to aortic involvement (n=2) or bronchiolitis obliterans organizing pneumonia (n=2). No FDG uptake was detected in one patient with venous lesions. In remaining 7 patients with incomplete manifestations suggesting BD, vascular involvement documented by FDG uptake in aorta and its branches (n=2), pulmonary arteries (n=2), carotid arteries (n=2) and splenic artery (n=1).

Conclusions. In BD patients with unexplained acute phase response, screening for vascular involvement is important, and PET/CT may contribute to diagnostic process by documenting medium-large size arterial activity. FDG uptake by arterial aneurysms and venous involvement in PET/CT is not clear, and several factors such as the size of the vessels and the thickness of vessel wall may affect FDG uptake. Parenchymal lesions possibly induced by small vessel vasculitis may also be another reason for positive PET/CT findings. Role of PET/CT in the diagnosis of patients with incomplete BD manifestations needs to be investigated further, since other disorders with mucocutaneous and vascular findings may mimic BD and cause diagnostic uncertainty.

P88.

TRANSVERSE MYELITIS – NEURO-BEHÇET'S ONSET

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We are presenting the case of a 51year old female that presents for the first time in the Internal Medicine and Rheumatology Department accusing low back pain with inflammatory characteristic and hypoesthesia of the upper abdominal wall with an insidious onset for 2 weeks.

Physical examination revealed mouth sores, nasal crusts and fetid secretions, painful fibromyalgia trigger points, hypoesthesia of the upper abdominal wall and paresthesias in both upper and lower limbs. Laboratory examination showed anemia (Hb 8.5mg/dl) and leucopenia (2700/ul), minimal inflammatory syndrome (ESR 31mm/h, RCP 6.09 mg/dl). Electromyography examination of the nerves of the upper and lower limbs was within the normal range.

A careful medical history revealed that approximately 8 years before, the patient presented recurrent mouth sores and an episode of inflammatory low back pain that irradiated in the anterior lower right quadrant, considered acute appendicitis, at that time and the appendix was removed surgically, with no clinical benefits. Seriate radiological examinations of the sacroiliac joints showed repeatedly, bilateral osteocondensation.

Two weeks before presentation, based on the low back pain, negative HLAB27, positive anti-Shigella antibodies and MRI osteocondensation of the sacroiliac joints, the patient was diagnosed with undifferentiated Spondylarthritis and received sulfasalazine therapy.

During hospitalization appeared urinal and fecal incontinence, a corset-like progression of hypoesthesia of the abdominal wall, muscular contraction in the lower limbs, intense occipital headache. The neurological examination revealed increased deep tendon reflexes, positive abdominal reflexes, positive Romberg test. The MRI examination of the spinal cord revealed transverse myelitis lesions between C3-T9.

The patient was transferred to a Neurology Department where the patient developed pustular lesions at the puncture sites, interpreted as pathergy. Genetic tests HLAB 51/HLA B35 were performed and they were positive. Taking into consideration the recurrent mouth sores, positive pathergy, positive genetic tests HLA B51 and 35, and the insidious onset, it is considered the diagnosis: Behçet's disease with neurological manifestations – Neuro-Behçet. Corticoids in pulse therapy are started promptly and also, it is considered opportune initiation of immunosuppression with cyclophosphamide pulse therapy 600 mg a month. Clinical evolution was good with total remission of abdominal wall hypoesthesia, mouth sores, and negative pathergy. Parenthesis in the lower limbs and muscular contraction at this level were persistent. After 5 courses of immunosuppression, spinal cord MRI showed no new lesions and sequelae lesions of transverse myelitis in the spinal cord.

P89.

CLINICAL FEATURES AND TREATMENT CHOICES IN BEHÇET'S DISEASE PATIENTS

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Background. Behçet's Disease is a rare type of systemic vasculitis with symptoms of varying severity across almost all systems. While mucocutaneous and articular diseases are the most common manifestations of Behçet's Disease, it is the cardiovascular and neurological manifestations which have the most potential to be serious.
Objectives. To Evaluate the unusual and potentially severe system-organ manifestations in patients diagnosed with Behçet's syndrome, the choices of treatment and their response to therapy.
Methods. We performed a study on a cohort of patients diagnosed with Behçet's Disease under surveillance in one tertiary Rheumatology Centre. All documented cases of Behçet's Disease have been diagnosed according to the International Study Group (ISG) guidelines (1990) and we used WindowsExcel/SPSS20.0
Results. 20patients were included in the study, with ages at the time of the diagnosis between 13 and 60years, most of them, 14 (70%), were under the age of 40 and 6(30%) were over 40 years of age, with a male predominance 60% (12 patients). Clinical classification criteria were met at the time of diagnosis in only 10 cases (50%), 8 male and 2 female patients. The pathergy test was performed for all 20 patients and was positive in 1 3cases. The genetic marker, HLA B51, was tested in 6 cases and in was positive in 5 patients (87%).
Ophthalmological involvement was present in 6cases, posterior uveitis (5cases), one patient presented chorioretinitis. One uncontrolled ophthalmologic involvement in the form of posterior uveitis led to vision loss.
Recurrent venous thrombosis was observed in 6cases while 1case presented thrombosis of the right atrium and inferior vena cava. Pulmonary vasculitis was seen in one case, in relation to a severe cardiovascular involvement. Neuro-Behçet's Disease was diagnosed in 3cases, 2of those patients presented cerebral involvement, sustained by cerebral imaging, while isolated lesions of the spinal cord were seen in 1 case-transverse myelitis, also being the first sign of the disease. The type of manifestations determined the course of treatment, 15patients received colchicine and in 9 patients cortisone was added for bipolar aphthous lesions and skin involvement.
In 10 (50%) cases, Immunosuppression was necessary due to severe systemic involvement. Pulse therapy with cyclophosphamide was initiated in 8cases and 1patient(who associated psoriatic arthritis) received biologic treatment (adalimumab).The cumulative dosage of cyclophosphamide was between 3,6g and 20 grams in 6 to20 pulses once a month. Immunosuppression once induced was maintained using Azathioprine.5 patients presented reactivation of the disease and needed another course of immunosuppressive therapy.
Conclusions. Clinical manifestations of Behçet's Disease are polymorphic and the classification criteria are not always met at the time of the diagnosis. Cardiothrombotic events, pulmonary and neurological involvement have the potential to be the most serious manifestations. Evolution and choices of treatment are mostly dictated by these types of manifestations and the severity of systemic involvement.
Acknowledgement. The first two authors contributed equally.

P90.

THE VESTIBULAR INVOLVEMENT IN BEHÇET'S DISEASE: A CROSS-SECTIONAL STUDY

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Introduction. The cochlear damage was a common symptom of Behçet Disease (B D) esteemed between 9 and 80% of cases. It was ranked second or third after cutaneous and ocular damage according to most studies.
Objective. To determine the frequency of cochlear involvement (CI) during BD and Identify their demographic, clinical and paraclinical particularities.
Patient and methods. We conducted a cross-sectional study including 55 patients with BD fulfilled the diagnostic criteria of the International Study Group on the BD, followed at Medicine Interne Department of the Hospital of Fattouma Bourguiba Monastir. All patients underwent clinical examination and cochleovestibular investigations. We compared the group with CI and its sub-groups to the control group consisted of patients with BD but without CI.
Results. The CI was objectified in 17 cases (31%). It was isolated in 12 cases (70.5%) and associated with vestibular dysfunction in 5 cases (29.4%). Deafness was bilateral and symmetric in 76.5% of cases, light in 70.6% of cases and focusing on high frequencies in 88.2% of cases. THE majority had sensorineural hearing loss (94.1%), classified deafness endocohléaire in 13 cases (81.25%) and retrocochlear in 3 cases (18.75%). Patients with CI were significantly older (p=0.048) with a late onset of BD compared to control patients (p=0.013). However, the duration of BD was longer in the group of sensorineural hearing loss compared to the control group without being statistically significant. The vascular injury was significantly less frequent in patients with CI and particularly those with sensorineural hearing loss. The frequency of the pseudofolliculitis necrotic was significantly higher in the group with sensorineural hearing loss (p=0.034).
Conclusion. CI is prevalent in BD, but remains underestimated. Therefore, all Behçet's patients should be regulary subjected to cochlear investigations to detect inner ear involvement.

P91.

MEAN PLATELET VOUME AS A BIOMARKER REPRESENTING TREATMENT RESPONSE IN BEHÇET'S DISEASE

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Background. Chronic inflammation is known to be associated with increased cardiovascular (CV) event rate in autoimmune diseases. Platelet activation may be a link in the pathophysiology of diseases leading to thrombosis and inflammation. Mean platelet volume (MPV), a platelet index, is an indicator of platelet activation. Several studies have shown increased MPV in Behçet's disease (BD) patients with higher disease activity. But, the others failed to find the relation between clinical activity and MPV in BD. Moreover, it is still not clear whether MPV increases or decreases with BD clinical activities and over the duration of treatment.
Objectives. The current study was conducted to evaluate platelet function by measuring MPV in a selected population of BD subjects. We also aimed to assess associations between MPV and various symptoms. Finally we investigate the changes of MPV in response to treatment.
Methods. We excluded those with established CV diseases or any conventional CV risk factors such as diabetes, hypertension, hyperlipidemia and smoking. Finally 86 BD patients (62 females, age: 49.2±11.3 years) and 160 age- & sex-matched healthy subjects (120 females, age: 49.1±11.6 years) as controls were enrolled for analysis. All patients started to receive treatment according to the spectrum of symptoms (corticosteroid: 65;75.6%, colchicine: 63;73.3%, DMARDs: 28;33.3%). They underwent laboratory evaluation including HLA-B51, MPV, platelet count, ESR, and CRP at baseline, 1 month, 3 months, 6 months and 12 months. Clinical findings such as oral aphthae, genital ulcer, erythema nodosum, acne, enteritis, uveitis, arthritis and vascular events were all recorded.
Results. At baseline, MPV was higher in BD patients as compared to healthy controls (9.053±0.916 vs. 7.988±0.538 fL, p=0.002). Baseline MPV was higher in patients with oral aphthae, skin manifestation, and vascular event (p<0.05). Initiation of treatment resulted in a significant decrease in MPV (6.952±1.700, 7.250±1.676, and 7.321±1.688 fL at 1 month*, 3 months* and 6 months, respectively; *p<0.001).
Conclusions. The result of this study provides additional evidence supporting the previous reports that MPV is higher in active BD. We also found the correlation of MPV with active symptoms and long-term treatment response in BD patients. A increased MPV seems to be a mirror activity of BD.

P92.

