
Behçet's syndrome

A bird's eye review of the recent literature

edited by Vedat Hamuryudan and Hasan Yazici

Reviews

Author: Barnes CG.

Title: Treatment of Behçet's syndrome.
Rheumatology 2006; 45: 245-7.

Authors: Bonfioli AA, Orefice F.

Title: Behçet's disease.
Semin Ophthalmol 2005; 20: 199-206.

Epidemiology

Authors: Mumcu G, Inanc N, Ergun T, Ikiz K, Gunes M, Islek U, Yavuz S, Sur H, Atalay T, Direskeneli H.

Title: Oral health related quality of life is affected by disease activity in Behçet's disease.
Oral Diseases 2006; 12: 145-51.

Summary: According to this cross-sectional study patients with BS have impaired oral and general health related quality of life scores compared to healthy controls. Patients with active disease have significantly impaired quality of life scores when compared to patients with inactive disease and to control patients with recurrent oral ulceration. The Turkish versions of oral healthy related quality of life questionnaires were also found to be valid and reliable in this study.

Pathogenesis

Authors: Nishiyama M, Takahashi M, Manaka K, Suzuki S, Saito M, Nakae K.

Title: Microsatellite polymorphisms of the MICA gene among Japanese patients with Behçet's disease.
Can J Ophthalmol 2006; 41: 210-5.

Summary: In contrast to previous work, this study did not find a difference between patients and controls in the phenotype frequencies of the MICA allele. On the other hand, the MICA-A6 allele showed an association with HLA B51.

Authors: Kötter I, Koch S, Vonthein R, Rückwaldt U, Amberger M, Günaydin I, Zierhut M, Stübiger N.

Title: Cytokines, cytokine antagonists and soluble adhesion molecules in patients with ocular Behçet's disease treated with human recombinant interferon alpha 2a. Results of an open study and review of the literature.
Clin Exp Rheumatol 2005; 23 (Suppl 38): S20-S26.

Summary: Serum of 50 BS patients with severe and resis-

tant uveitis were collected at several time points during interferon alpha 2a treatment. Compared to healthy controls, the influence of interferon alpha was mainly on cytokine antagonists and soluble adhesion molecules.

Authors: Yurdakul S, Hekim N, Soysal T, Fresko I, Bavunoglu I, Ozbakir F, Tabak F, Melikoglu M, Hamuryudan V, Yazici H.

Title: Fibrinolytic activity and d-dimer levels in Behçet's syndrome.
Clin Exp Rheumatol 2005; 23 (Suppl 38): S53-S58.

Summary: Thrombophlebitis is a prominent feature of BS but whether this is a result of endothelial damage or a defect in coagulation or fibrinolytic activity or a combination of them is not well understood. In this cross-sectional study the levels of tissue type plasminogen activator were significantly lower in BS patients with acute thrombophlebitis compared to patients with acute deep vein thrombosis related to other causes, whereas the levels of plasminogen activator inhibitor were not different between groups. These results combined with increased levels of d-dimer may point to impaired fibrinolysis in BS.

Authors: Ricart JM, Vaya A, Todoli J, Calvo J, Villa P, Estelles A, Espana F, Santolaria M, Coralla D, Aznar J.

Title: Thrombophilic risk factors and homocysteine levels in Behçet's disease in eastern Spain and their association with thrombotic events.
Thromb Haemost 2006; 95: 618-24.

Summary: This study found no differences regarding thrombophilic risk factors between patients with BS and healthy controls. Three out of 23 patients with thrombophlebitis had mutations of the prothrombin G20210A compared to none of 56 patients without thrombophlebitis.

Authors: Bozoglu E, Dinc A, Erdem H, Pay S, Simsek I, Kocar IH.

Title: Vascular endothelial growth factor and monocyte chemoattractant protein-1 in Behçet's patients with venous thrombosis.

Clin Exp Rheumatol 2005; 23 (Suppl 38): S42-S48.

Summary: The levels of angiogenic cytokines are significantly higher in BS patients with acute thrombophlebitis compared to BS patients with chronic thrombophlebitis and patients having only mucocutaneous involvement according to this cross-sectional study. The increase observed was comparable with that found among the controls who had acute thrombosis related to other causes.

Clinical aspects

Authors: Kaklamani VG, Tzonou A, Kaklamani PG.

Title: Behçet's disease associated with malignancies. Report of two cases and review of the literature.

Clin Exp Rheumatol 2005; 23 (Suppl 38): S35-S41.

