## P102.

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

Carriero A., Corrado A., Di Bello S., Tiso A., D'Onofrio F., Cantatore F.P.
Rheumatology Clinic, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy.

**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

Di Bello S., Corrado A., Di Bello V., Carriero A., d'Onofrio F., Cantatore F.P.
Rheumatology Clinic, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy.

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

# Treatment

## P103.

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

Karagiannidis I.[1], Altenburg A.[2], Kanaki T.[1], Zouboulis C.C.[1]
[1]Dessau Medical Center, Departments of Dermatology, Venereology, Allergology and Immunology, Dessau, Germany; [2]Specialist Clinic Bad Bentheim, Department of Dermatology and Allergology, Bad Bentheim, Germany

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

## P104.

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

Khabbazi A., Ebrahimi A., Hejazi M.E.
University of Medical Sciences, Internal Medicine Department, Connective Tissue Diseases Research Center, Tabriz, Iran

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

## P105.

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

Capittini C.[1], de Amici M.[2], De Silvestri A.[1], Scudeller L.[1], Aronico N.[3], Giuffrida P.[3], Antoniazzi E.[4], di Stefano M.[3], Tinelli C.[1]
[1]IRCCS Policlinico San Matteo Foundation , Biometry and Clinical Epidemiology, Pavia, Italy; [2]IRCCS Policlinico San Matteo Foundation , Immuno-Allergy Laboratory, Pavia, Italy; [3]IRCCS Policlinico San Matteo Foundation , Internal Medicine Department, Pavia, Italy; [4]IRCCS Policlinico San Matteo Foundation , Ophthalmology Department, Pavia, Italy

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

## P106.

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

Capittini C.[1], De Silvestri A.[1], Scotti V.[2], Scudeller L.[1], Tinelli C.[1]
[1]IRCCS Policlinico San Matteo Foundation, Biometry and Clinical Epidemiology, Pavia, Italy; [2]IRCCS Policlinico San Matteo Foundation, Scientific Documentation Service, Pavia, Italy

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

## P107.

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

Sfikakis P.P., Arida A., Panopoulos S., Fragkiadaki K., Pentazos G., Laskari A., Tektonidou M., Markomichelakis N.
Athens University Medical School, First Department of Propedeutic and Internal Medicine, Athens, Greece

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

## P108.

### THE EFFICACY OF TACROLIMUS AGAINST INTESTINAL BEHÇET'S DISEASE

Kobashigawa T., Omori T., Nanke Y., Iizuka B., Yamanaka H., Kotake S.
Tokyo Womens Medical University, Tokyo, Japan

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

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

**References**

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

## P109.

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

Benamour S.
47, Angle Bd D'ANFA, Bd MOulay Youssef, Internal Medicine Department, Casablanca, Morocco

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

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

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

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

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

## P110.

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

Echchilali K., Arif F., Rihani N., Bouissar W., Moudatir M., Allaoui F.-Z., Elkabli H.
University Hospital Ibn Rochd, Internal Medicine Department, Casablanca, Morocco

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

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

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

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

## P111.

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

Adeeb F., Stack A., Fraser A.
University Hospital Limerick, Rheumatology Department, Limerick, Ireland

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

## P112.

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

Adizie T., Situnayake D., Carruthers D.
Birmingham City Hospital, RheumatologyDepartment, Birmingham, UK

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

## P113.

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

Zheng W., Shi J., Zhao C., Zhang M.
Peking Union Medical College Hospital, Department of Rheumatology, Beijing, China

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

## P114.

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

Gül A.[1], Demir G.A.[2], Kürtüncü M.[2], Erer B.[1], Sevgi S.[3], Turgay S.[3]
[1]Istanbul University Faculty of Medicine, Internal Medicine Department, Rheumatology Division, Istanbul, Turkey; [2]Bilim University Faculty of Medicine, Neurology Department, Istanbul, Turkey; [3]Novartis Medical Department, Turkey

