P124.

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

Soriano A.[1], Croci S.[2], Cimino L.[3], Fontana L.[3], Bonacini M.[2], Zerbini A.[2], Parmeggiani M.[2], Salvarani C.[1]
[1]Rheumatology Unit, Arcispedale Santa Maria Nuova – IRCCS, Reggio Emilia, Italy; [2]Unit of Clinical Immunology, Allergy and Advanced Biotechnologies, Arcispedale Santa Maria Nuova – IRCCS, Reggio Emilia, Italy; [3]Ocular Immunology Unit, Ophthalmology Department, Arcispedale Santa Maria Nuova – IRCCS, Reggio Emilia, Italy

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

Epidemiology and Genetics

P18.

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

Elfishawi M.[1], Elgengehy F.[1], Mossallam G.[2], Elfishawi S.[2], Elfishawi M.[1], Metwally I.[1]
[1]Kasr Alainy Hospital, Cairo University , Department of Rheumatology, Egypt;
[2]National Cancer Instiute, Clinical pathology Department, Cairo University, Egypt

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

References

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

P20.

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

Izmailova F.[1], Kudaev M.[2], Alekberova Z.[1]
[1]V.A. Nasonova Research Institute of Rheumatology, Moskow. Russia; [2] Dagestan State Medical Academy, Makhachkala, Dagestan Republic, Russia.

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

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

P21.

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

Khabbazi A., Alipour S., Farhadi J., Sakhinia E.
Connective Tissue Diseases Research Center, Internal Medicine Department, Tabriz, Iran

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

P22.

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

Kirino Y.[1], Ideguchi H.[2], Suda A.[3], Sugiyama Y.[1], Tsuchida N.[1], Kunishita Y.[1], Kamiyama R.[1], Watanabe T.[1], Uehara T.[4], Minegishi K.[5], Tamura M.[1], Yoshimi R.[1], Yamazaki T.[6], Asami Y.[1], Sekiguchi A.[7], Ihata A.[8], Takeno M.[9], Ohno S.[5], Igarashi T.[6], Nagaoka S.[2], Ishigatsubo Y.[1], Ueda A.[1], Nakajima H.[1]
[1]Yokohama City University Graduate School of Medicine, Stell Cell and Immune Regulation Department, Yokohama City, Japan; [2]Yokohama Minami Kyosai Hospital, Yokohama City, Japan; [3]Yokosuka City Hospital, Yokosuka, Japan; [4]Chigasaki City Hospital, Chigasaki, Japan; [5]Yokohama City University Medical Center, Yokohama City, Japan; [6]Yamato City Hospital, Yamato, Japan; [7]Fujisawa City Hospital, Fujisawa, Japan; [8]National Hospital Organization Yokohama Medical Center, Yokohama City, Japan; [9]Nippon Medical School Graduate School of Medicine, Tokyo, Japan

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

P23.

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

Al-Okaily F., Al-Rashidi S., Al-Balawi M., Arfin M., Al-Asmari A.
Prince Sultan Military Medical City Riyadh, Rheumatology Department, Riyadh, Saudi Arabia

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

P24.

THE PREVALENCE OF BEHÇET'S DISEASE IN NORTH JORDAN

Madanat W.[1], Alawneh K.[2], Smadi M.[3], Saadeh S.[2], Omari M.[2], Anas, Hani B.[2], Yazici H.[4]
[1]Jordans Friends of Behçet's Disease Patients Society, Rheumatology Department, Amman, Jordan; [2]Department of Medicine, King Abdullah Hospital, Jordan University of Science and Technology, Irbid, Jordan; [3]Department of Mathematics and Statistics, Jordan University of Science and Technology, Irbid, Jordan; [4]Cerrahpaşa Medical School Hospital – University of Istanbul, Turkey

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

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

P25.

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

Kitaichi N.[1], Horie Y.[1], Namba K.[2], Ishida S.[2], Ohno S.[2]
[1]Health Sciences University of Hokkaido, Ophthalmology Department, Sapporo, Hokkaido, Japan; [2]Hokkaido University Graduate School of Medicine, Hokkaido, Japan

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

P26.

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

Meguro A.[1], Horita N.[1], Takeuchi M.[2], Ohno S.[3], Mizuki N.[1]
[1]Yokohama City University Graduate School of Medicine, Department of Ophthalmology and Visual Science, Yokohama City, Japan; [2]National Human Genome Research Institute, National Institutes of Health, Bethesda, USA; [3]Hokkaido University Graduate School of Medicine, Hokkaido, Japan

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

P27.

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

Fehim Esen
Devrek State Hospital, Ophthlamology Clinic, Zonguldak, Turkey

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

P28.

BEHÇET'S DISEASE: ETHNOS AND FAMILIAL AGGREGATION

Alekberova Z.[1], Izmailova F.[1], Kudaev M.[2], Denisov L.[1], Nasonov E.[1]
[1]V.A. Nasonova Research Institute of Rheumatology, Moskow. Russia;
[2]Dagestan State Medical Academy, Makhachkala, Dagestan Republic, Russia.