EVALUATION OF CHILDREN WITH BEHÇET'S DISEASE FROM REGIONALLY TWO DIFFERENT CENTERS OF A HIGHLY PREVALENT COUNTRY

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Behçet's disease is a complex multisystemic disease with variable vasculitis. The typical triad is oral ulcers, genital ulcers and ocular inflammation. But other clinical manifestations due to vasculitis and thrombosis, involvement of gastrointestinal system, nervous system and musculoskeletal system can be seen variably. Although it is a disease of young adulthood, one-forth of cases are diagnosed during childhood.
Objective. To evaluate the demographic data, clinical features and treatment modalities of children with Behçet's disease and to display the relationship of HLA B51 genotype with mild and severe system involvements of pediatric Behçet's disease patients.
Methods. Two large pediatric rheumatology centers; one from West and one from East of Turkey collected the data of patients with pediatric Behçet's disease retrospectively between January 2010 and May 2016. The children were

enrolled to the study if they fulfilled the Internationational classifications criteria for Behçet's disease. Children diagnosed ≤16 years of age were included to the study. The demographic, clinical, laboratory and medication reports were collected from data sheets.
Results. Fifty-four patients were included; 23 male (42,5%), 31 female (57.5%). Family history of Behçet's disease in a first-degree relative was present in 17 (31.5%) of cases. Of them, 11 (31,4%) were HLA B51 positive. The mean age of the patients was 15,1 (8-21) years. The mean age of onset was 11,1 (5-15,6) years. The mean age at diagnosis was 12,9 (6-16) years. All the patients had oral ulceration. Genital ulcers were present at 34 (62,9 %) patients. Skin findings were present in 35 (64,8 %) patients. Ten patients (18,5%) had uveitis during the course of disease. Seven patients (13 %) had thrombosis. Gastrointestinal involvement was reported in 15 patients (27,8%) and arthralgia/arthritis was present at 29 patients (53,7%). Five patients (9,3%) had neurological signs and symptoms. ANA positivity was seen at 9 (17 %) patients. HLA B51 positivity was detected at 35 (64,8%) children of whom 15 (42,8%) had a mild course of disease while 20 (57,2%) had a severe course with major organ involvement. All the patients were under colchicine treatment, 16 of them had aditional DMARD (azathiopurine or methotrexate) and 2 of them had biologic treatment. Steroids were used by 15 patients. The age that the first symptom ensues was significantly lower in males (9,9 vs 12,8). No relationship with the family history and age of onset of the diseaseand also severity of the disease was shown. The age of onset, the clinical features, treatment modalities reported from two centers from different regions of country were very similar to each other.
Conclusion. This is a retrospective evaluation of a large series of children with Behçet's disease from a country with high prevalance. HLA B51 positivity was assessed according to both demographic data and clinical features. Treatment modalities of two centers were also interpreted

P93.

EVALUATION OF COGNITIVE FUNCTION ELECTROPHYSIOLOGICALLY IN CHILDREN WITH BEHÇET DISEASE

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Introduction. Behçet disease (BD) is a systemic inflammatory condition characterized by recurrent oral aphthae and several systemic manifestations including genital aphthae, skin lesions, ocular, gastrointestinal, neurologic and vascular involvement, and arthritis. Generally, recurrent oral aphthous ulcers are the first symptoms and may begin during early childhood and in 4-26% of the cases full clinical picture is completed before the age of 16. Central nervous system involvement is uncommon but it is one of the most severe manifestation of pediatric BD. Evoked response potentials (ERPs) are commonly used as physiological measures of cognitive function as they are easily measured and noninvasive.
Objectives. This study was conducted to assess the cognitive function of children with the diagnosis of BD without neurological involvement.
Methods. Children included to the study were diagnosed as BD according to ISG criteria. Nine children with BD and 9 controls were enrolled in this study. All participants were good at school performance and examined by pediatric psychiatrist. Patients with any neurological symptoms were excluded from the study. The EEG were recorded from 19 scalp electrode sites. During the EEG recording, all participants were instructed to discriminate auditorially and visually the rare stimuli (target stimuli) from the frequent stimuli (standard stimuli) and to press the button of the mouse immediately following the target stimulus to perform ERPs and P300.
Results. Three of the children were female, 6 were male. the mean age of disease onset was 13.22±2.72. P300 amplitudes obtained from patients and controls were 13.13 mV and 12.2 mV respectively (p=0.21) P300 latencies from patients and controls were 394.8 and 406.1 ms respectively (p=0.03) after visual stimulations and after auditory stimulations amplitudes obtained from patients and controls were 9.467 and 9.681 mV respectively (p=0.69), latencies from patients and controls were 435.868 and 412.211 ms respectively (p=0.0001).
Discussion. Neurologic involvement in BD has a wide spectrum of symptoms consisting of acute type and chronic progressive type. Subclinical neurological involvement without neurological symptoms may also be possible. We aimed to look for the presence or absence of subclinical impairment of cognitive functions in pediatric BD patients. We did not find any difference in visual processing between patients and controls. But in auditory processing, latency of P300 in Behçet patients was longer than controls. We think that this finding may be due to subtle inflammation or vasculitis in different cerebral regions of pediatric BD patients.

P94.

COMPARATIVE STUDY OF CLINICAL CHARACTERISTICS IN TUNISIAN PATIENTS WITH BEHÇET DISEASE WITH OR WITHOUT ASSOCIATED OCULAR INVOLVEMENT

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Introduction. Ocular involvement can affect 30% to 60% of patients with Behçet disease (BD), revealing the disease in up to 20%. The aim of our study was to compare clinical characteristics of Tunisian patients with Behçet Disease (BD) with or without associated ocular involvement.
Methods. We retrospectively reviewed the medical records of BD patients diagnosed according to the International Study Group for Behçet Disease criteria admitted in the Internal Medicine or the ophthalmology Department of Fattouma Bourguiba University Hospital (Monastir, Tunisia) between January 2005 and February 2016. Clinical characteristics of patients with ophthalmic involvement were described then a comparative study between patients with (group 1) and without ocular manifestations (group 2) was performed.
Results. Of 211 patients with BD, 143 were male (67.8 %) and 68 (32.2 %) were female (sex ratio 2.1). The mean age was 31 years (range, 13- 60 years). Familial history of BD was recorded in 7.5% of patients. Oral aphthosis was detected in 98.6 % of patients at presentation, genital ulcers in 83.4%, pseudofolliculitis in 79.1%, and erythema nodosum in 10 %. Neurological and vascular involvement were found in 12.3% and 29.9% of patients, respectively.
Sixty-seven patients (31.8 %) were found to have ocular involvement (group 1) and 144 (68.2 %) had no ocular involvement (group 2). Ocular involvement had revealed the disease in 10.4% of patients. Comparative study between group 1 and group 2 revealed a significant prevalence of males in group 1 (p=0.007). Oral aphthosis at presentation and genital ulcerations were significantly more frequent in group 2 (p=0.031 (exact Fisher test); p<0.001 respectively).
Conclusion. Prevalence of ophthalmic involvement in our cohort seems to be in agreement with previous published data. Males are at higher risk of developing ocular manifestations, needing therefore a closer follow-up.

P95.

MARKERS OF SYSTEMIC INFLAMMATION IN BEHÇET'S SYNDROME

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Introduction. Behçet's syndrome (BS) is a chronic multisystemic disease with both autoimmune and autoinflammatory disease characteristics. Disease manifestations can be generally classified as vascular and non-vascular. These subtypes of BS are suggested to have different pathogenetic mechanisms. While deep vein, sinus vein, and hepatic vein thrombosis and pulmonary artery involvement are major vascular manifestations; mucocutaneous involvement (MCI), arthritis, uveitis, and parenchymal brain involvement (NBS) are typical non-vascular manifestations. Best indicators of systemic inflammation are serum sedimentation (ESR), and CRP levels in clinical practice. The aim of this study was to investigate the serum levels of ESR and CRP in different manifestations of BS.
Methods. A total of 111 patients who met the international diagnostic criteria were included in the study. All patients were during the active disease period. Laboratory values and clinical characteristics of the patients were recorded from medical records by the specialist who followed the patients in long-term. Patients with documented or suspected infections were not included in the study. Continuous variables were compared with using student's t test.
Results. 20 patients had vascular BS, 91 patients had non-vascular BS (42 MCI, 9 arthritis, 23 posterior uveitis, 17 NBS). Mean ESR/CRP±SD in vascular and non-vascular BS were 41.5 ±24.4/42.3±34.8 vs 24.2±16.4/13.4±20.7, p<0.05, Table I). In subgroup analyses, it is found that patients with MCI with erythema nodosum had higher levels of ESR and CRP than patients with MCI without erythema nodosum (p<0.05). Serum ESR and CRP levels of patients with different subtypes of non-vascular BS was shown in Table II.
Discussion. Patients with vascular BS had the highest levels of serum ESR and CRP levels than patients with non-vascular manifestations of BS. Patients with posterior uveitis and parenchymal NBS had low grades of systemic inflammation even they were in active disease period.

Table I. Serum ESR and CRP levels of patients with vascular and non-vascular BS.

	Vascular (n:20)	Non-vascular (n:91)	*p* value
ESR (mean ± SD) mm/h	45.3±2.2	24.2±1.6	0.004
CRP (mean ± SD) mg/L	46.3±3.4	13.4±2.0	0.001

Table II. Serum ESR and CRP levels of patients with different subtypes of non-vascular BS.

	MCI with erythema nodosum (n:15)	MCI without erythema nodosum (n:27)	Arthritis (n:9)	Posterior uveitis (n:23)	NBS (n:17)
ESR (mean ± SD) mm/h	23.1±1.72	21.4±1.19	36.1±2.08	16.5±1.12	25.4±1.93
CRP (mean ± SD) mg/L	29.9±3.03	5.63±5.07	25±2.36	6.91±7.21	10.9±2.51

P96.

NEUTROPHIL TO LYMPHOCYTE RATIO AND MEAN PLATELET VOLUME AND BEHÇET DISEASE ACTIVITY

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Introduction. Elevated neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and mean platelet volume (MPV) have been associated with many inflammatory diseases. Their role in Behçet disease (BD) however remains unclear. The purpose of our study is to evaluate these parameters in Tunisian patients with BD and to assess their association with disease activity.
Methods. Retrospective study including 35 patients with BD with ocular or cardiovascular involvement. BD was diagnosed based on ISGD criteria. C reactive protein (CRP), MPV, NLR, PLR, White blood cell (WBC), and neutrophils ratio were recorded at onset of the disease (acute active disease) and during follow-up after resolution of acute disease (inactive disease).
Results. Mean age of our patients was 32 years. M/F sex ratio was 4. Ophthalmic involvement was observed in 31.4% of patients, and cardiovascular involvement in 68.6%. CRP, neutrophils, MPV and NLR were significantly higher in active disease (p=0.001, p=0.003, p<0.001 and p=0.025 respectively). No significant difference was found for WBC or PLR between active and inactive disease (p=0.155 and 0.977, respectively).
Conclusion. In Tunisian patients with ocular or cardiovascular BD, high levels of CRP, PNN, MPV and NLR were found to be markers for disease activity.

P97.

PSEUDOTUMORAL NEURO-BEHÇET: 4 CASES

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Introduction. Behçet disease (BD) is a reccurent systemic vasculitis that is diagnosed on the basis of clinical criteria. Neurological involvement occurs in 10 to 28% of patients with Behçet's disease. The pseudotumoral presentation is an atypical form of neuro behçet. We report 4 cases of pseudotumoral neuro behçet.
Results. There were 3 males et 1 female. The average age was 36 years [25-51]. The diagnosis of Behçet disease was prior to the neurological manifestations in 3 cases. The pseudotumoral neuro Behçet revealed one case. The diagnosis of Behçet disease was based on clinical manifestations: oral aphtosis (n=4), genital aphtosis (n=3), pseudofolliculitis (n=3), uveitis (n=2), retinal vasculitis (n=1) and vein thrombosis (n=2). None of them had arterial thrombosis, anerysme nor Gastrointestinal manifestations. Pathergic test was positive in 3 cases. The neurological manifstations were: head ache (n=3), piriformis syndrome (n=3), irratability and change behaviour (n=1), seizure (n=1) and meningitis (n=1). The Brain magnetic resonance imaging (MRI) revealed pseudotumoral lesion in basal ganglia (n=3), cerebral pedoncule (n=2), periventricule (n=2) and thalamus (n=1). One had a cerebral veinus thrombosis. All the patients has pulses of methylprednisolone (1g per day 3 days) and maintained with oral prednisone (1mg per kg per day). All the patients had monthly pulses of cyclophosphamide during 6 months than azathioprine. The patient who had seizure received phenobarbital. Neurological manifestations had diseaperred under steroïds and immunosuppressive therapy. No relapse was observed after a medium follow up of 8,5 years [2-16].
Conclusion. The diagnosis of BD can be difficult if the pseudotumoral neuroBehçet reveales the disease. A pseudotumor in BD should be considered in the differential diagnosis of brain masses. A good response after treatment with glucocorticoids confirms the diagnosis. Biopsy may sometimes be necessary if there were no other clinical signs of BD.