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

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

## P115.

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

Yazici Y., Bernstein H., Swearingen C.J.
NYU Hospital for Joint Diseases, Rheumatology Department, New York, USA

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

## P116.

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

El-Haj N.[1], Nauf G.[1], Altenburg A.[2], Wild T.[1], Zouboulis C.C.[1]
[1]Dessau Medical Center, Departments of Dermatology, Venereology, Allergology and Immunology, Dessau, Germany; [2]Specialist Clinic Bad Bentheim, Department of Dermatology and Allergology, Bad Bentheim, Germany

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

**References**

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

## P117.

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

Padoan R., Felicetti M., Schiavon F.
University of Padua, Department of Rheumatology, Padua, Italy

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

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

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

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

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

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

## P118.

### THE EFFECT OF MEDICATION ON THE TREATMENT OUTCOMES OF BEHÇET DISEASE

Senusi A.[1], Buckland M.[2], Jawad A.[2], Kidd D.[2], Stanford M.[2], Fortune F.[1]
[1]Blizard Institute, Institute of Dentistry, Barts and the London School of Medicine and Dentistry, Centre for Clinical and Diagnostic Sciences, London, UK; [2]Behçet's Centre of Excellence, Royal London Hospital, London, UK

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

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

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

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

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

## P119.

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

Lopalco G.[1], Emmi G.[2], Gentileschi S.[3], Rotondo C.[1], Vitale A.[3], Silvestri E.[2], Becatti M.[4], Cavallo I.[2], Frediani B.[3], Iannone F.[1], Cantarini L.[3]
[1]Interdisciplinary Department of Medicine, Rheumatology Unit, University of Bari, Bari, Italy; [2]Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy; [3]Research Center of Systemic Autoinflammatory Diseases and Behçet's Disease Clinic, Department of Medical Sciences, Surgery and Neurosciences, University of Siena, Siena, Italy; [4]Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Italy

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

## P120.

### SURGICAL METHOD FOR AORTIC ROOT INVOLVEMENT OF BEHÇET DISEASE

Ghang B.[1], Choo S.J.[2], Kwon O.[1], Hong S.[1], Kim Y.-G.[1], Lee C.-K.[1], Yoo B.[1]
[1]University of Ulsan College of Medicine, Asan Medical Center, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea; [2]University of Ulsan College of Medicine, Asan Medical Center, Department of Thoracic and Cardiovascular Surgery, Seoul, Korea

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

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

## P121.

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

Caso F., Del Puente A., Foglia F., Benigno C., Bertolini N., Bottiglieri P., Girolimetto N., Scotti N., Bascherini V., Schiattarella A., Peluso R., Scarpa R., Costa L.
Rheumatology Unit, Department of Clinical Medicine and Surgery, University Federico II, Naples, Italy.

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

## P122.

### USTEKINUMAB EFFICACY IN REFRACTORY BEHÇET'S DISEASE

Costa L., Del Puente A., Foglia F., Benigno C., Bottiglieri P., Girolimetto N., Bascherini V., Scotti N., Schiattarella A., Peluso R., Scarpa R., Caso F.
Rheumatology Unit, Department of Clinical Medicine and Surgery, University Federico II, Naples, Italy

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

## P125.

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

Xenitidis T.[1], Berger C.[2], Jung T.[2], Henes J.[1], Koetter I.[3]
[1]Dept. Internal Medicine II, University Hospital, Tuebingen, Germany; [2]Delenex Therapeutics AG, Zurich, Switzerland; [3]Internal Medicine 4, Asklepios Clinic Altona, Hamburg, Germany.

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

**Disclosure of Interest:** T. Xenitidis Grant/research support from: Unrestricted grant from Delenex therapeutics, C. Berger: None declared, T. Jung: None declared, J. Henes Grant/research support from: Unrestricted grant from Delenex therapeutics, I. Koetter Grant/research support from: Unrestricted grant from Delenex therapeutics

DOI: 10.1136/annrheumdis-2016-eular.3898

**Reference**

Ann Rheum Dis 2016;75(Suppl2): 786.