
Behcet's Disease - A Bird's Eye Review of the Recent Literature

edited by V. Hamuryudan and H. Yazici

Pathogenesis

Author: Gül A.

Title: Behçet's disease: An update on the pathogenesis (review).
Clin Exp Rheumatol 2001; 19 (Suppl 24): S6-12.

Summary: A comprehensive review of the etio-pathogenesis of BS.

Authors: Mor F, Weinberger A, Cohen IR.

Title: Identification of alpha-tropomyosin as a target self-antigen in Behçet's syndrome.

Eur J Immunol 2002; 32: 356-65.

Summary: This study found auto-antibodies to alpha-tropomyosin in the sera of some Behçet's syndrome (BS) patients but failed to demonstrate T cell reactivity to alpha-tropomyosin in the peripheral blood lymphocytes of affected patients.

Genetics

Authors: Gül A, Hajeer AH, Worthington J, Ollier WE, Silman AJ.

Title: Linkage mapping of a novel susceptibility locus for Behçet's disease to chromosome 6p22-23.

Arthritis Rheum 2001; 44: 2693-6.

Summary: Using multi-case families, the authors found a second susceptibility locus for BS in the telomere of chromosome 6p.

Authors: Salvarani C, Boiardi L, Mantovani V, Olivieri I, Ciancio G, Cantini F, Salvi F, Malatesta R, Molinotti C, Govoni M, Trotta F, Filippini D, Paolazzi G, Viggiani M.

Title: Association of MICA alleles and HLA B51 in Italian patients with Behçet's disease.

J Rheumatol 2001; 28: 1867-70.

Summary: As in other populations HLA B51 is the most important susceptibility gene for BS in an Italian population. The association with MICA-A6 is secondary to the strong linkage disequilibrium with HLA B51.

Authors: Kotter I, Gunaydin I, Stubiger N, Yazici H, Fresko I, Zouboulis CC, Adler Y, Steiert I, Kurz B, Wernet D, Braun B, Muller CA:

Title: Comparative analysis of the association of HLA B*51 sub-alleles with Behçet's disease in patients of German and Turkish origin.

Tissue Antigens 2001; 58: 166-70.

Summary: In this study, the distribution of HLA B51 suballeles was analyzed among BS patients of German and Turkish origin along with ethnically matched healthy controls. HLA B51 was observed to be significantly associated with BS in Turkish (patients: 75%, controls: 25%; OR 9.13, $p < 0.001$) and German (patients: 58%, controls: 12%; OR 9.76, $p < 0.001$) populations. HLA B5101 was the most frequent suballele among patients and controls from two populations followed by HLA B5108. There was a tendency towards a higher frequency of HLA B51 homozygosity in patients from either population compared to their respective control groups. Furthermore there was a suggestion for a negative association between HLA B5107 and BS.

Authors: Gül A, Uyar FA, Inanc M, Ocal L, Tugal-Tutkun I, Aral O, Konice M, Saruhan-Direskeneli G.

Title: Lack of association of HLAB51 with a severe disease course in Behçet's disease.

Rheumatology (Oxford) 2001; 40: 668-72.

Summary: In this cross-sectional study, the prevalence of HLA

B51 was 63% among 148 BS patients and 25% among 191 matched healthy controls. The frequencies of genital ulceration, skin manifestations, positive pathergy test and eye disease were higher in HLA B51 positive patients. The authors divided the patients into three severity groups by using a modified disease activity index. Although there was a trend for HLA B51 positivity and B51 homozygosity among patients with severe disease, this did not reach statistical significance. Male sex, younger age of onset and a positive family history were associated with increased risk for disease severity.

Authors: Krause I, Mader R, Sulkes J, Paul M, Uziel Y, Adawi M, Weinberger A.

Title: Behçet's disease in Israel: the influence of ethnic origin on disease expression and severity.

J Rheumatol 2001; 28: 1033-6.

Summary: The clinical expression of BS was found to be similar among various ethnic groups in Israel. Jewish BS patients originating from North African countries tended to have more severe disease.

Authors: Ben-Chetrit E, Cohen R, Chajek-Shaul T.

Title: Familial mediterranean fever and Behçet's disease - are they associated?