P98.

THE SIGNIFICANCE OF NONORAL–APHTHOUS BEGINNING AND PREAPHTHOUS PHASE OF BEHÇET DISEASE ON THE DIAGNOSIS AND PROGNOSIS: A COMPARATIVE STUDY WITH THE WORLD LITERATURE

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Background. We began to be interested in and to investigate the prevalance and the significance of non-oral aphthous beginning (NOAB) in Behçet's disease (BD) since 1980. We reported our first results on the evaluation of this subject at 4th ICBD London in 1985 and expanded this research further.
Aim. Our objective was to compare and try to validate our results with the literature.
Methods. Our large cohort is composed of 645 cases observed and investigated at Istanbul Fac.Med, Dept.Int.Med, Div. Rheumatology and diagnosed according to our diagnostic criteria. We reevaluated the prevalence of NOAB cases and their correlation with demographic and clinical parameters. Major (vital) organ involvement (VOI) was particularly noted. Review of the literature was carried out by the books, Conference proceedings, Index Medicus, Medline, Internet and questionnaire sent to some of the experts.
Results. Particularly males with early age of onset (<25 yrs), present age <40, particularly patients belonging to NOAB group developed more major (vital) organ involvement. In our cohort the prevalance of NOAB was found to be 28.7 % .In literature review this ranged from 2 to 65 %. We could not find any analysis about demographic and clinical features in these cases.
Conclusions. This study revalidated our previous studies and revealed that the evaluation of demographic and clinical features both in Oral Aphthous Beginning and NOAB groups of BD help for early diagnosis and to predict the prognosis. Since we could not ascertain any data on this subject in our literature review we extend our hope for the near future.

References

1. KONICE M, DILŞEN N, ARAL O: *In*: LEHNER T, BARNES CG, Eds. Recent Advances *In* Behçet's Disease. *Royal Soc Med Sciences* London 1986; 199-203.
2. DILSEN N: *In*: BANG D, LEE E-S, LEE S, Eds, Behçet's Disease; Seoul;101-104,2000
3. DILSEN N: *In*: ZOUBULIS CC, Ed. Adamantiades-Behçet's Disease. Kluwer Academic / Plenum Publishers New York; 73-76, 2003.

P99.

A SYSTEMATIC LITERATURE REVIEW ON THE TREATMENT OF SKIN, MUCOSA AND JOINT INVOLVEMENT OF BEHÇET'S SYNDROME INFORMING THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF BEHÇET'S SYNDROME

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Objective. The aim of this systematic literature review was to inform the task force for updating the European League Against Rheumatism recommendations for the management of Behçet's Syndrome (BS), about the evidence for treatment of skin, mucosa and joint involvement of BS.
Methods. A systematic literature search, data extraction and statistical analyses according to pre-specified and protocolised eligibility criteria were performed using the GRADE approach. The protocol for the review was registered and is available at PROSPERO (CRD42015027033). The Cochrane Library, including the Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessments (HTA), MEDLINE (from

1950), EMBASE (from 1980) and International Pharmaceutical Abstracts Database (IPAD) were systematically searched. Randomised controlled trials (RCT), non-randomised controlled clinical trials and open label trials (OLT) on BS comparing an active intervention (alone or in combination) with any control or placebo were eligible. If controlled trials were not available for answering a specific research question, uncontrolled evidence from cohort studies or case series involving ≥ 5 patients were considered. The quality of evidence was assessed by using the GRADE approach. Risk ratios were calculated for the binary outcomes whereas for the continuous outcomes we calculated the standardized mean difference (SMD).
Results. Among the 3927 references that we have screened, 22 studies satisfied the inclusion criteria for mucocutaneous involvement and 15 studies for joint involvement. Seventeen of these studies were RCTs assessing mucocutaneous and/or joint involvement. RCTs with colchicine, azathioprine, interferon-alpha, thalidomide, etanercept and apremilast showed different levels of beneficial results on different types of skin and mucosa lesions and arthritis. Differences in the outcome measures that were used across the included studies made it difficult to compare the results. These agents were generally well tolerated with few adverse events causing withdrawal from the study in BS patients.
Conclusions. It was gratifying to see that randomised trials formed the majority (17/22, 77%) of the sources forming the basis for the recommendations related to skin mucosa and joint involvement in the updated EULAR recommendations for the management of BS.

P100.

BRAIN ^{18}F-FDG PET/CT ABNORMALITIES IN NEURO-BEHÇET'S DISEASE

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Introduction. Behçet's Disease (BD) is a chronic inflammatory disease characterized mainly by recurrent oral and genital ulcers and inflammatory eye disease. Neurological involvement (Neuro-Behçet's disease, NBD) is a relatively uncommon but potentially life-threatening manifestation (1). The gold-standard imaging modality for NBD is Magnetic Resonance Imaging (MRI) that is able to demonstrate both parenchymal and non-parenchymal disease (1). However a number of patients presents with neurological complaints (headache, cognitive impairment or neuropsychiatric manifestations) despite a normal MRI (2, 3), therefore other imaging techniques could be useful in the evaluation of such patients. Aim of this preliminary study was to investigate the differences in brain glucose consumption as detectable by means of 2-deoxy-2-(^{18}F) fluoro-D-glucose (^{18}F FDG) Positron Emission Tomography/Computed Tomography (PET/CT) in a selected population with NBD.
Methods. Six subjects (1 males and 5 females, mean age 42 (±12) years old, Table 1) with BD classified according to the International Criteria for Behçet's Disease (ICBD) (4) were enrolled in this study. All patients had NBD diagnosed by clinical evaluation (including neurophysiological studies when appropriate) and MRI findings. Seventeen healthy subjects (3 males and 14 females, mean age 40 (±12) years old) were enrolled as control group (CG). All the subjects underwent a PET/CT at rest in the same experimental conditions after the i.v. injection of 185-210 Megabequerels of ^{18}F FDG. Differences in brain glucose consumption were evaluated by means of statistical parametric mapping (SPM8) using age, sex and scholarship as covariates. The voxel-based analyses were performed using a two sample t-test.
Results. As compared to CG, NBD showed a significant reduction of brain glucose consumption (Pfwe corr. <0.001) in left and right cingulate gyrus [Brodmann Area (BA) 24, BA 23 and BA36], left precuneus (BA7) and in left temporal lobe (BA 38). At a sub-cortical level, we found a significant reduction of brain glucose consumption (Pfwe corr. < 0.01) in right and left brainstem that involved mainly the midbrain. We did not find any area of increased glucose consumption in NB as compared to CG.
Conclusions. Our preliminary results demonstrate a cortical and brainstem dysfunction in NBD patients. These abnormalities are topographically independent from lesional areas demonstrated by MRI.

References

1. KALRA S *et al*.: Diagnosis and management of Neuro-Behçet's disease: international consensus recommendations. *J Neurol* 2014; 261(9): 1662-76.
2. TALARICO R *et al*.: Epidemiology and management of neuropsychiatric disorders in Behçet's syndrome. *CNS Drugs* 2015; 29(3): 189-96.
3. TALARICO R *et al*.: Behçet's disease: features of neurological involvement in a dedicated centre in Italy. *Clin Exp Rheumatol* 2012; 30 (3 Suppl. 72): S69-72.
4. THE INTERNATIONAL CRITERIA FOR BEHÇET'S DISEASE (ICBD): A collaborative study of 27 countries on the sensitivity and specificity of the new criteria. *J Eur Acad Dermatol Venereol* 2014; 28(3): 338-47.

P101.

PREVALENCE OF TYPE 2 DIABETES IN BEHÇET'S DISEASE: A RETROSPECTIVE STUDY

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Introduction. Behçet's Disease (BD) is a chronic autoimmune disease characterized mainly by mucocutaneous, ocular, neurological and vascular manifestations. Despite the high prevalence of vascular involvement, current evidences suggest that atherogenesis is not significantly affected by the disease (1) and thus the risk of cardiovascular events is mainly attributable to the inflammatory phenotype. However, controversial evidences suggest an increased prevalence of metabolic syndrome (2) despite a normal insulin sensitivity (3). Aim of the present study was to investigate the prevalence of type 2 diabetes (T2DM) in an Italian BD population.
Methods. We retrospectively reviewed the clinical records of all BD patients (N = 99) admitted to our Inpatient Clinic during a 10-years period (January 2006 – December 2015) in order to evaluate the prevalence of T2DM and impaired fasting glucose (IFG). The presence of T2DM was defined according to the following criteria: 1) a past diagnosis of T2DM; 2) taking antidiabetic medications at the time of observation; 3) fasting plasma glucose (FPG) ≥126 mg/dL in at least 2 occasions. IFG was defined according to ADA criteria (4) if FPG ≥100 mg/dL and <126 mg/dL. Demographic (age, sex) and disease characteristics (disease duration, age at onset, mucocutaneous / neurological / vascular / ocular involvement, HLA-B51 status, current treatment) and laboratory data (glucose, ESR, CRP) were recorded, and disease severity was quantified with the score proposed by Krause *et al*. (5).
Results. General characteristics of the study population are reported in Table I. The overall prevalence of T2DM and IFG was 8.1% and 9.2% respectively. In a logistic regression analysis only age (OR: 1.08, 95% CI 1.02 – 1.15, p=0.01) and age at BD onset (OR: 1.08, 95% CI 1.02 – 1.14, p=0.007) were associated with an increased risk of being diagnosed with T2DM. No significant association was found for disease characteristics, medication used or ESR/CRP values.
Conclusions. According to our data the prevalence of T2DM in BD is comparable to that observed in Italian general population. T2DM was associated with age at BD onset, suggesting that prolonged corticosteroids exposure, more than current treatment, could influence the risk of T2DM in BD patients.

References

1. SEYAHI E *et al*.: Atherosclerosis in Behçet's Syndrome. *Semin Arthritis Rheum* 2008; 38 (1): 1-12.
2. YALCIN B *et al*.: Prevalence of metabolic syndrome in Behçet disease: a case-control study in Turkey. *Am J Clin Dermatol* 2013; 14 (5): 421-5.
3. SAHIN E *et al*.: Adiponectin levels, insulin resistance and their relationship with serum levels of inflammatory cytokines in patients with Behçet's disease. *J Eur Acad Dermatol Venereol* 2012; 26 (12): 1498-502.
4. STANDARDS OF MEDICAL CARE IN DIABETES-2016: Summary of Revisions. *Diabetes Care* 2016; 39 (Suppl 1): S4-5.
5. KRAUSE I, MOLAD Y ,WEINBERGER A: Association of HLA-B5 with Clinical Expression and Severity of Behçet's Disease in Israel. J Clin Rheumatol, 1999. 5(3): p. 137-40.

P102.

