P102.

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

Carriero A., Corrado A., Di Bello S., Tino A., D’Onofrio F., Cantatore F.P.
Rheumatology Unit of 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 diarrea 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 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 ulcerations, posterior uveitis and HLA-B51 positive. There may be a multifactorial etiology and other genetic pattern in addition to HLA B51.

P103.

PERSISTENT HYPERPROLACTINEMIA DURING THERAPY WITH INTERFERON-Α-2A IN A PATIENT WITH SYSTEMIC ADMANTIADES-BEHÇET’S DISEASE

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

Adamantiaides-Behçet’s disease is an immune-mediated vasculitis with relapsing course. It is characterised by the classic clinical triads of oral aphthous ulcers, genital ulcers and uveitis. We report on a 37-year-old woman suffering from Adamantiaides-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 (IFN-α2a) led to a reduction of the clinical manifestations except for occasional occurrence of oral ulcers. Two weeks after initiation of IFN-α2a, the patient complained about fatigue and mood fluctuations, so that after diagnosing an interferon-induced depression, treatment with citalopram 20 mg/d, lorazepam 4x0.5 mg/d and promethazine 20 mg/d was initiated. Moreover, after one-year treatment with IFN-α2a, 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 hypothroidism, chronic renal insufficiency, stress, pregnancy and several drugs. In our patient, it could be assumed that antidepressants and neuroleptics have led to increased circulating prolactin levels, although the latter insisted after discontinuation of the antidepressive therapy. On the other hand, IFN-α2a therapy could be the cause of the hyperprolactinemia. Mastodynia and hyperprolactinemia have not yet been described as potential side effects of IFN-α2a. The influence of interferon on the prolactin secretion is controversial: According to Hoffland et al. IFN-α2a inhibits the secretion of prolactin in cultured human pituitary adenomas. In contrast, Yamaguchi et al. showed that the interferon family stimulates the secretion of prolactin in vitro. Furthermore, patients with multiple sclerosis have been reported to develop hyperprolactinemia during IFN-β therapy. IFN-α and -β target the same receptor and they have therapeutic similarities, but not identical effects and side effects. The above observations could support, but are not sufficient to confirm a correlation between a symptomatic hyperprolactinemia and a treatment with IFN-α2a.

P104.

COMPLETE RESOLUTION OF PULMONARY ARTERY ANEURYSM IN A PATIENT WITH BEHÇET’S DISEASE WITH INFIXIMAB

Khabazii 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 38x34 mm, artery wall thickness and thrombosis in the lumen of left pulmonary artery. He refused conventional treatment with cyclophosphamide. Therefore, infliximab (IFX) 3 mg/kg, prednisolone 1mg/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.
PLASMA CYTOKINES AS BIOMARKERS FOR CLINICAL RESPONSE DURING NINE MONTHS OF INTRAVENOUS IMMUNOGLOBULINS THERAPY IN A BEHÇET DISEASE PATIENT UNSUITABLE FOR IMMUNOSUPPRESSION

Capitini C.1, de Amici M.2, De Silvestri A.1, Scudeller L.1, Aronica N.1, Giuffrida P.1, Antoniazzi E.1, de Stefano M.1, Tinelli C.1

1IRCCS Policlinico San Matteo Foundation, Biometry and Clinical Epidemiology, Pavia, Italy; 2IRCCS Policlinico San Matteo Foundation, Immunology Department, Pavia, Italy; 3IRCCS Policlinico San Matteo Foundation, Internal Medicine Department, Pavia, Italy; 4IRCCS 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 to severe herpetic reactivations in the trigeminal ganglion. She presented with oral and genital aphthosis, pseudoephidictia, papulopapulose 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 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 occurred: 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 paresis, headache, 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). Before each infusion, an aliquot of whole blood was collected in EDTA to assess the plasma concentrations of IL-1β, IL-2, IL-6, IL-10, CXCL8, IFN-γ and TNF-α by ELISA (normal values: IL-1β <5 pg/ml; IL-2 <11 pg/ml; IL-6 <10 pg/ml; IL-10 <15 pg/ml; CXCL8 <31 pg/ml; TNF-α <15 pg/ml; IFN-γ <15 pg/ml). Before treatment, only CXCL8 levels were high (254 pg/ml), and she presented with oral aphthosis, arthralgia, finger swelling in the morning, joint stiffness, pseudoephidictia on legs, asthenia, arm paresis, 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). After 15 days from the first IVIG infusion, her clinical signs started to improve and CXCL8 levels rapidly decreased (7 pg/ml). The IVIG infusion subsequently 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.

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=5). 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 oral, 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 remained 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.

P107.
OUTCOMES OF BIOLOGIC TREATMENT REGIMENS FOR SEVERE BEHÇET’S DISEASE: CURRENT EXPERIENCE FROM A SINGLE ACADEMIC CENTER

Silikakis P.P., Arika A., Panopoulos S., Fragkiadaki K., Pentazos G., Laskari A., Tektonidou M., Markomichelakis N.