J Rheumatol 2002; 29: 530-4.

Summary: The authors screened their registered patients with FMF and BS for the presence of co-existent disease. None of the 353 FMF patients but 2 of the 53 BS patients who were also homozygous for MEFV mutations had concomitant disease. The clinical picture of BS did not differ between 16 BS patients with MEFV mutation and 37 patients without mutation. (See also the Editorial in this issue)

Laboratory

Authors: Espinoza G, Font J, Tassies D, Vidaller A, Deulofeu R, Lopez-Soto A, Cervera A, Ordinas A, Ingelmo M, Reverter JC.

Title: Vascular involvement in Behçet's disease: relation with thrombophilic factors, coagulation activation and thrombomodulin.

Am J Med 2002; 112: 37-43.

Summary: In this cross-sectional study, several parameters of hemostasis were studied in 38 BS patients (14 had thrombotic events) and the results were compared to those of 38 patients with deep vein thrombosis without thrombophilia and 100 healthy controls. The thrombosis in BS was not related to the presence of activated protein C resistance due to heterozygous factor V Leiden mutation or heterozygous prothrombin gene G20210A mutation in BS. Compared to controls there was increased thrombin generation, fibrinolysis and thrombomodulin among BS patients but the levels did not differ between BS patients with or without thrombotic events. The authors concluded that thrombotic factors were not pivotal in explaining the thrombotic tendency in BS.

Authors: Akarsu M, Demirkan F, Ozsan GH, Onen F, Yuksel F, Ozkan S, Undar B.

Title: Increased levels of tissue factor pathway inhibitor may reflect disease activity and play a role in thrombotic tendency in Behçet's disease.

Am J Hematol 2001; 68: 225-30.

Summary: This study with no diseased controls found that tissue factor pathway inhibitor levels are higher in active BS patients compared to inactive patients and healthy controls.

Clinical

Authors: Kari JA, Shah V, Dillon MJ.

Title: Behçet's disease in UK children: clinical features and treatment including thalidomide.

Rheumatology (Oxford) 2001; 40: 933-8.

Summary: A retrospective report of 10 children with BS. The clinical spectrum was similar to that of the adults. Thalidomide even at low doses was useful in cases resistant to conventional treatment but caused neuropathy in 2 of the 5 patients.

Authors: Diri E, Mat C, Hamuryudan V, Yurdakul S, Hizli N, Yazici H.

Title: Papulopustular lesions are seen more frequently in patients with Behçet's syndrome who have arthritis: a controlled and masked study.

Ann Rheum Dis 2001; 60: 1074-6.

Summary: The frequency of acneiform skin lesions (papules and pustules but not comedones) were found to be more frequent among BS patients with arthritis compared to those without arthritis and controls, suggesting a possible relation between acne and arthritis.

Authors: Cengiz M, Altundag MK, Zorlu AF, Gullu IH, Ozyar E, Atahan IL.

Title: Malignancy in Behçet's disease: a report of 13 cases and a review of the literature.

Clin Rheumatol 2001; 20: 239-44.

Summary: A retrospective report of 13 malignancies among 400 BS patients. Solid tumors were the most frequent type. Six patients had received immunosuppressive treatment before the onset of malignancy.

Authors: Erkan F, Gul A, Tasali E.

Title: Pulmonary manifestations of Behçet's disease.

Thorax 2001; 56: 572-8.

Summary: A comprehensive review on the pulmonary manifestations of BS.

Authors: Lee CW, Lee J, Lee WK, Lee CH, Suh CH, Song CH, Park YB, Lee SK, Won YS.

Title: Aortic valve involvement in Behçet's disease. A clinical study of 9 patients.

Korean J Intern Med 2002; 17: 51-6.

Summary: A report on the postoperative course of 9 patients who underwent 17 prosthetic aortic valve replacement operations. Complications such as prosthetic valve detachment resulting in perivalvular leakage and dehiscence of the sternotomy wound were higher than those of other diseases.

Authors: Lee CR, Kim WH, Cho YS, Kim MH, Kim JH, Park IS, Bang D.

Title: Colonoscopic findings in Behçet's disease.

Inflamm Bowel Dis 2001; 7: 243-9.