FAMILIAL BEHÇET'S DISEASE: A REPORT OF 2 CASES FROM AN ITALIAN BEHÇET FAMILY

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Introduction. Behçet's disease (BD) is a systemic vasculitic disease, characterized mainly by recurrent oral and genital ulcerations, ocular and cutaneous lesions, vascular disease, arthritis and systemic manifestations of an unknown etiology. BD is in the majority of cases sporadic, but a familial aggregation has been reported.
We present a case of a family in which two of the members, father and daughter had BD. Human leukocyte antigen (HLA) studies were also performed for these patients to support genetic background of BD.
Case report. a 24-year-old woman was admitted to the Rheumatology outpatient clinic of the University of Foggia with a history of arthritis of the hands and the feet she suffered from the age of 4, recurrent oral and genital aphthous ulcerations and papulopustular lesions she suffered from the age of 11. In addition she reported blurring of vision when she was 16, diagnosed as uveitis. She reported also diarrhea and abdominal pain six months before her admittance to our clinic. HLA B51 was not found.
Her father, a 49 year-old man, was diagnosed as BD at the same time. He had a history of arthritis, oral aphthous ulcerations, pseudofolliculitis of the lower limbs and the back since he was 30. Eye involvement with episodes of bilateral anterior uveitis, peripheral nervous system involvement with polyneuropathy of the lower limbs and aphthous ulcers of the lower limbs appeared later. He did not experienced genital ulcers. HLA B51 was found.
Diagnosis of BD was made according to the diagnostic criteria developed by the International Criteria for Behçet's Disease.
Discussion. patients with familial BD have an onset of disease almost 10 years earlier, on average, than sporadic cases. Association with human leukocyte antigen (HLA)-B51 is known as the strongest genetic susceptibility factor for BD. In this familial case of BD father was B51 positive while daughter was not B51 positive. There may be a multifactorial etiology and other genetic pattern in addition to HLA B51.

P123.

A CASE OF BEHÇET'S DISEASE PRESENTING WITH DEEP VENOUS THROMBOSIS

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Background. In 2008 the European League Against Rheumatism (EULAR) developed evidence-base recommendations for the management of Behçet's Disease (BD). The recommendations related to the eye, skin, mucosa and joints are mainly evidence based, but the recommendations on vascular disease, neurological and gastrointestinal involvement are based largely on expert opinion.
Introduction. There is no evidence to guide the management of major vessel disease in BD. For the management of acute deep vein thrombosis in BD, immunosuppressive agents such as corticosteroids, azathioprine, cyclophosphamide or ciclosporine A are recommended.
Case report. A 47-year-old-man affected by BD presented recurrent deep venous thrombosis from five years. He had a ten years history of recurrent oral and genital ulcers, posterior uveitis and HLA-B51 positive. After a therapeutic attempt with cyclosporine A and methylprednisolone 8 mg per day, the ophthalmic course worsened. A progressive improvement was observed after azathioprine administration associated with low doses of oral prednisolone, but after one year, the patient developed the first event of deep venous thrombosis, treated with heparin. The patient was tapered off the heparin and was managed on a low steroid dose and azathioprine, but in one year he had three events of deep venous thrombosis. After anticoagulant oral therapy in association with azathioprine the patient has not developed thrombotic events.
Conclusion. A combined use of azathioprine and oral anticoagulant therapy resulted in a long-term suppression of major vessel disease without any safety concern.

Treatment

P103.

PERSISTENT HYPERPROLACTINEMIA DURING THERAPY WITH INTERFERON-A-2A IN A PATIENT WITH SYSTEMIC ADAMANTIADES-BEHÇET'S DISEASE

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Adamantiades-Behçet's disease is an immune-mediated vasculitis with relapsing course. It is characterised by the classic clinical trias of oral aphthous ulcers, genital ulcers and uveitis. We report on a 37-year-old woman suffering from Adamantiades-Behçet disease with recurrent uveitis, oral ulcers, genital ulcers, arthralgias, erythema nodosum and folliculitis. During a treatment with cyclosporin the patient developed hypertrichosis, whereas azathioprin and prednisolone did not improve the ocular symptoms. Long term interferon-α-2a (IFNα-2a) led to a reduction of the clinical manifestations except for occasional occurrence of oral ulcers. Two weeks after initiation of IFNα-2a, the patient complained about fatigue and mood fluctuations, so that after diagnosing an interferon-induced depression, treatment with citalopram 20 mg/d, lorazepam 4×0.5 mg/d and promethazine 20 mg/d was initiated. Moreover, after one-year treatment with IFNα-2a, the patient developed mastodynia and hyperprolactinemia of unknown etiology. A magnetic resonance imaging of sella turcica excluded repeatedly a prolactinoma and the thyroid values were normal. The patient received a therapy with bromocriptine 2.5 mg/d. A chronic hyperprolactinemia cannot only be induced by prolactinoma, but also by hypothyroidism, chronic renal insufficiency, stress, pregnancy and several drugs. In our patient, it could be assumed that antidepressants and neuroleptics have led to increased circulating prolactin levels, although the latter insisted after discontinuation of the antidepressive therapy. On the other hand, IFNα-2a therapy could be the cause of the hyperprolactinemia. Mastodynia and hyperprolactinemia have not yet been described as potential side effects of IFNα-2a. The influence of interferon on the prolactin secretion is controversial: According to Hofland *et al*. IFNα-2a inhibits the secretion of prolactin in cultured human pituitary adenomas. In contrast, Yamaguchi *et al*. showed that the interferon family stimulates the secretion of prolactin *in vitro*. Furthermore, patients with multiple sclerosis have been reported to develop hyperprolactinemia during IFNβ-therapy. IFN-α und -β target the same receptor and they have therapeutically similar, but not identical effects and side effects. The above observations could support, but are not sufficient to confirm a correlation between a symptomatic hyperprolactinemia and a treatment with IFNα-2a.

P104.

COMPLETE RESOLUTION OF PULMONARY ARTERY ANEURYSM IN A PATIENT WITH BEHÇET'S DISEASE WITH INFLIXIMAB

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We present a case of BD which treatment with infliximab induced complete resolution of pulmonary artery aneurysm (PAA).
A 24-year-old male with known Behçet's disease (BD) was admitted to our hospital because of life threatening hemoptysis. Recurring painful oral ulcerations, erythema nodosum, unilateral panophthalmitis, and positive pathergy led to a diagnosis of BD 14 months earlier. Treatment with prednisolone 60 mg/day and azathioprine 150 mg/d was started. He was followed in the BD clinic of our hospital and prednisolone was tapered gradually to 10 mg/d and his disease was in remission. However, he developed chest pain and mild hemoptysis one month before admission and finally massive hemoptysis. Chest radiography showed rounded left para hilar opacity. Computed tomographic angiography (CTA) showed an aneurysm (PAA) with the size of 38×34 mm, artery wall thickness and thrombosis in the lumen of left pulmonary artery. He refused conventional treatment with cyclophosphamide. Therefore, infliximab (IFX) 3 mg/kg, prednisolone 1 mg/kg/d and isoniazid 300 mg/d (because of positive PPD test) were started. The clinical response was impressive. The symptoms resolved within a few days. IFX was continued as a protocol (0, 2, 6 weeks) and then every 8 weeks. Prednisolone was gradually tapered over 12 weeks to 5 mg/day. In the follow-up, the patient had no cough, hemoptysis or dyspnea. After 3 months, another CTA was done which showed decreasing of the arterial wall thickness and thrombosis size. Finally, after 6 months of treatment with IFX, the third CTA showed a complete resolution of aneurysm. IFX was continued over a period of 10 months. In the last visit, the patient was in a good condition without cough, hemoptysis, dyspnea, oral aphthous ulcer, and ophthalmologic problem.

P105.

PLASMA CYTOKINES AS BIOMARKERS FOR CLINICAL RESPONSE DURING NINE MONTHS OF INTRAVENOUS IMMUNOGLOBULINS THERAPY IN A BEHÇET DISEASE PATIENT UNSUITABLE FOR IMMUNOSUPPRESSION

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The etiopathogenesis of Behçet's Disease (BD) is still unknown, but current treatments aim at dampening the immune system by a combination of corticosteroids, immunosuppressants, and antibodies against TNF-α. However, an increasing number of patients become refractory to the most used biologics and new needs have emerged for alternative therapies. Besides the recognized use of IntraVenous ImmunoGlobulins (IVIG) for immunodeficiencies, they are an effective cure for several autoimmune pathologies affecting the skin and the neuromuscular system. We first used plasma cytokines to monitor the clinical response during 9 months of IVIG therapy in a 39-year-old Italian female BD patient unsuitable for immunosuppression due severe herpetic reactivations in the trigeminal ganglion. She presented with oral and genital aphtosis, pseudofolliculitis, papulopustular nodules, episcleritis, severe arthralgia (back, shoulders and hands), and abdominal pain (diarrhea/constipation). After a failed therapy with steroids, she was treated with cycles of IVIG (0.3 mg/kg) fortnightly for 5 times, then every 3 weeks for 9 months. Before each infusion, an aliquot of whole blood was collected in EDTA to assess the plasma concentrations of IL-1b, IL-2, IL-6, IL-10, CXCL8, IFN-γ and TNF-α by ELISA (normal values: IL-1b <5pg/ml; IL-2 <31pg/ml; IL-6 <10pg/ml; IL-10 <15pg/ml; CXCL8 <31pg/ml; TNF-α <15pg/ml; IFN-γ <15pg/ml). Before treatment, only CXCL8 levels were high (254 pg/ml), and she presented with oral aphtosis, arthralgia, finger swelling in the morning, joint stiffness, pseudofolliculitis on legs, asthenia, arm paresthesia, headaches, abdominal pain (Fig). After 15 days from the first IVIG infusion, her clinical signs started to improve and CXCL8 levels rapidly decreased (7 pg/ml). As of today, the patient returned to her normal daily activities. Two noteworthy episodes occured: a dental gangrene increased TNF-α level (37 pg/ml) without affecting BD symptoms, while an emotional trauma (bereavement) reactivated articular, mucocutaneous and gastrointestinal symptoms, asthenia, arm paresthesia, and headaches concurrently with an increase of CXCL8 (226 pg/ml) and TNF-α (47 pg/ml) levels. The IVIG infusion subsequent to the grief lowered CXCL8 and TNF-α levels and symptoms improved in 15 days. Several studies have correlated CXCL8 levels with severity and duration of BD symptoms, including the number of involved organs. Moreover, high levels of CXCL8 and IL-6 in the cerebrospinal fluid of BD patients are more suggestive of a Central Nervous System (CNS) involvement than TNF-α. In our patient, the plasma levels of CXCL8 confirmed to be a good marker for BD activity. Although we cannot identify the molecular pathway linking the activity of the Central Nervous System to the increase of CXCL8 levels, the recent discovery of lymphatic vessels lining the dural sinuses and directly connecting the nervous and immune systems strongly supports a tight molecular exchange between these two systems. We think that IVIG therapy deserves to be considered for further investigations, especially in BD patients with CNS involvement.

P106.

