

**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.

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### 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.

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### 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 electrochemoluminescence 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.

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### 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 simplex 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 Lancet (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 response 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 ( $p\text{-value}<0.0001$ ). On the contrary mucosal lesions were more common in P (+) subset ( $p\text{-value}<0.0001$ ). Skin manifestations were more common in P (+) subset ( $p\text{-value}<0.0001$ ). Furthermore P (+) patients were more prone to gastrointestinal ( $p\text{-value}=0.038$ ) and neurological lesions ( $p\text{-value}=0.038$ ). 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 ( $297.4\pm81.0\text{ }\mu\text{m}$ ) than in the IUBD ( $253.0\pm77.2\text{ }\mu\text{m}$ ,  $p=0.042$ ) and control ( $261.2\pm78.6\text{ }\mu\text{m}$ ,  $p=0.047$ ) 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 ( $M\pm m$ ) of BD patients was  $32.5\pm0.88$  years, RA –  $47.4\pm1.01$  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 ( $\pm$  standard deviation [SD]) follow-up after initiating ICCT was  $5.6\pm2.3$  years. The mean ( $\pm$ SD) number of ocular attacks were  $2.9\pm1.6$  times during the 6 months before initiating ICCT (baseline period),  $0.6\pm0.9$  times during months 1-6, and  $0.5\pm0.9$  times during months 7-12 ( $p<0.01$ , Friedman test). The mean ( $\pm$ SD) BOS24 was  $5.2\pm2.4$  during baseline period,  $1.5\pm2.1$  during months 1-6, and  $1.7\pm3.1$  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 potential role 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's Syndrome 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 associated 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 (4 cases), 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 immunosuppressive 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 immunosuppressive 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 ( $\geq 30.005$  ng/mL and  $<30.005$  ng/mL): the EMRAI scores and the proportion of patients in the active phase of BD presenting with  $\geq 2$  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 ICBT 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) ICBT 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 aphthosis (100 vs 3.5 %), genital aphthosis (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 involvement (45.3 vs 53.4%) and intestinal involvement (1.6 vs 13%). Different statistic results of application of ICBT and ICBDr are shown in Table I:

Statistic result	ICBT	ICBDr
Sensitivity (%)	100	99.3
Specificity (%)	97.5	98.6
Positive predictive value (%)	96.8	98.4
Negative predictive 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 ICBT and ICBDr criteria to ISG criteria, we noted a gain of sensitivity of 8 and 7.3% respectively, and a gain of specificity 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 VEIN THROMBOSIS ASSOCIATED WITH BEHÇET'S DISEASE TO IDIOPATHIC DEEP VEIN THROMBOSIS**

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**Objective.** to compare epidemiological, clinical and evolutive characteristics of patients with deep vein thrombosis related to Behçet's disease (DVT-BD) to patients with idiopathic deep vein thrombosis (Id-DVT)

**Methods.** We compared two groups of patients hospitalized for management of deep vein 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.** Comparison 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-phlebotic syndrom (%)	30.47	11.86	<0.05
Recurrence (%)	31.42	6.75	<0.05

**Conclusions.** Behçet's 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 demonstrates 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 aphthosis (%)	95.84	100	0.001
Genital aphthosis (%)	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 significantly 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 conducted 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 occurred 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 occurred 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 aphthosis (%)	97.5	98.2	NS
Genital aphthosis (%)	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)	<i>p</i>
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 aphthosis (%)	97.6	98.9	NS
Genital aphthosis (%)	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 aphthosis, pseudofolliculitis 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 aminotransferase levels 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 severe 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 insufficiently 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. Immunosuppressive (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;  $6.8 \pm 4$  vs  $10.9 \pm 4.5$ ,  $p=0.003$  for FMD,  $0.55 \pm 0.13$  vs  $0.47 \pm 0.1$ ,  $p=0.004$ ). 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 aphthous 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 Cerrahpaşa 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  $36 \pm 8$  and mean disease duration of  $9 \pm 6$  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).

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## 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 aphthous 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 epidemittitis (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.

