Behçet's Syndrome - A Bird's Eye View of the Recent Literature

edited by V. Hamuryudan and H. Yazici

Author: Yazici H.
Title: Behçet's syndrome: An update.
Curr Rheumatol Rep 2003; 5: 195-9.
Summary: A comprehensive review on Behçet's syndrome.

Pathogenesis

Authors: Ahmad T, Wallace GR, James T, Neville M, Bunce M, Mulcahy-Hawes K, Armuzzi A, Crawshaw J, Fortune F, Walton R, Stanford MR, Welsh KI, Marshall SE, Jewell DP.
Title: Mapping the HLA association in Behcet's disease: A role for tumor necrosis factor polymorphisms?
Arthritis Rheum 2003; 48: 807-13.
Summary: The authors have searched for additional loci, besides the well known HLA B51, as susceptibility loci in BS. Among 133 BS patients and 354 ethnically matched controls, the TNF1031C allele was found in 55.6% of the BS patients and 35% of the controls. More work is needed to clarify the functional significance of this association.

Authors: Lee KH, Chung HS, Kim HS, Oh SH, Ha MK, Baik JH, Lee S, Bang D.
Title: Human alpha-enolase from endothelial cells as a target antigen of anti-endothelial cell antibody in Behcet's disease. *Arthritis Rheum* 2003; 48: 2025-35.
Summary: Anti-endothelial cell antibodies (AECA) have been well described in many vasculitides, including BS. On the other hand, their specificity has been questioned not only for the diseases for which they had been described but also for their antigen.
The study by Lee *et al.* seems to cast light at least on the latter of these two areas of concern. Using the proteinase technique, which searches the specific protein to which an antibody is targeted to, they showed that 18/40 of the BS patients studied had IgM AECA and of those 18, sera from BS patients reacted with recombinant α-enolase. None of the 5 SLE patients had sera reactive with α-enolase while 1/6 rheumatoid arthritis and 2/2 Wegener granulamotosis sera were reactive.
As the authors admit, the biological explanation of this finding is not apparent. After more specificity studies α-enolase might indeed turn out to be an interesting marker antigen for BS.

Authors: Karasneh J, Hajeer AH, Barrett J, Ollier WE, Thornhill M, Gul A.
Title: Association of specific interleukin 1 gene cluster polymorphisms with increased susceptibility for Behcet's disease.
Rheumatology (Oxford) 2003; 42: 860-4.
Summary: The contribution of single nucleotide polymorphisms in the interleukin-1 gene cluster (IL-1A, IL-1B and IL-1RN genes) to the genetic susceptibility to BS was investigated using 132 Turkish patients and 105 healthy controls. An increased susceptibility to BS was identified in individuals carrying the IL-1A -889C allele and the IL-1A -889C / IL-1B +5887T haplotype, and homozygosity for this haplotype increased two-fold the risk of developing BS (OR = 2.2, p = 0.003).

Laboratory aspects

Authors: Krause I, Monselise Y, Milo G, Weinberger A.
Title: Anti-*Saccharomyces cerevisiae* antibodies – a novel serologic marker for Behçet's disease.
Clin Exp Rheumatol 2002; 20 (Suppl. 26): S21-4.
Summary: Antibodies to *Saccharomyces cerevisiae* (ASCA) are considered to be specific for Crohn's disease and are used to differentiate it from ulcerative colitis. This cross-sectional study demonstrated for the first time the presence of ASCA in patients with BS. Of note, none of these patients had gastrointestinal symptoms and no correlation was found between the presence of ASCA and any clinical manifestation of BS.

Authors: Korkmaz C, Bozan B, Kosar M, Sahin F, Gulbas Z.
Title: Is there an association of plasma homocystein levels with vascular involvement in patients with Behçet's syndrome?
Clin Exp Rheumatol 2002; 20 (Suppl. 26): S30-4.
Summary: In contrast to a previous study reporting that hyperhomocysteinemia might be an independent risk factor for thrombosis in BS, this cross-sectional study found no association between homocystein levels and vascular involvement. The paper provides a detailed discussion on the possible factors leading to this conflicting result. Furthermore, this study for the first time proposed smoking as a possible risk factor for vascular involvement in BS.