SYSTEMATIC REVIEW OF THE LITERATURE FOR THE USE OF INTRAVENOUS IMMUNOGLOBULINS IN BEHÇET DISEASE

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We reviewed the use of Intravenous Immunoglobulins (IVIG) in Behçet's Disease (BD) by a systematic literature search in the major biomedical databases. We performed a comprehensive search of MEDLINE, EMBASE, and WEB of SCIENCE retrieving clinical trials, clinical studies, case series, and case reports reporting the use of IVIG in BD patients. We searched all English articles published from inception to January 2016. An expert librarian (V.S.) performed the search using the following terms: "Immunoglobulins, Intravenous"[Mesh] AND "Behçet Syndrome"[Mesh] in MEDLINE and EMBASE databases, "Behçet Disease" AND "Intravenous Immunoglobulins" in WEB OF SCIENCE database. Two authors (C.C. and A.D.S.) screened the articles and excluded the irrelevant ones. The pertinent data were extracted by two authors (C.C. and A.D.S.) and checked by a third one (L.S.). We found three reports describing six BD patients who underwent IVIG therapy due to comorbidities or refractoriness to previously failed therapies. Four patients had refractory ocular BD, one had gastrointestinal BD, and one had BD combined with common variable immunodeficiency. All patients received at least the first-line therapy with systemic corticosteroids without clinical improvement. IVIG allowed remission of symptoms in all patients (varying from ocular to gastrointestinal signs) in a period ranging from 7 days to 12 months. Two patients experienced a flare up that was successfully treated with additional IVIG or steroids and, after 12 months, the patients were in a quite phase. No side effects were observed. Nava and colleagues have recently highlighted the lack of multicenter well-designed Randomized Clinical Trials in order to address the efficacy of the current use of several drugs with life threatening side effects in Neuro-BD patients. Due to the limited side-effects of IVIG and to the effecacy observed in replacing failed classic therapy (although in few cases), we think that IVIG therapy deserves to be considered for further investigations especially in Neuro-BD patients.

P107.

OUTCOMES OF BIOLOGIC TREATMENT REGIMENS FOR SEVERE BEHÇET'S DISEASE: CURRENT EXPERIENCE FROM A SINGLE ACADEMIC CENTER

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Background. During the last 15 years TNF blockade has been established as an important therapeutic advancement for Behçet's patients with severe and resistant, or intolerant, to standard immunosuppressive regimens disease. We report our current experience on the outcomes of biologic treatment regimens in such patients.
Methods. This retrospective flow-chart review included all patients followed up at least once yearly since 2007; that year anti-TNF agents became fully reimbursed for patients fulfilling the recommended criteria (Rheumatology 2007;46:736-41). Information on clinical manifestations, treatment and disease course was recorded.
Results. A total of 57 patients (aged 39±12 years, with disease duration 11±8 years, 63% men,) was studied. Biologic treatment has been given in 28/57 patients (49%), however, the proportion of patients at such need is probably lower because those with milder disease forms are not being regularly followed-up in our center. The first agent prescribed was infliximab (Remicade, n=24; Inflectra, n=2) or adalimumab (n=2). Anti-TNF treatment was initiated for refractory ocular (n=20), mucosa/skin (n=4), central nervous system (CNS) (n=2), or gastrointestinal involvement (n=2). Azathioprine was always co-administered, unless not tolerated (n=3). Currently, 6/28 patients are on continuous, uninterrupted anti-TNF treatment for 1 up to 13 years, for either ocular (1 and 4 patients with partial and complete responses, respectively) or mucosa/skin disease (partial response). The remaining 22/28 patients discontinued anti-TNF treatment after achieving remission (n=20) or due to pregnancy (n=2). However, anti-TNF treatment was resumed in 15/22 patients who relapsed within 6 to 18 months after discontinuation (9, 3, 2, 1, for ocular, mucosa/skin, CNS, gastrointestinal involvement, respectively). Anti-TNF treatment either continues to date in 9/15 (3 were switched to tocilizumab, of whom 1 did not respond and was successfully switched back to infliximab), or discontinued successfully in 4/15, whereas the remaining 2/15 patients lost their vision either due to discontinuation of infliximab for logistic reasons, or due to refractory disease to anti-TNF, anakinra, tocilizumab and interferon. Overall 11 patients (50%) of those who discontinued anti-TNF treatment after achieving remission remain severe disease-free (ocular, n=9; CNS, n=1; mucosa/skin, n=1) for a period of 5.2±3.1 years (range 3 to 12 years). No serious safety issues were observed.
Conclusion. The efficacy of biologic agents for severe forms of Behçet's disease in our center is compatible with the published experience. Importantly, our data suggest that long term remission after discontinuation of anti-TNF agents is feasible in a good proportion of these patients.

P108.

THE EFFICACY OF TACROLIMUS AGAINST INTESTINAL BEHÇET'S DISEASE

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Tacrolimus (TAC) is one of the famous immunosuppressive agents. The name of this agent stands for Tsukuba mACROLide IMmUnoSuppressant, and Tsukuba is a region in about 50 kilometers north of Tokyo, Japan. This agent is using against refractions of post-transplantation, grafts versus host disease due to the born marrow transplantation, some rheumatic diseases (rheumatoid arthritis, systemic lupus erythematosus, and polymyositis/dermatomyositis), ulcerativecolitis, and atopic dermatitis. Here, we succeeded in the treatment for intestinal Behçet's disease (BD) using TAC. This agent may be useful to treat mucosal lesion of intestinal BD.

Case. A 39 year-old male, who had the history of recurrent oral aphtous ulcer (ROA) from childhood, recurrent arthritis without distraction on his right ankle, recurrent erythema nodosum (EN) on his legs since his 24 year-old, with the septal panniculitis from skin biopsy, and he had genital ulcer (GU) in his childhood, though it was only once. In November 2005, he fulfilled the BD criteria (ROA, EN, arthritis, and GU) in our clinic (1,2). Thus, the colchicine was started and it controlled his arthritis. In July 2007, he was admitted to another hospital with his arthritis on right ankle by MRI T2WI view and laboratory data: WBC 9,440/μL (neutrocyte 79.1%, lymphocyte 14.2%), C-reactive protein (CRP) 60.6 mg/L. He was then suspected something bacterial infection, and Cefazolin 3 g/day was started; however, his inflammation did not improve. Thus, according to the therapy for BD, colchicines (1 mg/day) and sulphasalazine (SSZ) (1 g/day) were started, and his arthritis and vasculitis of skin on his legs improved, and he could be discharged. In January 2007, he was admitted to our hospital to examine his colon with colonoscopy. We could see multiple ulcers around ileocecul valve; thus, he was diagnosed with having intestinal BD and he was treated with predonisolon (PSL) (30 mg/day) and 5-aminosalicylic acid (2,250 mg/day, switched from SSZ). His condition was controlled and his CRP level kept less than 1.0 mg/L with taking PSL 10 mg/day. The PSL dose was tapered to 50 mg/L in March 2008. The EN was recurred. Then the dose of PSL was increased to 30 mg/day. His EN improved. The dose of PSL was tapered, and cyclosporine 150 mg/day was added. In July 2015, he caught a common cold. Water diarrhea and merena occurred in September. His abdominal pain was worsening with fever. He was admitted to our hospital in September 2015, the abdominal CT showed colon wall was thickened; he was diagnosed as recurring intestinal BD. After colonoscopy in October TAC 2.5 mg/day was started. Then, his abdominal condition improved and his findings of colonoscpy showed mucosal hearing; thus, the dose of PSL could be tapered and his CRP level decreased. In conclusion, TAC may be useful to treat mucosal lesion of intestinal BD.

References

1. MIZUSHIMA Y: Recent research into Behçet's disease in Japan. *International Journal of Tissue Reactions* 1988; 10: 59-65.
2. INTERNATIONAL TEAM FOR THE REVISION OF THE INTERNATIONAL CRITERIA FOR BEHÇET'S DISEASE: Revision of the International Criteria for Behçet's Disease (ICBD). *Clin Exp Rheumatol* 2006; 24: S14-5.

P109.

BENZATHINE PENICILLIN IN TREATMENT OF ORAL AND GENITAL ULCERS IN BEHÇET'S DISEASE

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Purpose. To confirm the value of Benzathine Penicillin (BP) in the treatment of oral and genital ulcers of Behçet's Disease (BD) and to recommend its use by doctors around the world.

Materials and Methods. 12 patients with BD were included in this Study (9 patients fulfilled all criterias for BD). Benzathine Penicillin (BP) 2.4 million units, every 2ou 3 weeks were used in oral, genital or cutaneous ulcers which are not improved with colchicine or is required forte dosage of corticosteroids. Patients needed 3 or 4 intramuscular injections .It was used in numerous or Giant ulcers. Patients had negative serology of Syphilis before treatment by BP.

Results. 7 males and 5 females. The onset of the disease is 3 months for the youngest and 52 for the oldest. There were arthritis in 9 patients, ocular lesions were observed in 5 cases and fever in 8 patients. BP was used in 8 cases of oral ulcers, Genital ulcers (4 cases), oral and genital ulcers (2 cases) and cutaneous aphtosis in 2 patients .In all these patients, recovery from oral, genital and cutaneous ulcers was achieved. BP was administrated a second time with success, in 8 patients who have developed ulcers (numerous or Giant), after several months or years of recovery.

Discussion. In previous meeting, we presented a few cases treated successfully. In this study, we confirm that the treatment with BP is rather easy in outpatients, it is efficient, it has a low cost and have few side effects.

Conclusion. In this Study, we confirm the recovery from oral, Genital and cutaneous ulcers in these 12 patients with Benzathin Penicillin .We recommend using more frequently BP, worldwide in BD with ulcers which are not improved with colchicine , or is required high dose of corticosteroids causing many side effects. Is Behçet's Disease an infectious disease and streptococcus has the role on the pathogenesis of BD?

P110.

ANTI-TNF-α THERAPY IN PATIENTS WITH BEHÇET'S UVEITIS

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Purpose. Behçet's disease (BD) is a systemic inflammatory disorder of unknown etiology. It frequently involves the ocular system. The aim of this study is to demonstrate the importance and efficiency of early treatment with anti-tumor-necrosis factor-alpha antibodies (anti-TNFα) include Infliximab in severe ocular manifestation refractory to immunosuppressants and corticosteroids, in Behçet's disease.

Methods. retrospective study in internal medicine department over 4 years and including 7 patients with severe or/and refractory ocular Behçet's disease which anti-TNFα" Infliximab" was added. The diagnosis was performed by the International Study Group for Behçet's Disease and/or the International Criteria for Behçet's Diseas. The outcome measures were visual acuity, intraocular inflammation, reduction of daily corticosteroid dose, and adverse effects.

Results. 7 patients (2 women and 5 men) had BD with severe ocular involvement, recurrent and refractory to immunosuppressive treatment requires the use of anti-TNF alpha (Infliximab). It was 5 men and 2 women with a mean age of 27,14 years (range 18-35 years). These patients have debuted their Behçet's disease between 6 and 28 years (mean: 18.7), 4 of them (57,14%) had a juvenil BD. Ocular involvement revealed BD in all our patients with a diagnostic delay of MB from some months to 19 years (mean 7.8 years). This achievement was severe at diagnosis in our patients with visual acuity <1/10 involving one eye and 3 cases were already at the stage of unilateral blindness. It was made of sequelae of anterior uveitis in 4 cases, posterior uveitis in 5 patients and panuveitis in 2 patients. The vasculitis lesions were noted in 5 cases bilaterally. Other complications were noted (intra vitreous hemorrhage: 3 patients, macular edema: 4 patients , macular atrophy: 2 patients and papillary edema 2 patients). The retinal detachment was noted in 4 patients. Infliximab was given immediately in 2 cases and after failure of conventional therapy in the remaining five. Our patients received an average of 7 Infliximab infusions (range: 3- 13). The evolution was marked by a transient improvement in 2 cases including one patient went from counting fingers to 10/10 after the 2nd Infliximab infusion, but the treatment was arrested because of the appearance of miliary tuberculous. A continuous improvement was noted in 3 patients and therapeutic failure in one patient who received biotherapy quite late.

