Behçet's syndrome
A bird's eye review of the recent literature

edited by Vedat Hamuryudan and Hasan Yazıcı

Epidemiology

Authors: Calamia KT, Wilson FC, Icen M, Crowson CS, Gabriel SE, Kremers HM
Title: Epidemiology and clinical characteristics of Behçet's disease in the US: a population-based study.
Arthritis Rheum 2009; 15: 600-4.
Summary: This is a retrospective study reporting the incidence, prevalence and clinical characteristics of patients who had been diagnosed as having BS over a period of 45 years in Olmstead County, Minnesota, USA. The authors identified 13 BS patients by using a comprehensive diagnostic indexing and medical records linkage system, which covers all medical information from all health care providers. The overall age and sex adjusted incidence and point prevalence rates were 0.38 per 100.000 and 5.2 per 100.000 population respectively. These figures were similar to those reported from other Western countries but lower than from the Mediterranean countries and Japan. The incidence rate of BS was higher among women than men and ocular and CNS complications were more common.

Authors: Mahr A, Belarbi L, Wechsler B, Jeanneret D, Dhote R, Fain O, Lhote F, Ramanoelina J, Coste J, Guillevin L
Title: Population-based prevalence study of Behçet's disease: differences by ethnic origin and low variation by age at immigration.
Arthritis Rheum 2008; 58: 3951-9.
Summary: This study was performed in a suburb of Paris which has a multi-ethnic population. Information on BS patients in this area was ascertained from different sources that provide health care for this area. Capture-recapture analysis was done to assess the completeness of case findings. The overall prevalence rate of BS was 7.1 per 100.000 population with prominent differences between ethnic subgroups. It was interesting to note that BS was almost as common as the sum frequency of other primary vasculitides (Wegener's, PAN, MPA and Churg Strauss syndrome) from the same region as reported earlier (Mahr A *et al.: Arthritis Rheumatism* 2004). BS was substantially higher among the North African and Asian subpopulations compared to the native European population. The prevalence rates of BS in the non-European subgroups were within the ranges reported in their original countries. The risk of developing BS among immigrants was found to be independent of their ages at the time of their immigration to France. These findings again underline the importance of hereditary factors in BS pathogenesis. Also note the accompanying editorial by Yazici H *et al*. in the same issue.

Authors: Yi SW, Kim JH, Lim KY, Bang D, Lee S, Lee ES.
Title: The Behcet's Disease Quality of Life: reliability and validity of the Korean version
Yonsei Med J 2008; 49: 698-704.
Summary: BD-QoL is a patient based questionnaire developed in Leeds and has sufficient reliability and validity for assessing the quality of life of BS patients. The purpose of this study was to adapt the BD-QoL questionnaire into the Korean language. The Korean version of BD-QoL was developed following all the necessary steps for translation and cross-cultural adaptation procedures and showed high internal consistency and test-retest reliability. The Korean version of BD-QoL also showed significant correlations with self-rated well being, depression scales and the clinical activity form for Korean patients.

Pathogenesis

Authors: Takemoto Y, Naruse T, Namba K, Kitaichi N, Ota M, Shindo Y, Mizuki N, Gul A, Madanat W, Chams H, Davatchi F, Inoko H, Ohno S, Kimura A
Title: Re-evaluation of heterogeneity in HLA-B*510101 associated with Behçet's disease.
Tissue Antigens 2008; 72: 347-53.
Summary: In this study, full sequences of the HLA*B5101 gene were determined in 37 individuals consisting of Japanese, Turkish, Jordanian and Iranian BS patients and healthy controls. All the HLA*B5101 sequences from the samples were found to be HLA*B510101 and not HLA*B510102. There were no variations in the 5′-flanking region. Seven single nucleotid polymorphysms forming six haplotypes were found in the 3′- flanking region. The variations in the 3′- flanking region of HLA*B510101 were also observed in other HLA-B alleles. The entire sequence of HLA*B510101 was found to be conserved in the phylogenetic analysis. These results suggest that the susceptibility to BS is conferred by the HLA*B510101 itself and not by any genes in linkage disequilibrium with HLA*B510101.

Authors: Tomiyama R, Meguro A, Ota M, Katsuyama Y, Nishide T, Uemoto R, Iijima Y, Ohno S, Inoko H, Mizuki N.
Title: Investigation of the association between Toll-like receptor 2 gene polymorphisms and Behçet's disease in Japanese patients.
Hum Immunol 2009; 70: 41-4.
Summary: This study looked for 5 common polymorphysms in the TLR-2 gene among 200 Japanese BS patients and 128

healthy controls and did not find significant differences for any SNP between patients and controls. According to these results the association of TLR-2 gene polymorphisms with the pathogenesis of BS seems to be low.