Summary: Of the 128 BS patients from a database, 2 developed solid malignancies during a median follow-up of 10 years. The age standardized ratio for cancer in BS patients was 1600 per 100,000 in 10 years which was lower but not significantly different from that in the Greek general population. The paper continues with a comprehensive review of the literature and discusses the reported discrepancies in the frequency of malignancy in BS.

Authors: Bozkurt A, Akpinar O, Uzun S, Akman A, Arslan D, Birand A.

Title: Echocardiographic findings in patients with Behçet's disease.

Am J Cardiol 2006; 97: 710-5.

Summary: This study evaluated cardiac functions in 54 BS patients with mainly mucocutaneous involvement by using Doppler tissue imaging and pulse wave Doppler methods. The dimensions of the cardiac chambers and left ventricular systolic function of the patients were not different from those of healthy controls while at rest and following exercise. The limited disease of the study patients and exclusion of those with cardiovascular morbidity could have influenced the results.

Authors: Keser G, Aksu K, Tamsel S, Ozmen M, Kitapcioglu G, Kabaroglu C, Killi R, Bayindir O, Doganavsargil E.

Title: Increased thickness of the carotid artery intima media assessed by ultrasonography in Behçet's disease.

Clin Exp Rheumatol 2005; 23 (Suppl 38): S71-S76.

Summary: Endothelial cell dysfunction is widely regarded as the initial lesion in atherosclerosis. Increased intima-media thickness of the carotid artery is significantly correlated with endothelial cell dysfunction. Carotid intima media thickness and plaque frequency of BS patients were significantly higher compared to that observed among the healthy controls but significantly lower compared to patients with SLE. These findings further support the contention that atherosclerosis is mild in BS compared to other inflammatory diseases like SLE and RA.

Authors: Chang HK, Kim SK, Lee SS, Rhee MY.

Title: Arterial stiffness in Behçet's disease: increased regional pulse wave velocity values.

Ann Rheum Dis 2006; 65: 415-6.

Summary: Measurement of pulse wave velocity is an indicator of arterial stiffness which develops as a result of endothelial dysfunction. The importance of this study was that it measured pulse wave velocity values at 4 different sites. The values were higher in all sites among 53 BS patients compared to controls indicating to increased arterial

stiffness. The lack of a suitable diseased control group in the study is a problem.

Authors: Duzgun N, Ates A, Aydintug OT, Demir O, Olmez U.

Title: Characteristics of vascular involvement in Behçet's disease.

Scand J Rheumatol 2006; 35: 65-8.

Summary: In this retrospective study the frequency of vascular involvement was found to be 39% among 180 BS patients followed up in a tertiary referral clinic in Turkey. The study protocol excluded patients with isolated superficial thrombophlebitis (ie. with no accompanying deep vein thrombosis). Venous involvement constituted the vast majority of vascular involvement (96%). Deep vein thrombosis of the lower extremities (34%) and superficial thrombophlebitis (27%) were the most frequent types of venous involvement and not surprisingly, a significant correlation was found between deep vein thrombosis and superficial thrombosis. Arterial involvement was found in 11% of the patients, all were men and 85% of them had accompanying venous involvement.

Authors: Fresko I, Ugurlu S, Ozbakir F, Celik A, Yurdakul S, Hamuryudan V, Yazici H.

Title: Anti-*saccharomyces cerevisiae* antibodies (ASCA) in Behçet's syndrome.

Clin Exp Rheumatol 2005; 23 (suppl 38): S67 –S70.

Summary: Antibodies against *saccharomyces cerevisiae* are helpful for differentiating Crohn's disease from ulcerative colitis with positivity favoring the diagnosis of Crohn's disease. This study found significantly less ASCA positivity among BS patients compared to patients with Crohn's disease. On the other hand, ASCA positivity was more frequent among a small number of BS patients with gastrointestinal involvement compared to the rest of BS cohort. More BS patients with gastrointestinal involvement need to be studied to better appreciate these findings.

Authors: Kose O, Arca E, Akgul O, Erbil K.

Title: The levels of serum neopterin in Behçet's disease: objective marker of disease activity.

J Dermatol Sci 2006; 42: 128-30.

Summary: This cross-sectional study found significantly higher serum neopterin levels in BS patients compared to healthy controls. Neopterin levels were higher in BS patient with active disease compared to those with inactive disease and showed a correlation with CRP and ESR in active patients.

Authors: Hamzaoui K, Hamzaoui A, Bouajina L, Houman H.

Title: Circulating soluble CD28 in patients with Behçet's disease: Relationship to clinical manifestations.

Clin Exp Rheumatol 2005; 23 (Suppl 38): S49-S52.