Conclusion. The biological therapies have increased the treatment options for severe ocular involvement that threaten the visual prognosis in Behçet's disease. The lack of data from randomized controlled studies limits our understanding of which agent to choose, when to start treatment and how long to continue it. However, it seems that only early treatment allows a better therapeuthic answer. In addition, the high cost and potential side effects of all biological agents have limited current use of uveitis refractory to immunosuppression.

P111.

BEHÇET'S DISEASE IN IRELAND: PATIENT ACCESS AND RESPONSE TO ANTI-TNF BIOLOGICS

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Background. Based on promising efficacy and safety data of anti-TNF use in Behçet's disease (BD), European League Against Rheumatism (EULAR) developed evidence-based recommendations supplemented with expert opinion for use of anti-TNF in the management of different aspects of BD in 2009.
Objectives. The aim was to establish the current prescription practice of anti-TNF in a cohort of BD patients in Ireland including the indications, response and the serious adverse risks associated with it.
Methods. A retrospective analysis was performed on all BD patients attending our rheumatology service and satisfying ISGBD or ICBD criteria. Response was evaluated on new/worsening clinical features and improvement/resolution of clinical symptoms. Management was benchmarked against current EULAR guidelines published in 2009.
Results. From a cohort of 22 patients, 18 (81.9%) received anti-TNF (6 males, 12 females) with mean age of 38.9 years. 14 patients (77.8%) achieved complete remission and 4 patients (22.2%) achieved low disease activity on anti-TNF. Three patients (16.7%) were successfully switched to a different agent due to secondary failure, six patients (33.3%) needed 3 different anti-TNFs and one required a fourth to achieve remission. Five allergic reactions encountered, all with administration of infliximab. Five serious infections were documented involving three patients aged 50 years or above. No other serious side effects were observed.
Conclusions. Response rates to anti-TNF were excellent and treatment was well tolerated but should be used with caution in patients age 50 or above. BD patients who fail one anti-TNF due to intolerance, ineffectiveness or secondary failure may benefit from switching to another drug from this group or even re-trial of a previously administered anti-TNF.

P112.

ANEURYSMAL ARTERIAL DISEASE REQUIRING SURGICAL INTERVENTION IN BEHÇETS: A CASE SERIES

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Background. Vasculitis is thought to underlie many of the clinical manifestations of Behçet's disease, with both arteries and veins of all sizes commonly affected. The aorta and femoral artery are commonly involved, but any extremity or visceral vessel may be involved, including the coronary arteries, splenic artery, and the inferior mesenteric artery. The prevalence of vascular involvement in BD varies from 12.8 to 16.8%. Arterial aneurysms are associated with a poor prognosis because of a fairly high risk of rupture, recognized in aneurysms even less than 5 cm in diameter. We report the clinical course and outcomes of 5 patients with Behçet's and major vascular involvement who required surgical intervention.
Methods. We retrospectively reviewed the clinical, laboratory and imaging data of a cohort of BD patients, followed in our tertiary referral, multidisciplinary hospital outpatient clinic.
Results. We identified 5 patients with severe arterial aneurysmal involvement requiring surgical intervention. Among our cohort there 7 arterial aneurysms suffered, in various anatomical sites including the popliteal, femoral, innominate, coronary and abdominal aorta. The commonest procedures performed in this group were graft (6 procedures) and stent insertion (4 procedures). 1 pateint had a limb amputation and another had a renal artery pseudoaneurysm embolisation.4 of our 5 cases also suffered concurrent venous thromboses. In addition, 3 out of our 5 cases experienced post operative complications. Case 1 requiring several procedures due to stenotic lesions associated with her grafts and eventually required a right leg, above knee amputation following a presentation with acute limb ischaemia due to an occlusion of a previously inserted right popliteal stent. Case 2 suffered a false abdominal aortic aneurysm at the proximal end of his EVAR graft, with an associated left renal artery pseudoaneurysm. Case 5 suffered an anastamotic leak at the site of his previous right femoral arterial graft. Cases 1, 2 and 5 were on immunosuppression at the time of their operative complications, Case 1 while on Prednisolone 20mg and both Case 2 and 5 were taking Azathioprine and Prednisolone. Cases 1 and 2 patients were anticoagulated and suffered complications while on Warfarin. Our first case had been taking warfarin for 2 months at the time of her ruptured right femoral aneurysm, while case 2 had been on warfarin for 6 months at the time of his false abdominal aortic aneurysm at the proximal end of his previous EVAR graft. Both patients had warfarin stopped and were commenced on Clopidogrel following developing these complications. Case 5 was on Clopidogrel at the time of his anastamotic leak. Case 1 is the first case to our knowledge in the literature of Tocilizumab efficacy in arterial aneurysmal disease in Behçets., while cases 2 and 5 received cyclophosphamide, with case 2 suffering a further aneurysm while on this.
Conclusions. It is known is that patients with Behçets and aneurysmal disease suffer significant mortality and complication rates. We present 5 cases of vascular Behçet's with varied clinical outcomes, but exhibiting a high complication rate.

P113.

INTERFERON ALFA-2A IN TREATMENT OF REFRACTORY UVEITIS ASSOCIATED BEHÇET'S DISEASE: A SINGLE-CENTRE EXPERIENCE iN CHINA

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Ocular manifestation of Behçet's disease mostly involved bilateral panuveitis and retinal vasculitis, which are very challenging to treat. Interferon alfa-2a (IFN-α2a) has been reported to successfully treat the BD Uveitis refractory to conventional immunosuppressive treatment, but mainly in Turkey. But up to now, the information for the efficacy and safety of IFN in Chinese BD patients with refractory uveitis is very limited.
Objectives. To report on the efficacy and safety of IFN-α2a in the treatment of refractory uveitis associated with BD.
Methods. Clinical data of IFN-α2a therapy in eight BD patients with refractory ocular symptoms were retrospectively analyzed at Peking Union Medical College Hospital between January 2015 and May 2016.
Results. Eight BD patients with severe uveitis (seven males, average age (32.4±10.6) who had suffered from relapses despite corticosteroids as well as multiple immunosuppressive were given INF-α2a. All of these patients fulfilled both 1990 International Study Group BD criteria and 2013 International Criteria for BD. Besides the ocular involvement, oral ulceration was present in all patients, and other findings included genital ulcers in 5 cases, skin lesions in 7 cases, positive pathergy test in 2 cases. The initial dose of IFN-α2a was 3 MIU/day subcutaneously for 4 weeks, tapered down to 3 MIU every other day for 3 months, and then to 3 MIU three times per week, according to the individual ocular manifestations. The median duration of IFN treatment was 4.9 months (range 3-15 months). All patients showed positive response to IFN-α2a, among whom six patients remained relapse free during the treatment, while one patient had one relapse and the other experienced twice. Ocular inflammation was suppressed completely or partially in all cases. Other BD symptoms improved during the follow-up period as well. The required dose of oral corticosteroids was reduced in most cases, indicating a potential steroid-sparing effect. The visual acuity, however, failed to acquire significant improvement in our patients. No severe side effects were observed in all patients. Four patients experienced flu like symptoms responding to oral NSAIDs, and Leukopenia were seen in 2 patients during treatment with IFN-α-2a.
Conclusions. IFN-α2a therapy is effective and relatively safe in BD patients with refractory ocular manifestations, who are unresponsive to conventional agents, leading to remission of both ocular and system symptoms. Due to limited observation period, long-term efficacy and safety of IFN-α2a along with the possible discontinuation of the agent need further investigation.

P114.

CANAKINUMAB TREATMENT IN BEHÇET'S DISEASE PATIENTS WITH NEUROLOGIC OR VASCULAR INVOLVEMENT

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Background. Vascular and neurologic involvements are the main causes of mortality in Behçet disease (BD), and both conditions are also associated with serious morbidity. High dose corticosteroids and immunosuppressive treatments are the standard of care, but there is no clinical trial data showing the efficacy of any drug in vascular and neurologic involvement in BD (VBD and NBD). Some new medications including canakinumab were reported to be effective in selected refractory cases, however since VBD and NBD are rare manifestations of BD with no established outcome measures, none of the observations were followed by clinical trials.

Design. We designed an exploratory open-label trial with canakinumab to evaluate interleukin-1β inhibition in patients with VBD or NBD. A total of 10 patients will be recruited to receive 300 mg IV canakinumab as the first dose, which will be followed by monthly 150 mg IV infusions for 6 months. Responding patients will continue to receive SC injections. For VBD, improvement in the relevant symptoms (i.e. localised pain, abdominal pain, calf thickness, haemoptysis) by using physician and patient's global assessment with using a 10-cm visual analogue scale (VAS), improvement in systemic inflammatory findings (CRP, ESR, SAA), any improvement in radiological findings depending on the involved vessels (MR, CT or Doppler findings) will be recorded. For patients with NBD; improvement of muscle strength, ataxia, or other relevant neurologic findings, improvement in systemic inflammatory findings, decrease in the size of the MRI lesion, or disappearance of contrast enhancement and improvement in patients' and physicians global assessment using a 10-cm visual analogue scale (VAS) will be recorded by each visit. Behçet Disease Current Activity Form (BDCAF), Modified Rankin Score, Neuro Behçet Disease Score, and modified Extended Disability Status Scale (mEDSS) questionnaires will also be used. The primary endpoint of the study is resolution of acute exacerbation findings at the end of the first month in parenchymal brain or major vessels related to NBD or VBD, which will be assessed by clinical, radiological and laboratory measures. Complete response is defined as clinical and laboratory improvement based on ≥50% improvements in patient's and physician's global assessments by using VAS, and ≥50% reduction in CRP values; along with stable or ≥20% reduction in aneurysm size in patients with arterial involvement, and stable or ≥20% reduction calf swelling in patients with lower extremity venous thrombosis. Samples will also be collected for the analysis of potential biomarkers.
Summary. This pilot trial (ClinicalTrials.gov registration no. NCT02756650) is aimed to evaluate the efficacy and safety of canakinumab in NBD and VBD using preliminary outcome measures. In addition to the investigation of IL-1β blockade in these settings, this study is expected to provide important information about the performance of the proposed outcome measures as well as potential biomarkers.

P115.

APREMILAST FOR THE TREATMENT OF BEHÇET'S SYNDROME: ROUTINE CARE, REAL WORLD EXPERIENCE

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Background. Apremilast has been approved for the treatment of psoriasis and psoriatic arthritis in the US. Apremilast has also been studied for the treatment of mucocutaneous manifestations of Behçet's syndrome (BS). This provides opportunities for the off label use of apremilast in BS patients.
Methods. NYU Behçet's Syndrome Center was established in 2005 and since then over 1000 patients have been seen. The NYU ARMD Registry collects data from routine care for all patients seen at the Behçet Center, including demographic data, medical history, BS related medical history, family history, medication use, MDHAQ and RAPID3 outcomes, BSAS scores for BS activity and adverse event profiles. We identified all patients treated with apremilast for their BS from 2014 to 2016 and analyzed use patterns and response.
Results. Nine patients (female 8 (89%), mean age 37.1+8.6 years and disease duration 11.8+7.2 years) were identified. They were on azathioprine (n=3), colchicine (n=2), hydroxychloroquine (n=5), abatacept (n=1) and adalimumab (n=3). On average they were on apremilast for 18.8+3.2 months. Their baseline RAPID3 and BSAS scores were 13.3+7.3 and 42.7+25.7, respectively. RAPID3 improved to 5.4 + 11.8 for subjects continuing apremilast, while RAPID3 worsened 5.3 + 8.1 for subjects discontinuing at last follow up visit. Patients were able to stop azathioprine, colchicine, hydroxychloroquine and abatacept in one case each and adalimumab in 2 cases.
Conclusions. Apremilast was effective in controlling signs and symptoms of BS in this small group of patients. There were few discontinuations and the treatment was overall well tolerated. Larger studies are needed in routine clinical care to better assess the role of apremilast in the treatment of BS.