Authors: Hamzaoui K, Houman H, Hentati F, Hamzaoui A
Title: BAFF is up-regulated in central nervous system of neuro-Behçet's disease.
J Neuroimmunol 2008; 200: 111-4.
Summary: BAFF and BAFF-R levels were found to be significantly increased in CSF of 8 BS patients with CNS involvement and 6 patients with multiple sclerosis (MS) compared to 9 patients with non-inflammatory neurological diseases. The levels of soluble BAFF were increased in BS patients but there was no correlation between serum and CSF BAFF levels of BS and MS patients suggesting in situ production of BAFF in CSF.

Clinical aspects

Authors: Saadoun D, Wechsler B, Resche-Rigon M, Trad S, Le Thi Huong D, Sbai A, Dormont D, Amoura Z, Cacoub P, Piette JC
Title: Cerebral venous thrombosis in Behçet's disease.
Arthritis Rheum 2009; 61: 518-26.
Summary: This retrospective study reported 64 BS patients diagnosed as having central venous thrombosis (CVT) in a single center during a period of 32 years. Consistent with previous work, patients with CVT were found to have significantly more frequent (63%) extracranial vascular involvement than the patients without CVT (39%). Parenchymal central nervous system (CNS) disease was also significantly less frequent among those having CVT (5%) compared to those without CVT (29%). The onset of CVT was acute in 36% of the patients. Headache, papilledema, nausea, vomiting, focal neurologic deficits, seizures and confusion were the most frequent signs and symptoms. Cerebrospinal fluid examination showed elevated pressure in 62% of the studied specimens. Pleocytosis with a lymphocytic predominance and elevated protein levels were other findings. Anticoagulation was the mainstay of treatment (96% of the patients) which was combined with high dose corticosteroids in 77%. Short term response was good in 88% of the patients. Repeated cerebral imaging during follow-up showed recanalization of the CVT in 58% of the patients. Seven patients experienced a relapse of CVT during their follow-up. Papilledema was associated with the development of sequela whereas the presence of prothrombotic risk factors and peripheral venous involvement were found to be associated with recurrence of thrombosis. According to the authors anticoagulation appears to be an effective and safe treatment for CVT. However, the outcome of patients receiving the combination of anticoagulation and corticosteroids was not compared with those receiving anticoagulation alone in this study.

Authors: Hatemi I, Hatemi G, Celik AF, Melikoglu M, Arzuhal N, Mat C, Ozyazgan Y, Yazici H
Title: Frequency of pathergy phenomenon and other features of Behçet's syndrome among patients with inflammatory bowel disease.
Clin Exp Rheumatol 2008; 26 (Suppl. 50): S91-5.
Summary: Inflammatory bowel disease and BS share some common features such as oral ulcers, erythema nodosum, uveitis and arthritis making the differential diagnosis difficult in some patients. Furthermore, the intestinal ulcers of BS may be indistinguishable from those of Crohn's disease. This study looked at the features of BS and frequency of positive pathergy test in 93 patients with Crohn's disease and 130 patients with ulcerative colitis. The investigators were masked to the diagnoses of the patients. Approximately 20% of the patients had oral ulcers and papuloustular lesions. None of the Crohn's disease patients but 2 patients with ulcerative colitis fullfilled the International Study Group (ISG) Criteria for BS. 8% of the patients were evaluated as having a positive pathergy test by at least one of the 2 examiners. According to these results the performance of ISG criteria is good in differentiating BS from inflammatory bowel disease.

Authors: Oran M, Hatemi G, Tasli L, Garip F, Kadioglu P, Mat C, Yazici H
Title: Behçet's syndrome is not associated with vitiligo.
Clin Exp Rheumatol 2008; 26 (Suppl. 50): S107-9.
Summary: Vitiligo is associated with various autoimmune disorders. This controlled study tested the hypothesis that vitiligo was rare in BS patients. 253 patients with BS, 32 patients with Hashimoto's thyroiditis, 34 patients with Grave's disease and 439 healthy controls were examined by a dermatologist masked to the clinical diagnoses of the patients. Vitiligo was diagnosed in 0.9% of the healthy controls, 18% of the patients with Grave's disease, 19% of the patients with Hashimoto's thyroiditis and in none of the patients with BS. All patients with vitiligo were women excluding one patient with Grave's disease. These results further suggest that traditional autoimmune mechanisms are not prominent in BS.