Authors: Korman U, Cantasdemir M, Kurugoglu S, Mihmanli I, Soylu N, Hamuryudan V, Yazici H.
Title: Enterocylisis findings of intestinal Behçet disease: A comparative study with Crohn disease.
Abdom Imaging 2003; 28: 308-12.
Summary: Gastrointestinal involvement is infrequent among BS patients from the Mediterranean basin but rather common among patients from the Far East. This study describes the enterocylisis findings of 17 Turkish BS patients having gastrointestinal involvement. The most frequent findings were multiple superficial ulcers localized prominently at the terminal ileum. Since these lesions have been reported to occur as single, large, deep ulcers with distinct borders in studies from the Far East, it might be that not only the frequency but also the type of bowel disease differs among regions.

Clinical aspects

Authors: Seyahi EK, Fresko I, Seyahi N, Ozyazgan Y, Mat C, Hamuryudan C, Yurdakul S, Yazici H.
Title: The long term mortality and morbidity of Behçet's syndrome. A 2-decade outcome survey of 387 patients followed at a dedicated center.
Medicine 2003; 82: 60-76.
Summary: This is the most comprehensive outcome survey performed on a cohort of BS patients. Forty-two of 387 patients (39 males, 3 females; 9.8%) had died mainly due to major vessel disease and neurologic involvement during a period of 20 years. Mortality and morbidity were highest among young males. On the other hand, the mortality ratios tended to decrease significantly with the passage of time and this was also true for the mucocutaneous lesions and articular manifestations. Both the onset of eye disease and its greatest damage usually occur within the first few years of disease onset and those patients with a late onset had a better visual prognosis. These observations suggest that the disease burden of BS is usually confined to the early years during its course and in many patients the disease eventually burns out. However, major vessel disease and neurologic involvement are exceptions and can have their onset late in the course.

Authors: Idil A, Gurler A, Boyvat A, Caliskan D, Ozdemir O, Isik A, Tuncbilek A, Kocyigit P, Calikoglu E.
Title: The prevalence of Behçet's disease above the age of 10 years. The results of a pilot study conducted at the Park Primary Health Care Center in Ankara, Turkey.
Ophthalmic Epidemiol 2002; 9: 325-31.
Summary: This study screened a population of 17,256 individuals above the age of 10 years for the presence of BS. The reported prevalence of 0.11% was in line with 2 previous community surveys from Turkey which found prevalence rates of 0.08% and 0.3%, respectively.

Authors: Al-Araji A, Sharquie K, Al-Rawi Z.
Title: Prevalence and patterns of neurologic involvement in Behçet's disease: a prospective study from Iraq.
J Neurol Neurosurg Psychiatry 2003; 74: 608-13.
Summary: Out of 140 BS patients registered at a multidisciplinary outpatient clinic 20 (14%) had neurologic involvement. The mean duration of BS was 3 years at the emergence of neurologic involvement. Ten patients (50%) had parenchymal CNS involvement and 6 (30%) had intracranial hypertension. This study is interesting in that it reports the simultaneous occurrence of parenchymal CNS involvement and cerebral venous thrombosis in one fifth of the patients. This concurrence in the same patient is generally believed to be unusual.

Authors: Ben Taarit C, Turki S, Ben Maiz H.
Title: Neurological manifestations in Behçet's disease. Forty observations in a cohort of 300 patients.
J Mal Vasc 2002; 27: 77-81.
Summary: In this retrospective study, 40 of 300 patients seen over a 20-year period developed neurological involvement. The most common type of neurological involvement was meningo-encephalitis followed by intracranial hypertension. This study re-confirmed that peripheral nervous involvement was unusual for BS in that it was seen in only one patient in the form of polyneuropathy.

Authors: Chang HK, Cheon KS.
Title: The clinical significance of a positive pathergy reaction in patients with Behçet's disease.
J Korean Med Sci 2002; 17: 371-4.
Summary: The frequency of a positive pathergy reaction was 36% among 64 Korean BS patients. The low frequency of pathergy positivity as well as the lack of association with any of the clinical and demographic features is another example to the regional variability of BS.