P116.

DEEP ABDOMINAL WALL ULCERATION IN A ADMANTIADES-BEHÇET'S DISEASE PATIENT

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A 35-year-old German male patient was admitted diagnosed with Admantiades-Behçet's Disease (ABD) since 2008. Recurrent oral and genital apthous ulcers, in addition to vascular brain involvement were successfully treated with interferon-alpha-2a (3x 3 million IU s.c. per week).
Wound infections and local ulcers occured on the lower abdomen at injection sites. Despite the operative management of the 4cm wide ulcers at an external hospital, wound healing could not be achieved. Continous pus secretions and deterioration of the general condition including fatigue and abdominal pain were seen. A second operative management, fasciectomy, was carried out. Few days following hospital discharge, the ulceration recurred again and led to recurrent deep abdominal wall invading ulcers. A 10 cm wide, 3-4 cm deep subumbilical ulcer involving the abdominal wall was present, lacking signs of infection. Despite lack of wound infection signs, we carried out a disinfectant preventive measure with Braunol tamponade. Interferon s.c. treatment was carried out on the upper thighs. Additionally, a systemic oral treatment with prednisolone 100mg/d, and vacuum therapy were implemented. The above therapy led to tissue granulation. After 27 days in-patient treatment we discharged the patient and treated him as an outpatient with 20mg prednisolone orally, reducing 5mg every 7 days till the constatnt dose of 5mg was reached. The above lead to remission.
Pathergy phenomenon, skin sensitivity due to trauma, leads to wound healing disturbances. CRP is an indication of disease activity in ABD patients, especially, with no evidenece of infection and normal WBC count. One third of patients treated surgically, develop dehiscence, ulcers or transplantation-rejection (1), particularly when the disease is active. The initial deterioration of the ulcer on the lower abdominal wall after the operative mangament, without the pre-operative steroidal management, confirms this statement. Therefore, before indispensable operative managemet or invasive approch, preventive systemic prednisolone should be carried out (2). In our Patient having a deep wound on the lower abdomen, a 20-day vaccum therapy and systemic prednisolone was sufficient to induce wound healing. This progress confirms the positive effects of systemic steroids on would healing in ABD patients. The literature lacks publications regarding ABD and vacuum therapy.

References

1. PARK M-C, HONG B-K, KWON HM, HONG Y-S: Surgical outcomes and risk factors for postoperative complications in patients with Behçet's disease. *Clin Rheumatol* 2007; 26: 1475-1480.
2. HOXHA FT, HASHANI S, KRASNIQI A *et al*.: Intestinal vasculitis in Adamantiades-Behçet disease presenting as acute abdomen. *J Eur Acad Dermatol Venereol* 2009; 23: 1461-1463.

P117.

BEHÇET'S DISEASE IN A PATIENT WITH VERTICALLY TRANSMITTED HIV INFECTION SUCCESSFULLY TREATED WITH ANTI TNF-ALPHA THERAPY – A CASE REPORT AND SYSTEMATIC LITERATURE REVIEW.

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Background. Behçet's disease (BD) is a systemic syndrome with protean manifestations that has been occasionally described in association with human immunodeficiency virus (HIV) infection. Tumor necrosis factor (TNF)-alpha inhibitors in HIV infected patients with refractory autoimmune disorder are only rarely reported.
Methods. Starting from our case, a complete literature review was conducted using searching engine in PubMed and as mesh terms, "Behçet's disease", "HIV infection", "infliximab" and "TNF alpha inhibitor". We focused on clinical features, treatment strategy and outcomes.
Results. In 2008 a 22-year old man, presented with a 10-month history of fever, fatigue and recurrent oral and genital ulcerations. He also complained swelling and pain of the left knee. His past medical history revealed vertically acquired HIV infection, without AIDS symptoms and without antiretroviral therapy. Blood

Author	Year	Patient	First symptom	HIV infection	Therapy	Outcome
Routy JP	1989	69 y/M	Oral and genital ulcers and polyarthritis	Heterosexual	Colchicine	Successful
Buskila D	1991	27 y/F	Fever, fatigue, oral and genital ulcers, cutaneous nodules and arthritis	Heterosexual	PDN, Thalidomide, Colchicine, Zidovudine	Successful
Stein CM	1991	33 y/M	Genital ulcers, polyarhtritis, uveitis and AIDS	Heterosexual	PDN	Death **
Belzunegui J	1994	25 y/M	Oral and genital ulcers and polyarthritis	IV drug abuse	PDN, AZT	Death *
Chahade WH	1994	31 y/F	Oral and genital ulcers, polyarthritis, deep venous thrombosis, AIDS	Unknown	PDN, acycolvir,	Death *
Olivè A	1999	40 y/F	Oral and genital ulcers and polyarthritis	IV drug abuse	PDN, Estavudine, Amivudine, Indinavir	Relapsing
Merciè P	2002	41 y/M	Oral ulcers	Homosexual	Colchicine, Thalidomide, triple antiretroviral therapy	Successful
Cicalini S	2004	34 y/F	Fever, fatigue, oral and genital ulcers, bilateral conjunctivitis	Unknown	HAART	Successful ***
Mahajan V	2005	38 y/M	Oral and genital ulcers, polyarthritis and erythema nodosum	Unknown	Stavudine, Lamivudine, Nevirapine, Colchicine	Relapsing ***
Gomez-Puerta J	2006	38 y/M	Oral and genital ulcers, polyarthritis and erythema nodosum	Blood transfusion	PDN, Colchicine, Cyclosporine	Successful
Mrih L	2012	28 y/M	Fever, oral and genital ulcers, deep venous thrombosis	Unknown	PDN, Colchicine, Cyclophosphamide, zidovudine, lamivudine, efanvirenz	Successful
Roscoe C	2014	29 Y/M	Feever, bloody stools, polyarthralgias, skin rash, oral and ulcers	IV drug abuse	PDN, atazanavir, ritonavir, emtricitabine, tenofovir, raltegravir, Colchicine, HCQ, Dapsone, MMF	Successful ***
Present case	2016	22 Y/M	Fever, fatigue, oral and genital ulcers and polyarthritis	Mother-to-child transmission	PDN, Colchicine, Azathioprine, efanvirenz, emtricitabina, tenofovir, **Infliximab**	Successful

Table. HIV: human immunodeficiency virus; PDN: prednisone; AZT: azidothymidine; HAART: highly active antiretroviral therapy; HCQ: hydroxychloroquine; MMF: mycophenolate mofetil; N/A: not available. *AIDS-related; **Not AIDS-related; ***mainly due to antiretroviral therapy.

test showed elevated C-reactive protein, normal WBC and CD4 count and undetectable plasma HIV-RNA. Polymerase chain reaction for HSV-1 and HSV-2 performed on oral and genital ulcer smears was negative. Knee aspiration yielded a yellow fluid with 2900/mm3 WBC (22% polymorphonuclear, 60% monocytes, 18% lymphocytes). Erythematous papular lesion developed within 24h after skin prick by sterile needle was considered consistent with a positive pathergy test. HLA-B51 was present. An ophtalmological examination was normal. The patient was diagnosed with BD, according to International Study Group (ISG) Criteria. Colchicine 1 mg daily and mouth washes were not completely effective, so Cyclosporin (150 mg/day) and oral prednisone (25 mg/day) were added. When prednisone was tapered to 10 mg, the arthritis and oral and genital ulcers recurred. During the next two years the patient developed several flares of oral ulcers and arthritis so Azathioprine was added, without improvement. Both drugs were discontinued and, in 2013, Infliximab 300 mg/month and Atripla (efanvirenz, emtricitabina, tenofovir) therapy were started with marked improvement.

Twelve articles were found in literature which comprehend, including our case, 13 patients. Most of them were male (69.2%), mean age ± SD 33±11.8 years, mainly presenting with recurrent oral and genital ulcers, arthritis and fever. In three patients an improvement was noted after starting antiretroviral therapy, but only one patient was treated with highly active antiretroviral therapy (HAART) alone. Clinical features, treatment and outcomes are reported in Table. The majority of the patients were treated with prednisone, colchicine and antiretroviral therapy; treatment was successful in 10 out 13 patients (76.9%). Notably, only our case was treated with TNF-alpha inhibitors. In literature Gallitano et al recently reported 27 HIV-positive patients treated with TNF alpha inhibitors, none of them was affected by BD.

Conclusion. A relationship between BD and HIV infection appears to exist and this caseraises the question of whether HIV can serve as a trigger for autoimmune hyperactivity. TNF-alpha inhibitors could be used in patients treated with antiretroviral therapy. Further studies are needed.

P118.

THE EFFECT OF MEDICATION ON THE TREATMENT OUTCOMES OF BEHÇET DISEASE

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Objectives. The main objectives of this study were to examine the medication which appears to be most effective in our cohort of patients with BD. The additional effects of patients receiving vitamin D and anticoagulants including the thrombotic, factor protein C (PC) and protein S (PS) on systemic activity of BD patients were assessed.

Methods. A total of 522 (179 males: 343 females) BD patients were studied. The data collected included; ulcer severity score tools, BD activity form, patients' medication, vitamin D, and thrombophilia screen; anti-thrombin (AT), free protein C (PC), protein S (PS), activated protein C resistance (APCR), factor V Leiden mutation (FVL), prothrombin gene mutation (PGM), heritable thrombophilia (HT) and lupus anticoagulant (LA) were also included. This clinical data was collected from the London, Behçet's Centre.

Results. On the day of clinical assessment 176 BD patients (33.7%) their disease was inactive, and 327 (62.6%) had active disease. The multivariate regression and Principal Component Analysis (PCA) suggested that the activity of BD was increased when Colchicine was combined with therapies such as; Humira, Infliximab and Mycophenolate mofetil (MMF). When MTX was combined with Azathioprine or MMF the patient's symptoms remained active. Factor analysis showed that Vitamin D had a strong positive loading value, indicating that it may add positively to the management of both CNS and fatigue symptoms (0.7 and 0.6, respectively).

The results of the thrombophilia screen analysis using the independent t-test showed that level of PC and PS for inactive patients was higher than active group; the mean of level of PC for inactive patients was (135.50± 27.10; p=0.012), and for PS the mean level for inactive patients was (116.42± 24.23; p=0.005). The rest of thrombophilia screen did not show any statistical significance. Also ANOVA test showed that there was a significant difference between anticoagulants and level of PC and PS, and P values were (p=0.001) each.

Conclusion. The available information suggests that the most effective treatment regimes for controlling BD symptom activity were; Azathioprine combined with Colchicine and Prednisolone. Thereafter, Infliximab combined with either MMF or Cyclosporine. In addition prescribing Colchicine with a biological agent in a patients' treatment plan may increase skin and CNS complications. This study also indicated that anticoagulants, when required clinically, may have an important role of suppressing BD activity. Deficiency of PC and PS may act as risk factors for the activation BD symptoms. From these findings, it is recommended routinely to include thrombophilia screen for BD patients

P119.

