387 Behçet's Syndrome

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DEFINITION, INCIDENCE, AND PREVALENCE

Behçet's syndrome is a multisystem disorder presenting with recurrent oral and genital ulcerations as well as ocular involvement. The diagnosis is clinical and based on internationally agreed diagnostic criteria (Table 387-1).

The syndrome affects young males and females from the Mediterranean region, the Middle East, and the Far East, suggesting a link with the ancient Silk Route. Males and females are affected equally, but males often have more severe disease. Blacks are very infrequently affected.

PATHOGENESIS

The etiology and pathogenesis of this syndrome remain obscure. The disease appears to be in the crossroads of autoinflammatory and autoimmune disorders. The main pathologic lesion is systemic perivasculitis with early neutrophil infiltration and endothelial swelling. In some patients, diffuse inflammatory disease, involving all layers of large vessels and resulting to formation of pseudoaneurysms, suggests vasculitis of vasa vasorum. Apart from activated neutrophils, increased numbers of infiltrating T_H1, T_H17, cytotoxic CD8+, and γδ T cells are observed, suggesting a link between innate and adaptive autoreactive immune response. Circulating autoantibodies against α-enolase of endothelial cells, selenium binding protein, and anti-*Saccharomyces cerevisiae* antibodies have been observed, but their pathogenic role remains unclear. A recent genome-wide association study confirmed the known association of Behçet's syndrome with HLA-B*51 and identified a second, independent association within the major histocompatibility complex (MHC) class I region. In addition, an association with interleukin (IL) 10 and the IL-23R–IL-12RB2 locus was also observed. Interestingly, the disease-associated IL-10 variant was correlated with diminished mRNA expression and low protein production.

CLINICAL FEATURES

The recurrent aphthous ulcerations are a sine qua non for the diagnosis. The ulcers are usually painful, are shallow or deep with a central yellowish necrotic base, appear singly or in crops, and are located anywhere in the oral cavity. Small ulcers, less than 10 mm in diameter, are seen in 85% of patients, whereas large or herpetiform lesions are less frequent. The ulcers persist for 1–2 weeks and subside without leaving scars. The genital ulcers are less common but more specific, are painful, do not affect the glans penis or urethra, and produce scrotal scars.

Skin involvement is observed in 80% of patients and includes folliculitis, erythema nodosum, an acne-like exanthem, and, infrequently, vasculitis, Sweet syndrome, and pyoderma gangrenosum. Nonspecific skin inflammatory reactivity to any scratches or intradermal saline injection (pathergy test) is a common and specific manifestation.

Eye involvement with scarring and bilateral panuveitis is the most dreaded complication, since it occasionally progresses rapidly to blindness. The eye disease, occurring in 50% of patients, is usually present at the onset but may also develop within the first few years. In addition to iritis, posterior uveitis, retinal vessel occlusions, and optic neuritis can be seen in some patients with the syndrome.

Nondeforming arthritis or arthralgias are seen in 50% of patients and affect the knees and ankles.

TABLE 387-1 DIAGNOSTIC CRITERIA OF BEHÇET'S SYNDROME

Recurrent oral ulceration plus two of the following:
Recurrent genital ulceration
Eye lesions
Skin lesions
Pathergy test

Superficial or deep peripheral vein thrombosis is seen in 30% of patients. Pulmonary emboli are a rare complication. The superior vena cava is obstructed occasionally, producing a dramatic clinical picture. Arterial involvement occurs in less than 5% of patients and presents with aortitis or peripheral arterial aneurysm and arterial thrombosis. Pulmonary artery vasculitis presenting with dyspnea, cough, chest pain, hemoptysis, and infiltrates on chest roentgenograms has been reported in 5% of patients and should be differentiated from thromboembolic disease since it warrants anti-inflammatory and not thrombolytic therapy.

Neurologic involvement (5–10%) appears mainly in the parenchymal form (80%); it is associated with brainstem involvement and has a serious prognosis (*central nervous system [CNS]-Behçet's syndrome*). IL-6 is persistently raised in cerebrospinal fluid of these patients. Cerebral venous thrombosis is most frequently observed in the superior sagittal and transverse sinuses and is associated with headache and increased intracranial pressure. Magnetic resonance imaging (MRI) and/or proton magnetic resonance spectroscopy (MRS) are very sensitive and should be employed if CNS-Behçet's syndrome is suspected.

Gastrointestinal involvement is seen more frequently in patients from Japan and consists of mucosal ulcerations of the gut, resembling Crohn's disease.

Epididymitis is seen in 5% of patients, whereas amyloidosis of AA type and glomerulonephritis are uncommon.

Laboratory findings are mainly nonspecific indices of inflammation, such as leukocytosis and elevated erythrocyte sedimentation rate, as well as C-reactive protein levels.

TREATMENT BEHÇET'S SYNDROME

The severity of the syndrome usually abates with time. Apart from the patients with CNS-Behçet's syndrome and major vessel disease, the life expectancy seems to be normal and the only serious complication is blindness.

Mucous membrane involvement may respond to topical glucocorticoids in the form of mouthwash or paste. In more serious cases, thalidomide (100 mg/d) is effective. Thrombophlebitis is treated with aspirin, 325 mg/d. Colchicine can be beneficial for the mucocutaneous manifestations and arthritis. Uveitis and CNS-Behçet's syndrome require systemic glucocorticoid therapy (prednisone, 1 mg/kg per day) and azathioprine (2–3 mg/kg per day). Cyclosporine (5 mg/kg) has been used for sight-threatening uveitis, alone or in combination with azathioprine. Pulse doses of cyclophosphamide are useful early in the course of the disease for pulmonary or peripheral arterial aneurysms. Anti–tumor necrosis factor therapy is recommended in panuveitis refractory to immunosuppressives. Administration of this therapy improves visual acuity in more than two-thirds of patients.

388 Polymyositis, Dermatomyositis, and Inclusion Body Myositis

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The inflammatory myopathies represent the largest group of acquired and potentially treatable causes of skeletal muscle weakness. They are classified into three major groups: polymyositis (PM), dermatomyositis (DM), and inclusion body myositis (IBM).

CLINICAL FEATURES

The prevalence of the inflammatory myopathies is estimated at 1 in 100,000. PM as a stand-alone entity is a rare disease. DM affects both