Authors: Tunc R, Keyman E, Melikoglu M, Fresko I, Yazici H.
Title: Target organ associations in Turkish patients with Behçet's disease: a cross sectional study by exploratory factor analysis.
J Rheumatol 2002; 29: 2393-6.
Summary: Factor analysis is a statistical tool that is suitable to find associations between the different clinical manifestations of a multisystem disease like BS. In this cross-sectional study the analysis identified 4 independent factors explaining 69% of the diverse clinical findings in 277 consecutive BS patients: an association between the mucocutaneous manifestations of oral and genital ulcers as well as erythema nodosum (Factor 1); an association between superficial and deep vein thrombosis (Factor 2); uveitis as a single feature (Factor 3); and an association between papulopustular skin lesions and joint involvement (Factor 4). This last association confirms earlier work by the same group on a different set of patients and suggests that the arthritis of BS may be of the reactive type.

Treatment

Author: Sfikakis PP
Title: Behçet's disease: A new target for anti-tumour necrosis factor treatment.
Ann Rheum Dis 2002; 61 (Suppl. ii): 51-3.
Summary: A comprehensive review on the current status of anti-cytokin therapy in BS.

Authors: Kötter I, Zierhut M, Eckstein AK, Vonthein R, Ness T, Günaydin I, Grimbacher B, Blaschke S, Meyer-Riemann W, Peter HH, Stübiger N.
Title: Human recombinant interferon alpha-2a for the treatment of Behçet's disease with sight threatening posterior or panuveitis. *Br J Ophthalmol* 2003; 87: 423-31.
Summary: In this open, uncontrolled study, 50 BS patients with treatment-resistant ocular involvement received interferon alpha 2a 6 million units daily for at least 14 days. The dosage was then adjusted according to the clinical res-

ponse of the patients. The onset of the effect of interferon was rapid (2 – 4 weeks) and the response rate was high (92%). There was a significant increase in the mean visual acuity and a significant decrease in ocular symptoms and the overall activity of BS. These encouraging results still need to be confirmed in controlled studies.

Authors: Hamuryudan V, Ozyazgan Y, Fresko Y, Mat C, Yurdakul S, Yazici H.
Title: Interferon alpha combined with azathioprine for the uveitis of Behçet's syndrome: An open study.
Isr Med Assoc J 2002; 4 (Suppl.): 928-30.
Summary: This open trial reports for the first time the effect of the combination of interferon alpha 2b and azathioprine in a small group of BS patients with retinal vasculitis. The rationale for choosing this combination was the expectation that the rapid effect of interferon would prevent structural changes until a substantial effect of azathioprine was seen. At the end of 24 weeks the combination treatment significantly improved the visual acuity compared to study entry. Reversible hematologic toxicity mainly in the form of leukopenia was common and necessitated close monitoring.

Authors: Sharquie KE, Najim Ra, Abu-Raghif AR.
Title: Dapsone in Behçet's disease: A double blind, placebo controlled, cross-over study.
J Dermatol 2002; 29: 267-79.
Summary: Dapsone is being used anecdotally in the treatment of the mucocutaneous lesions of BS. Although conducted on a small number of patients, this is the first controlled trial of dapsone in BS. The results suggest that dapsone 100 mg per day is superior to placebo in the treatment of the mucocutaneous lesions of BS.

Authors: Matsuda T, Ohno S, Hirohata S, Miyanaga Y, Ujihara H, Inaba G, Nakamura S, Tanaka SI, Kogure M, Mizushima Y.
Title: Efficacy of rebamipide as adjunctive therapy in the treatment of recurrent oral apthous ulcers in patients with Behçet's disease. A randomized, double blind, placebo controlled study.
Drugs 2003; 4: 19-28.
Summary: Rebamipide is a gastric mucoprotective agent that is widely used for the treatment of gastritis and gastric ulcer in the Far East. The efficacy of this drug on oral ulceration has been tested against placebo in a double blind trial. The results suggest the efficacy of rebamipide in improving the number and pain score of oral aphthae in BS. On the other hand, the power of this multi-center trial is low in that it studied only a total of 35 patients.

Authors: Cantasdemir M, Kantarci F, Mihmanli I, Akman C, Numan F, Islak C, Bozkurt AK.
Title: Emergency intravascular management of pulmonary artery aneurysms in Behçet's disease: Report of 2 cases and review of the literature.
Cardiovasc Intervent Radiol 2002; 25: 533-37.
Summary: The authors report their successful experience with 2 BS patients suffering from pulmonary arterial aneurysms who continued to bleed despite ongoing medical treatment. Emergency endovascular embolization could represent a life-saving intervention in selected patients who are resistant to medical therapy and may otherwise be considered as candidates for surgery.