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## 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 (33.7%). 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/ $\mu$ l, 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/ $\mu$ l, 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**Pain C.<sup>1</sup>, Al Badri S.<sup>2</sup><sup>1</sup>Alder Hey Children's NHS Foundation Trust, Paediatric Rheumatology Department, Liverpool, UK; <sup>2</sup>Liverpool University Dental Hospital, Liverpool, UK

Behçet's syndrome is a rare multi-system inflammatory condition, which can have an onset in childhood in between 4-26% of cases<sup>1</sup>. 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 1.** 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 conducted 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 pseudofolliculitis 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, coxsackie 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 cutaneous 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 familial 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 vasculitis 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 Enhanced 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 immunosuppressive 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 specific quality of life can be explained by the long period of time (mean±SD:74,23±59,5) post DVT.

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

	Baseline mean±SD	Last visit mean±SD	change mean±SD	P value
VEINES-QoL	89,73±16,93	91,25±16,18	1,52±12,07	<sup>a</sup> 0,499
VEINES-Sym	39,23±9,32	40,20±9,28	0,98±6,44	<sup>a</sup> 0,285
PCS-1	43,22±10,56	45,55±10,24	2,33±8,36	<sup>a</sup> 0,111
MCS-1	46,43±9,03	51,38±8,81	4,95±10,96	<sup>a</sup> 0,006**
BSAS	21,36±15,24	19,86±14,82	-1,50±13,54	<sup>a</sup> 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 ( $p<0.0001$ ) comorbidities.

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 ( $<50\text{nmol/L}$ ) 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 systematically 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. Eleven cases were treated with glucocorticoid (mean dose 58.5 mg/d, prednisone or equivalent), including one case treated with methylprednisolone pulse 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 ( $\geq 4$ ). 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 ( $27.1\pm16.6$  versus  $20.1\pm17.6$ ) 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 acrocyanosis, 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 branches, 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 sub-cortical bilateral front. Cyclophosphamide 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 from 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- $\gamma$ 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  $\geq 70\%$  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  $\geq 70\%$  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,  $\geq 70\%$  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  $44\pm 9$  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  $150 \mu\text{g/g}$  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  $>150 \mu\text{g/g}$  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  $1125\pm 800 \mu\text{g/g}$  (95%CI: 341 to 1908) among symptomatic patients with ulcers (n=4) and  $209\pm 213 \mu\text{g/g}$  (95%CI: 22 to 396) among symptomatic patients without ulcers (n=5). On the other hand, the mean FC was  $243\pm 73 \mu\text{g/g}$  (95%CI: 158 to 328) among asymptomatic patients with ulcers (n=3) and  $95\pm 160 \mu\text{g/g}$  (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  $>150 \mu\text{g/g}$  (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.

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## P84.

### A BEHÇET'S DISEASE PATIENT WITH PERICARDIAL 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 systems. 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.

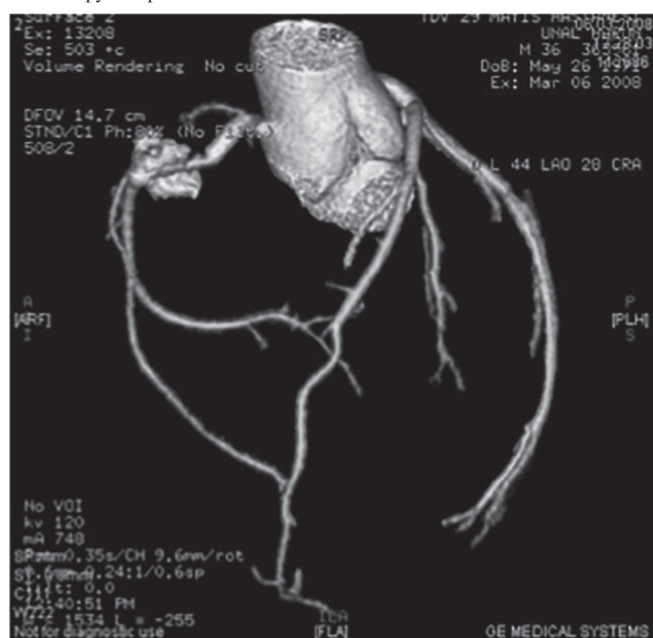


Fig. 1. Coronary artery pseudoaneurysm demonstrated on right coronary CT angiography.

