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 320-1).

Table 320-1 Diagnostic Criteria of Behçet's Disease

<table>
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<th>Criteria</th>
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<td>Recurrent oral ulceration plus two of the following:</td>
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<td>Recurrent genital ulceration</td>
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<td>Eye lesions</td>
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<td>Skin lesions</td>
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<td>Pathergy test</td>
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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 main pathologic lesion is systemic perivasculitis with early neutrophil infiltration, endothelial swelling, and fibrinoid necrosis. Apart from neutrophils, increased numbers of infiltrating T cells are observed. Circulating autoantibodies against α-enolase of endothelial cells and anti-Saccharomyces cerevisiae antibodies (ASCA—characteristic of Crohn’s disease) are found to be present in the later stages of the disease. A tendency toward venous thrombus formation accounts for many of the consequences of Behçet’s syndrome, though it is not clear whether it is due to additional thrombophilic factors (e.g., factor V–Leiden mutation, reduced activated protein C levels) or to the inflammatory vasculitis per se. Finally, the strong association with HLA-B5 (B51) alloantigen (present almost exclusively on areas of the aforementioned Silk Route) and the fact that ~1 in 10 patients has an affected relative underscore the genetic basis of Behçet’s syndrome.

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. The ulcers persist for 1–2 weeks and subside without leaving scars. The genital ulcers are less common but more specific, do not affect the glans penis or urethra, and produce scrotal scars.

Skin involvement includes folliculitis, erythema nodosum, an acne-like exanthem, and, infrequently, vasculitis. 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 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. Hypopyon uveitis, a specific but rare manifestation, is a layer of pus visible on the anterior chamber; it usually indicates severe retinal vascular disease.

The arthritis of Behçet’s syndrome is not deforming and affects the knees and ankles. Superficial or deep peripheral vein thrombosis is seen in one-fourth of patients. Pulmonary emboli are a rare complication. The superior vena cava is obstructed occasionally, producing a dramatic clinical picture. Arterial involvement occurs infrequently 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 recently 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 (CNS-Behçet’s syndrome). Dural sinus thrombi (20%) are associated with headache and increased intracranial pressure. MRI and/or proton magnetic resonance spectroscopy (MRS) are very sensitive and should be employed if CNS-Behçet’s syndrome is suspected.

Gastrointestinal involvement consists of mucosal ulcerations of the gut, resembling Crohn’s disease. Laboratory findings are mainly nonspecific indices of inflammation, such as leukocytosis and elevated erythrocyte sedimentation rate, as well as C-reactive protein levels; autoantibodies (see above) may be found.

**Behçet’s Syndrome: Treatment**

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 of the syndrome. Uveitis and CNS-Behçet’s syndrome require systemic glucocorticoid therapy (prednisone, 1 mg/kg per day) and azathioprine, 2–3 mg/kg per day. Interferon has proved to be very effective not only for CNS-Behçet’s syndrome but also for refractory uveitis. Preliminary data suggest that anti–tumor necrosis factor therapy may be an alternative treatment modality for panuveitis. Early initiation of azathioprine tends to favorably affect the long-term prognosis of Behçet’s syndrome.

**Further Readings**