Authors: Cho YK, Lee W, Choi SI, Jae HJ, Chung JW, Park JH
Title: Cardiovascular Behçet disease: the variable findings of rare complications with CT angiography and conventional angiography and its interventional management.
J Comput Assist Tomogr 2008; 32: 679-89.
Summary: Invasive radiological interventions can lead to the development of aneurysms or occlusions at the puncture site of BS patients and are considered to be relatively contraindicated unless a therapeutic intervention is planned. This comprehensive review gives an overview of various vascular and cardiac complications of BS and also discusses the place of computerized tomographic angiography as a new tool in diagnosing the vascular complications of BS.

Authors: Chung YM, Lin YC, Tsai CC, Huang DF
Title: Behcet's disease with uveitis in Taiwan.
J Chin Med Assoc 2008; 71: 509-16.
Summary: Although one of the earliest descriptions of a disease resembling BS was from ancient China, BS appears to be less frequent among the Chinese as compared to the other Silk Road populations. In this retrospective study the clinical characteristics and outcome of 227 Chinese BS patients that were seen in a uveitis center during a period of 20 years are presented. The male to female ratio was 1.6 and the mean age of the patients at the onset of BS was 30 years. Eye involvement was bilateral in 82% of the patients. At the first decade of this survey colchicine was the most frequently used drug and immunosuppressives were given only after the failure of colchicine in controlling uveitis. However, during the last decade of this survey a combination of cyclosporine A with corticosteroids was the choice of treatment for patients with posterior involvement and recurrent attacks. Loss of useful vision was seen in 23% of the patients at 5 years and in 43% at 10 years. Visual prognosis was better for female patients. However, Kaplan Meier analysis did not reveal a significant difference in the visual prognosis of patients regardless of the time point they entered this survey.

Authors: Yi SW, Cheon JH, Kim JH, Lee SK, Kim TI, Lee YC, Kim WH
Title: The prevalence and clinical characteristics of esophageal involvement in patients with Behçet's disease: a single center experience in Korea.
J Korean Med Sci 2009; 24: 52-6.
Summary: Esophageal involvement is a rare but severe complication of BS even among Korean BS patients who have a relatively high incidence of gastrointestinal involvement. In this retrospective study the records of 129 who had upper and lower endoscopic examination because of gastrointestinal symptoms were reviewed. Six patients (4.7%) had esophageal ulcerations which responded to treatment with proton pump inhibitors. The clinical characteristics of the patients with esopageal involvement were similar to those with other types of intestinal involvement.

Treatment

Authors: Gueudry J, Wechsler B, Terrada C, Gendron G, Cassoux N, Fardeau C, Lehoang P, Piette JC, Bodaghi B
Title: Long-term efficacy and safety of low-dose interferon alpha2a therapy in severe uveitis associated with Behçet disease.
Am J Ophthalmol 2008;146: 837-44.
Summary: This is a retrospective survey of 32 BS patients who received low dose (3 MU three times a week) interferon alfa 2a for refractory posterior uveitis or panuveitis. This treatment regime led to significant improvement in visual acuity, suppression in the number of ocular attacks and decrease of corticosteroid dosage in 28 (88%) patients. Interferon treatment could be stopped in 19 patients (68%) after a mean of 32 months which led to relapses in 6 patients (32%) after a mean delay of 8 months. Flu like symptoms and moderate leukopenia, which responded to dose tapering were the main side effects of interferon treatment. The authors conclude that low dose interferon is an effective and safe treatment for severe uveitis of BS which can also lead to long term drug free remission in some patients.

Title: Cyclosporine for Behçet's uveitis: is it associated with an increased risk of neurological involvement?
Authors: Akman-Demir G, Ayranci O, Kurtuncu M, Vanli EN, Mutlu M, Tugal-Tutkun I
Clin Exp Rheumatol 2008; 26 (Suppl. 50): S84-90.
Summary: Cyclosporine is widely used in BS especially for sight-threatening refractory eye involvement. There is a concern that it may increase the risk of neurological involvement in BS. This retrospective study examined 269 BS patients who were admitted to an uveitis clinic within a period of 5 years. None of these patients had been referred from neurology department. The patients were divided into 3 groups based on their treatments. During follow-up, parenchymal neurological involvement developed in 8.6% of the 92 patients receiving cyclosporine containing treatment, whereas it was found only in 1 of the 132 patients receiving immunosuppressives other than cyclosporine and in none of the 45 patients receiving colchicine. Patients receiving cyclosporine alone tended to develop more frequent neurological involvement than those receiving combination of cyclosporine and azathioprine. There was no correlation between the severity of ocular involvement and development of neurological involvement. These results again underline that patients using cyclosporine should be closely monitored for the development of neurological symptoms. Stopping of cyclosporine treatment is recommended in case of neurological involvement.