Summary: In this study 94 patients with intestinal involvement were studied. Abdominal pain, followed by diarrhea and gastrointestinal bleeding was the most frequent symptom. Typical colonoscopic findings were single, large and deep ulcers with discrete margins that were seen mostly at the ileocecal area in the nonoperated patients and at the anastomotic site in the operated patients.

Authors: Akpolat T, Akkoyunlu M, Akpolat I, Dilek M, Odabas AR, Ozen S.

Title: Renal Behçet's disease: a cumulative analysis.

Semin Arthritis Rheum 2002; 31: 317-37.

Summary: A report of six BS patients with renal involvement from a nephrology center and a cumulative review of the literature. Amyloidosis and glomerulonephritis were the most commonly reported complications followed by renal vascular disease among the 159 cases with renal involvement reported so far in the literature. Male gender predominated in all types of renal involvement.

Treatment

Authors: Kaklamani VG, Kaklamani PG.

Title: Treatment of Behçet's disease - an update.

Semin Arthritis Rheum 2001; 30 (5): 299-312.

Summary: An extensive review of the treatment of BS.

Authors: Sfikakis PP, Theodossiadi PG, Katsiari CG, Kaklamani P, Markomichelakis NN.

Title: Effect of infliximab on sight threatening panuveitis in Behçet's disease.

Lancet 2001; 358 (9278): 295-6.

Summary: A single dose of 5 mg/kg infliximab was added to the treatment of 5 BS patients immediately after they experienced exacerbations of uveitis while taking immunosuppressives. Improvement of ocular and extra-ocular symptoms was prompt and dramatic.

Authors: Travis SP, Czajkowski M, McGovern DP, Watson RG, Bell AL.

Title: Treatment of intestinal Behçet's disease with chimeric tumour necrosis factor alpha antibody.

Gut 2001; 49: 725-8.

Summary: Treatment with infliximab followed by thalidomide resulted in long lasting remission in two BS patients with intestinal involvement.

Authors: Yurdakul S, Mat C, Tuzun Y, Ozyazgan Y, Hamuryudan V, Uysal O, Senocak M, Yazici H.

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

Arthritis Rheum 2001; 44: 2686-92.

Summary: A double blind, placebo controlled, 2-year study of colchicine in the treatment of mucocutaneous lesions of BS. A significant effect of colchicine was found only in arthritis in the male patients whereas it was significantly effective for genital ulcers, erythema nodosum lesions and arthritis in the females. This study is important in that it for the first time showed different responses to colchicines between the males and females which, in turn, might be a reflection of the more severe disease expression among the males.

Authors: Nichols JC, Ince A, Akduman L, Mann ES.

Title: Interferon alpha 2a treatment of neuro-Behçet disease.

J Neuroophthalmol 2001; 21: 109-11.

Summary: A single case report of a BS patient with neurologic and ocular involvement treated with interferon alpha 2a.

Authors: Adler YD, Mansmann U, Zouboulis CC.

Title: Mycophenolate mofetil is ineffective in the treatment of mucocutaneous Adamantiades Behçet's disease.

Dermatology 2001; 203: 322-4.

Summary: A prospective study of mycophenolate mofetil in BS with mucocutaneous involvement was stopped early when an interim analysis of the first 6 patients suggested inefficacy of the drug.

Authors: Alpsoy E, Durusoy C, Yilmaz E, Ozgurel Y, Ermis O, Yazar S, Basaran E.

Title: Interferon alfa 2a in the treatment of Behçet's disease:

A randomized placebo controlled and double blind study.

Arch Dermatol 2002; 138: 467-71.

Summary: A double blind, placebo controlled study for 3 months with pre and post-treatment evaluation. Fifty BS patients with mainly mucocutaneous disease were treated with either interferon alpha 2a 6 MU 3 times weekly or placebo and the results were compared in an efficacy analysis. Treatment with interferon improved significantly the duration and pain of oral ulcers and the frequency of genital ulcers and papulopustular lesions. There was a trend towards suppression of erythema nodosum, thrombophlebitis, articular symptoms and eye disease but the difference was not significant mainly due to small numbers of patients. The symptoms tended to return when interferon was stopped.