CERTOLIZUMAB PEGOL TREATMENT IN BEHÇET'S DISEASE: A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY

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The purpose of the present study was to describe our experience with the recombinant Fab' antibody fragment against TNF-α Certolizumab Pegol (CZP) in patients with Behçet's disease (BD) refractory to standardized therapies and previous biologic agents. Retrieved data including demographic characteristics, clinical manifestations, and previous treatments were collected in three different specialized Rheumatologic Units in Italy. In order to evaluate disease activity, the Behçet's disease current activity form (BDCAF) has been used before starting CZP therapy and at each visit during treatment. Thirteen BD patients (mean age 42.6±8.8 years) with a disease duration of 8.80±6.9 years, underwent CZP treatment for 6.92±3.52 months. Six patients (46.15%) experienced a worsening of symptoms after 4.16±1.21 months, whereas a satisfactory response was achieved in seven patients (53.84%) who were still on CZP therapy at the last follow-up visit (after 9.28±3.03 months of treatment). The mean decrease of BDCAF between the first and last visit was 0.308±1.84 without reaching significant difference (mean 8.3±1.3 and 8 ± 2.08, respectively; p=0.51). During the whole study period CZP was well tolerated in all patients except one who developed a generalized cutaneous reaction after the third administration. These results suggest that CZP can represent a reliable alternative for the treatment of otherwise refractory BD patients. Whether the increase of CZP dosage may ensure a better clinical response remains an unsolved issue that needs to be considered.

P120.

SURGICAL METHOD FOR AORTIC ROOT INVOLVEMENT OF BEHÇET DISEASE

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Background. Aortic regurgitation (AR) in Behçet disease is a rare but very fatal condition. Many patients required a second or third operation after simple aortic valve replacement (AVR) as a result of prosthetic valve dehiscence or destruction because of flare. Recently, several case series have been published aortic root replacement (ARR) have shown favorable outcome. However, because lack of evidences, we wonder if the surgical outcome of AR in Behçet disease was dependent on surgical methods or materials.
Objectives. To identify factors associated with the long-term outcome of AR in the patients with Behçet disease who performed surgical treatment.
Methods. From January 1996 through December 2013, 33 patients with AR caused by Behçet disease have been surgically treated. Twenty-three patients were fulfilled the international criteria for Behçet disease. AVR was performed in 9 cases and ARR in 14 cases. Bioprosthesis ARR was performed in 8 cases and composite graft ARR in 6 cases. According to the definition of the event; aortic valve/graft problem, infective endocarditis, cerebral infarction caused by thromboembolism or re-operation of aortic valve; we compared events after first operation between two groups. The duration of follow-up was 10.7(median; IQR=8.9-13.5) years (bioprosthesis ARR group) and 6.4(median; IQR=4.8-7.7) years (composite graft ARR group).
Results. In the 9 patients with AVR, events occurred in 6 patients (2.3 (median; IQR=0.3-10.3) years after operation) and 11 cases required re-operations. In the 14 patients with ARR, events occurred in 7 patients (4.7 (median; IQR=1.6-6.9) years after operation) and 6 cases required re-operations. Overall mortality was 17.3% (2 of 9 patients in AVR group, 2 of 14 patients in ARR group). Steroid was prescribed for significantly more patients and higher dosage in ARR group than those of AVR group.
In the 8 patients with bioprosthesis ARR, events occurred in 6 patients (3.0 (median; IQR=1.5-5.4) years after operation) and re-operations were performed in 6 cases. Interestingly, in the 6 patients with composite graft ARR, events occurred in 1 patient (6.2 (median; IQR=4.8-7.5) years after operation), there is no case required re-operation. Kaplan-Meier curves displayed higher event free rate in composite graft ARR group compared to bioprosthesis ARR group (Figure 1). Overall mortality was 14.3% (2 of 8 patients in bioprosthesis ARR group, 0 of 6 patients in composite graft ARR group). As post operational medications, administration of steroid and immunosuppressants were not significantly different between both groups.
Conclusion. In patients with AR related with Behçet disease, the rate of event was lower in patients with composite graft ARR compared to those with bioprosthesis ARR. Composite graft ARR might be a surgical option in patients requiring ARR for aortic root involvement of Behçet disease.

Disclosure. Byeongzu Ghang, None; Ohchan Kwon, None; Wook Jang Seo, None; Seokchan Hong, None; Yong-Gil Kim, None; Chang-Keun Lee, None; Bin Yoo, None.

P121.

THE EFFICACY AND SAFETY OF ANTI-TNF-ALPHA IN BEHÇET'S DISEASE: A CASE SERIES

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Behçet's disease (BD) is a chronic and relapsing multisystemic inflammatory disorder (1).
Major pathogenetic mechanisms underlying BD are linked to innate immune cell activation and dysregulation and overproduction of proinflammatory cytokines, such as tumor necrosis factor- (TNF)-α, interleukin- (IL-) 1β, IL-6, and IL-17 (2).
The aim of the study was to report the efficacy and safety of TNF-α inhibitors in case series of patients with Behçet's disease (BD).
Twelve BD patients (F/M: 6/6; mean age 34.91 years, range 24-50 years; disease duration 72.41 months, range 12-120 months) refractory to disease-modifying antirheumatic drugs (DMARDs) are reported in this study. Eight patients were positive for the HLA-B51 allele. The diagnosis of BD was made on the basis of the International Study Group Criteria (ISGC).
All patients had recurrent oral and genital ulcerations, ten patients had skin lesions and all patients had arthritis. Regard ocular involvement six patients had anterior uveitis, 1 posterior uveitis and 2 panuveitis.
Four patients had gastrointestinal involvement, one patient a thrombosis and 5 patients had fever.
All patients were treated with anti-TNF-α, seven with adalimumab (40 mg/biweekly) and five with infliximab (5 mg/kg IV at 0, 2, and 6 weeks, then every 8 weeks). Two patients were also in therapy with DMARDs and 5 with oral steroid. Mean disease duration of anti-TNF-α was of 37.83 months (range 6-84 months). After 6 months of therapy with anti-TNF-α, eleven patients showed a good response with a relapse in one or more clinical manifestations over time, while one patient had a partial remission on mucosal and musculoskeletal involvement. In all patients no serious adverse events occurred. In conclusion, all patients had a good response to therapy with anti-TNF-α, supporting the pathologicalrole of TNF-α in BD.

P122.

USTEKINUMAB EFFICACY IN REFRACTORY BEHÇET'S DISEASE

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We describe the successful use of ustekinumab in a 37-year-old woman with Behçet Disease (BD).
The diagnosis of BD was made eleven years before on the basis of the International Study Group Criteria (ISGC).
The patient showed recurrent oral and genital ulcerations, skin lesions, fever, abdominal pain, diarrhea and myalgia. She also complained for musculoskeletal involvement, in the form of arthralgia and arthritis. Laboratory investigations revealed increased inflammatory markers and the HLA-B51 allele was positive.
Over the past years, the patienthad been treated with several drugs, including cyclosporine A (CYC) (3-5 mg/kg/day), non-steroidal anti-inflammatory drugs (NSAIDs), prednisone (PDN) (up to 50 mg/daily), methotrexate (10 mg/weekly), etanercept (50 mg/weekly) and adalimumab (40 mg/biweekly). Each of these regimens failed to induce clinical remission and normalization of acute phase reactants.
Infliximab had also been administered at a dose of 5 mg/kg IV at 0, 2, and 6 weeks, then every 8 weeks. However, it was withdrawn after 8 months for loss of efficacy. When infliximab therapy was stopped, ustekinumab was started at a dose of 45 mg, at weeks 0, 4, and every 12 weeks thereafter.
After three months of therapy, the patient showed the remission of fever, skin lesions and gastrointestinal symptoms. After 6 months of therapy, there was also a partial remission of oral and genital ulcerations and a complete remission of arthritis.
We have described the case of a refractory BD patient, in whom only the use of ustekinumab was able to inducean almost complete clinical remission. BD is a multisystemic disease and the treatment should be tailored according to the extent and severity of clinical manifestations.
Ustekinumab is a human monoclonal antibody that binds with high affinity and specificity to the p40 protein subunit used by both the interleukin (IL)-12 and IL-23. IL-12 and IL-23 are involved in inflammatory and immune responses, such as natural killer cell activation and CD4+ T-cell differentiation and activation.
To the best of our knowledge, data reported represent the second case described in literature, only one case have recently been published on treatment of BD with ustekinumab with partial remission.
In conclusion, we report herein a case of BD successfully treated with ustekinumab. The number of published reports is still low, making difficult to draw firm conclusions. For these reasons, further investigation involving a wider population with BD with a longer-term follow-up is needed to validate these recent observations.

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EFFECTIVE AND RAPID TREATMENT OF FLARES IN PATIENTS WITH BEHÇET'S DISEASE BY THE SINGLE CHAIN ANTI-TNF ANTIBODY DLX105

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Background. Behçet's Disease is a rare, chronic variable vessel vasculitis presenting with oral and genital aphthous lesions, a variety of skin symptoms, arthritis and depending on its severity with uveitis, CNS and GI symptoms. Most often used drugs are colchicine, corticosteroids, azathioprine and cyclosporine. TNF inhibitors are used off-label (only in Japan approved) in particular for patients with uveitis to prevent blindness. Usually given TNF inhibitors are infliximab and adalimumab. These monoclonal antibodies are large molecules and as such they do not penetrate well into tissues following systemic administration.
We explored the clinical effect of a single chain anti-TNF antibody fragment (DLX105) consisting of 246 amino acids (molecular weight: 26 kDa) for flaring mucocutaneous Behçet's Disease.
Objectives. The primary objective of this study was the describe the pharmacokinetics of DLX105 after a single fixed dose in patients with Behçet's Disease. The exploratory objective was to explore the preliminary efficacy of a single fixed dose of DLX105 on mucocutaneous lesions in patients with Behçet's Disease.
Methods. A total of 6 patients with flaring Behçet's Disease received a single dose of 10 mg/kg i.v. DLX105. The main inclusion criteria were: males and females aged 18 to 65, with flaring Behçet's Disease defined by the criteria of the "International Study Group for Behçet's Disease (ISBD)" with at least two oral ulcerations for at least 3 days prior to enrollment. Patients were allowed to be on colchicine or low dose corticosteroids (≤7,5 mg/d). After a dosing visit (Day1) all patients attended two follow-up visits (Day 5 and 8) and an end-of-study-visit (Day 15).
Results. Each patient had oral lesions at baseline (mean 3.7 ulcers, SD 2) which rapidly and almost completely disappeared within one week (mean 1 ulcer, SD 1.3) and stayed improved even after 2 weeks (mean 1.5 ulcers, SD 1). Genital lesions in one patient also resolved. Two patients with erythema nodosum showed a prompt and complete disappearance of skin nodules after one week of treatment. The number of papulo-pustular skin lesions in 5 patients also rapidly declined (mean 14.3 at baseline, after one week 7.2). Arthralgia present in 3 patients resolved within one week of treatment. The ISBD questionnaire score (range 0–12) dropped from 4.3 to 3.3 within one week and to 3.0 within two weeks indicating a sustained response. There were no SAEs and adverse events were mild and disappeared within 2 weeks.
Conclusions. These data suggest that DLX105 has a rapid and strong onset of action likely due to its unique property to penetrate effectively into inflamed tissues. The duration of the response is far longer than its serum pharmacokinetics with a half-life of roughly one day suggested. Thus, DLX105 is a strong development candidate to treat flaring mucocutaneous Behçet's Disease.

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