**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.

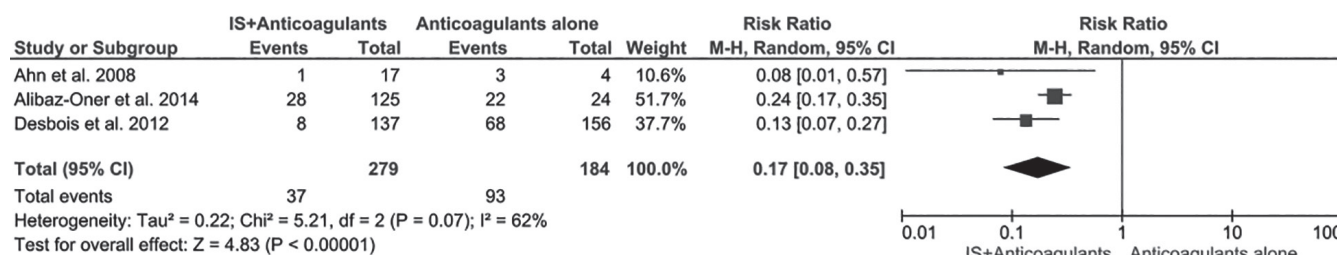


Fig. 1. (P-85)

## 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 cough 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 deficiency 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  $\geq 2$  (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.** 20 patients were included in the study, with ages at the time of the diagnosis between 13 and 60 years, 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 13 cases. The genetic marker, HLA B51, was tested in 6 cases and in 5 patients (87%).

Ophthalmological involvement was present in 6 cases, posterior uveitis (5 cases), one patient presented choriorretinitis. One uncontrolled ophthalmologic involvement in the form of posterior uveitis led to vision loss.

Recurrent venous thrombosis was observed in 6 cases while 1 case 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 3 cases, 2 of 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, 15 patients 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 8 cases and 1 patient (who associated psoriatic arthritis) received biologic treatment (adalimumab). The cumulative dosage of cyclophosphamide was between 3.6g and 20 grams in 6 to 20 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. Cardio-thrombotic 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 endocochléaire 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 regularly subjected to cochlear investigations to detect inner ear involvement.

## P91.

## MEAN PLATELET VOLUME 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:  $49.2 \pm 11.3$  years) and 160 age- & sex-matched healthy subjects (120 females, age:  $49.1 \pm 11.6$  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 ( $9.053 \pm 0.916$  vs.  $7.988 \pm 0.538$  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 ( $6.952 \pm 1.700$ ,  $7.250 \pm 1.676$ , and  $7.321 \pm 1.688$  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-fourth 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 International classifications criteria for Behçet's disease. Children diagnosed  $\leq 16$  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 additional 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 disease and 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 prevalence. 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 $\pm$ 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 $\pm$ SD in vascular and non-vascular BS were 41.5  $\pm$ 24.4/42.3 $\pm$ 34.8 vs 24.2 $\pm$ 16.4/13.4 $\pm$ 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 recurrent 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 aphthosis (n=4), genital aphthosis (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 manifestations were: head ache (n=3), piriformis syndrome (n=3), irritability 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 peduncle (n=2), periventricule (n=2) and thalamus (n=1). One had a cerebral vein thrombosis. All the patients had 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 phe-

nobarbital. Neurological manifestations had disappeared under steroids 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 reveals 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 prevalence 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 prevalence 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.

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**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  $\geq 5$  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 <sup>18</sup>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-(<sup>18</sup>F) fluoro-D-glucose (<sup>18</sup>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 ( $\pm 12$ ) 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 ( $\pm 12$ ) 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 Megabecquerels of <sup>18</sup>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 (P<sub>fwe</sub> 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 (P<sub>fwe</sub> 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.

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## 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)  $\geq 126$  mg/dL in at least 2 occasions. IFG was defined according to ADA criteria (4) if FPG  $\geq 100$  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.

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## 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 ADAMANTIADIS-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- $\alpha$ -2a (IFN $\alpha$ -2a) led to a reduction of the clinical manifestations except for occasional occurrence of oral ulcers. Two weeks after initiation of IFN $\alpha$ -2a, the patient complained about fatigue and mood fluctuations, so that after diagnosing an interferon-induced depression, treatment with citalopram 20 mg/d, lorazepam 4x0.5 mg/d and promethazine 20 mg/d was initiated. Moreover, after one-year treatment with IFN $\alpha$ -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, IFN $\alpha$ -2a therapy could be the cause of the hyperprolactinemia. Mastodynia and hyperprolactinemia have not yet been described as potential side effects of IFN $\alpha$ -2a. The influence of interferon on the prolactin secretion is controversial: According to Hofland *et al.* IFN $\alpha$ -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 IFN $\beta$ -therapy. IFN- $\alpha$  and - $\beta$  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 IFN $\alpha$ -2a.

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## 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 38x34 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.