Summary: Concentrations of soluble CD28 are increased in patients with BS and rheumatoid arthritis. This increase showed a correlation with disease activity and vascular

involvement in BS. Longitudinal measurements showed the decrease of CD28 levels with remission which also correlated with CRP levels. Measurement of CD28 levels may be helpful in evaluating disease activity.

Treatment

Authors: Tugal-Tutkun I, Mudun A, Urgancioglu M, Kamali S, Kasapoglu E, Inanc M, Gul A.

Title: Efficacy of infliximab in the treatment of uveitis that is resistant to treatment with the combination of azathioprine, cyclosporine and corticosteroids in Behçet's disease. *Arthritis Rheum* 2005; 52: 2478- 84.

Summary: In this open study infliximab was used in men with BS who had active uveitis under combination immunosuppressive treatment. Infliximab was given at a dose of 5 mg/kg at weeks 0, 2, 6, and 14. Out of 13 patients, 4 were attack free during treatment with infliximab but only 1 patient remained attack free during the posttreatment observation period (weeks 23 – 54). Infliximab was effective in reducing the numbers of uveitis attacks and improved the visual acuity but these beneficial effects were not preserved during the observation period. These results suggest that the beneficial effect of infliximab may be not long lasting.

Authors: Ribi C, Sztajzel R, Delavelle J, Chizzolini C.

Title: Efficacy of TNF alpha blockade in cyclophosphamide resistant neuro-Behçet disease. *J Neurol Neurosurg Psychiatry* 2005; 76: 1733-5.

Summary: Infliximab was effective in a BS patient with treatment resistant neurological involvement. The patient experienced a relapse 7 months later after stopping infliximab while being on azathioprine and cortisone. Reintroduction of infliximab was again successful.

Authors: Tugal-Tutkun I, Guney-Tefekli E, Urgancioglu M.

Title: Results of interferon-alfa therapy in patients with Behçet uveitis.

Graefe's Arch Clin Exp Ophthalmol 2006; May 4 (Epub ahead of print)

Summary: This is a retrospective analysis of 44 BS patients with uveitis who had been treated with interferon alfa in a tertiary referral center. The indication for interferon was active and resistant uveitis among 34 patients and the side effects of previous immunosuppressives in 10 patients. The induction dose of interferon was mostly 6 MU per day followed by a maintenance dose of 3 MU twice of three times a week. With this treatment the authors observed a relapse free response in 36% of the patients during a mean treatment

period of 12 months. Side effects necessitated cessation of interferon in 3 patients. These results are in line with previous observations from other centers reporting the beneficial effect of interferon in the treatment of active and resistant uveitis and again underline the need of comparative studies.

Authors: Mat C, Yurdakul S, Uysal S, Gogus F, Ozyazgan Y, Uysal O, Fresko I, Yazici H.

Title: A double blind trial of depot corticosteroids in Behçet's syndrome.

Rheumatology 2006; 45: 348-52.

Summary: In this double blind trial, 86 BS patients having active genital ulcerations were treated either with intramuscular injections of 40 mg methylprednisolone or placebo every 3 weeks for 27 weeks. The assessment continued for additional 8 weeks after the treatment had ended. The trial failed to show the superiority of depot steroid injections over placebo in suppressing the occurrence of oral and genital ulcers and folliculitis. On the other hand, the treatment was effective for eythema nodosum like lesions especially among women. No cushingoid side effects were seen during the trial.

Authors: Ohguro N, Yamanaka E, Otori Y, Saishin Y, Tano Y.

Title: Repeated intravitreal triamcinolone injections in Behçet's disease that is resistant to conventional therapy. *Am J Ophthalmol* 2006; 141: 218-20.

Summary: Repeated intravitreal steroid injections might be an alternative in patients with resistant uveitis. In this open prospective study 9 eyes of 5 patients were treated with intravitreal triamcinolone injections. Injections were repeated during monthly visits if the volume of triamcinolone particles in the vitreous decreased to one sixth of the initial volume. This treatment prevented recurrences in 8 eyes; earlier than expected disappearance of intravitreal triamcinolone particles was detected in the only non-responding eye.

Authors: Cil BE, Turkbey B, Canyigit M, Kumbasar OO, Celik G, Demirkazik FB.

Title: Transformation of a ruptured giant pulmonary artery aneurysm into an air cavity after transcatheter embolization in a Behçet's patient.

Cardiovasc Intervent Radiol 2006; 29: 151-4.

Summary: Emergent transcatheter embolization of a massively bleeding pulmonary artery aneurysm can be a life saving procedure and may prevent surgery. Based on a case report, this paper gives a comprehensive overview on the techniques and difficulties of transcatheter embolization.