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

P29.

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

Kono H., Asako K., Kikuchi H.
Teikyo University School of Medicine, Internal Medicine Department, Kawasaki, Kanagawa, Japan

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

P30.

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

Pain C.[1], Rice H.[1], Beresford M.[2], Brogan P.[3], Fortune F.[4], Moots R.[5], Murphy R.[6]
[1]Alder Hey Children's NHS Foundation Trust, Paediatric Rheumatology Department, Liverpool, UK; [2]Institute of Translational Medicine, University of Liverpool & Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [3]Great Ormond Street Hospital, London, UK; [4]Queen Mary School of Medicine and Dentistry, London, UK; [5]University Hospital Aintree, Liverpool, UK; [6]Royal Hallamshire Hospital, Sheffield, UK

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

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

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

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

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

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

Discussion. Study findings are limited at this stage related to the small number of completed cases which have been analysed. Incidence and prevalence rates will be calculated once completed 12 month's data is obtained. However, case reporting highlights the extreme rareness of Behçet's syndrome in children within the UK. Comparison of frequency of disease manifestations with non-UK cohorts will be important in future analysis as there may be differences in our UK population, for example a low frequency of ocular involvement. This is important when considering the design of healthcare services that address the needs of children.
Funding. Alder Hey Children's Charity, Behçet's Syndrome Society, Vasculitis UK, unrestricted grants under direction of Professor Fortune & Professor Moots.
REF The ICBD. J Eur Acad Derm Ven 2014

P31.

ARTICULAR MANIFESTATION OF BEHÇET DISEASE IN NORTHERN ITALY

Berti A.[1], Felicetti M.[2], Bortolotti R.[3], Cavatorta F.[3], Paolazzi G.[3]
[1]IRCCS San Raffaele Scientific Institute, Department of Medicine and Clinical Immunology, Milan, Italy; [2]University of Padua, Department of Rheumatology, Padua, Italy; [3]Santa Chiara Hospital, Department of Rheumatology, Trento, Italy

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

P32.

A DARWINIAN VIEW OF BEHÇET'S DISEASE

Wallace G.[1], Smith R.[2], Roberts A.[1]
[1]University of Birmingham, Institute for Inflammation and Ageing, Birmingham, UK; [2]University of Liverpool, Liverpool, UK

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

P33.

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

Schirmer M.[1], Sadeghi Abdollahi B.[2], Davatchi F.[2], Zouboulis C.[3]
[1]Medical University of Innsbruck, Department of Internal Medicine, Clinic VI (Infectiology/Immunology, Pulmology, Rheumatology), Innsbruck, Austria; [2]Tehran University of Medical Sciences, Tehran, Iran; [3]Dessau Medical Center, Division of Evidence Based Dermatology, and Departments of Dermatology, Venereology, Allergology and Immunology, Dessau, Germany

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

P34.

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

Esatoglu S.N., Seyahi E., Ugurlu S., Hatemi G., Melikoglu M., Hamuryudan V., Yurdakul S.
Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey

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

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

References

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

P35.

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

Gerardi M.C., Batticciotto A., Talotta R., Ditto M.C., Atzeni F., Sarzi-Puttini P.
ASST Fatebenefratelli L. Sacco University Hospital, Rheumatology Unit, Internal Medicine Department, Milan, Italy

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

P36.

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

Lee Y.-A., Hong S.-J.
Kyung Hee University Hospital, Rheumatology Department, Seoul, South Korea

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

P37.

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

Padula M.C.[1], D'Angelo S.[2], Pellizzieri E.[1], Gilio M.[2], Leccese P.[2], Lofrano M.[2], Olivieri I.[2], Martelli G.[1]
[1]Department of Science, University of Basilicata, Potenza, Italy; [2]Rheumatology Division, San Carlo Hospital, Potenza, Italy

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

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

References

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

P38.

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

Padula M.C.[1], D'Angelo S.[2], Amato G.C.[1], Giuzio R.[1], Pellizzieri E.[1], Gilio M.[2], Leccese P.[2], Olivieri I.[2], Martelli G.[1]

[1]Department of Science, University of Basilicata, Potenza, Italy; [2]Rheumatology Division, San Carlo Hospital, Potenza, Italy

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

References

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

Clinical and Outcome Measures

P39.

ELEVATED SERUM PROLACTIN IN EGYPTIAN PATIENTS WITH BEHÇET'S SYNDROME

Elfishawi M.[1], Elgengehy F.[1], Mossallam G.[2], Elfishawi S.[2], Elfishawi M.[1], Metwally I.[1]

[1]Kasr Alainy Hospital, Cairo University , Department of Rheumatology, Egypt; [2]National Cancer Instiute, Clinical pathology Department, Cairo University, Egypt

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

References

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

P40.

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

Kaneko F.[1], Togashi A.[1], Nomura E.[1], Nakamura K.[2]

[1]Southern TOHOKU Research Institute for Neuroscience, Institute of Dermato-Immunology and Allergy, Koriyama, Japan; [2]Saitama Medical University, Saitama, Japan

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