Athenos 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 regimes 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=5). 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 oral, 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 remained 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., Nankan 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 MacRoloide 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), ulcerative colitis, 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 aphthous 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 9.44 x 10^9/L (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, colchicine (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 ileocecal valve; thus, he was diagnosed with having intestinal BD and he was treated with prednisolone (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 recurrent. 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 menora 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 colonoscopy showed mucosal healing; 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

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 aphthosis 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?
Methods. 5 patients with Behçet’s and major vascular involvement who required surgical 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.

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 hand and vascular 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 patient had a limb amputation and another had a renal artery pseudoaneurysm embolisation. 4 of our 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 anastomotic leak at the site of his previous right femoral arterial graft. Cases 1, 2 and 5 were on immunosuppression at the time of their respective 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 aneurysm disease in Behçets, while cases 2 and 5 received cyclophosphamide, with case 2 suffering a further aneurysm while on this.

Conclusions. It is known that patients with Behçet’s 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.
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 a 10-cm visual analog 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 a ≥50% improvements in patient’s and physician’s global assessments by using VAS, and a ≥50% reduction in CRP values; along with stable or a ≥20% reduction in anemia in patients with arterial involvement, and stable or ≥20% reduction of 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.

P116. DEEP ABDOMINAL WALL ULCERATION IN A ADMANIATODES-BEHÇET’S DISEASE PATIENT

El-Haj N.1, Nauf G.1, Altenburg A.2, Wild T.2, Zouboulis C.C.1
1Dessau Medical Center, Departments of Dermatology, Venerology, Allergology and Immunology, Dessau, Germany; 2Specialist 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 aphthous 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 occurred 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. Continuous 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 submucosal 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 constant dose of 5mg was reached. The above led to remission.

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

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

Background. Behçet’s disease (BD) is a systemic syndrome with protein 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
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 popular lesion developed within 24h after skin prick by sterile needle was considered consistent with a positive pathergy test. HLA-B51 was present. An ophthalmological 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 Cyto- sporin (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 (efavirenz, 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

Sensui A.1, Buckland M.2, Jawad A.3, Kidd D.2, Stanford M.2, Fortune F.1

1Blizard Institute, Institute of Dentistry, Barts and the London School of Medicine and Dentistry, Centre for Clinical and Diagnostic Sciences, London, UK; 2Behçet’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 (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.

S-186
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 impor-
tant 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
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.4, Vitale A.4, Silvestri E.3, Becati M.4, Cavallo I.4, Frediani B.1, Iannone F.1, Cantarini L.1
1Interdisciplinary Department of Medicine, Rheumatology Unit, University of Bari, Bari, Italy; 2Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy; 3Research Center of Systemic Autoinflammatory Diseases and Behçet’s Disease Clinic, Department of Medical Sciences, Surgery and Neurosciences, University of Siena, Siena, Italy; 4Department 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 re-
combinant 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 (BDCF) has been used before start-
ing 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 worsen-
ing of symptoms after 4.16±1.21 months, whereas a satisfactory response was achieved in seven patients (55.84%) who were still on CZP therapy at the last follow-up visit (after 9.28±3.03 months of treatment). The mean decrease of BD-
CZF between the first and last visit was 0.306±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 sug-
gest 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.3, Hong S.4, Kim Y.-G.4, Lee C.-K.1, Yoo B.1
1University of Ulsan College of Medicine, Asan Medical Center, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea; 2University of Ulsan College of Medicine, Asan Medical Center, Division 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 destruc-
tion 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 AVR was performed in 8 cases
and composite graft ARR in 6 cases. According to the definition of the event;
aortic valve/graff 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 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 (me-
dian; 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, ad-
ministration 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 biopro-
thesis ARR. Composite graft ARR might be a surgical option in patients requir-
ning ARR for aortic root involvement of Behçet disease.

Disclosure. Byongzgu Ghang, None; Ohchun 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
Casó F., Del Puente F., Foglia F., Benigno C., Bertolini N., Bottiglieri P.,
Giroliminetto N., Scotti N., Bascherini V., Schiattarella A., Peluso R., Scarpa R.,
Costa L., Rhenumatology Unit, Department of Clinical Medicine and Surgery, University Federico II, Naples, Italy.

Behçet’s disease (BD) is a chronic and relapsing multisystemic inflammatory
disease (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 le-
sions 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/bi-
weekly) 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 of was 37.83 months (range 6-84 months).
After 6 months of therapy with anti-TNF-α, eleven patients showed a good re-

course 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.
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 patient had 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 induce 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.

In conclusion, we report herein a case of BD successfully treated with ustekinumab at a 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). 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 (Day 1), 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: None declared, J. Koetter: None declared, I. Koetter Grant/research support from: unrestricted grant from Delenex therapeutics, C. Berger: None declared, T. Jung: None declared. DLX105 is a strong development candidate to treat flaring mucocutaneous Behçet’s Disease.

Reference