AMERICAN UVEITIS SOCIETY

Behçet's Disease

A Patient Education Monograph prepared for the American Uveitis Society **January 2003**
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Introduction
Behçet's disease is a chronic, relapsing-remitting, occlusive vasculitis affecting multiple organ systems in the body. It is a multifaceted syndrome, characterized by mouth and genital ulcerations (sores) and uveitis. The disease occurs worldwide, however it has a much higher incidence in the latitudes between 30˚ and 45˚ N, around the Mediterranean basin extending through Middle East and Orient. The striking similarity of the distribution of Behçet's disease to the ancient Silk Road suggests that an inherited tendency to develop Behçet's Disease was spread by merchants who traveled these trading routes.

History
Behçet's disease was first described in 1937 by the Turkish dermatologist, Hulusi Behçet, but probably has been recognized since ancient times. In his original report, Behçet referred to a complex of recurrent oral ulcers, genital aphthae (sores), and hypopyon uveitis that could lead to blindness. Hypopyon occurs when white blood cells accumulate inside the front of the eye and actually form a layer visible by microscope or even by the naked eye.

Course of Disease
Adult males are most commonly affected. The mean age at onset ranges from the mid 20s to the 50s. Behçet's disease is relatively rare in children and the elderly. Although a definitive pattern of inheritance has not been proven, cases that appear to run in families have been reported. While Behçet's classically has periods of active and inactive disease, it can become chronic in a given organ system. Behçet's disease may produce a wide variety of symptoms. In mild cases, oral aphthous ulcers, genital sores and skin lesions (pustules or painful, red raised lesions called erythema nodosum) may be the only signs . Involvement of the gastrointestinal tract, central nervous system (brain and spinal cord) and large blood vessels is less common, but sometimes life-threatening.

Eye inflammation, which occurs in 70% of cases, is considered one of the major criteria upon which the diagnosis is based. Its complications are frequently sight threatening and require

constant attention. The ocular disease is characterized by unpredictable, repetitive, explosive inflammatory attacks, which can subside spontaneously (without treatment). Between attacks, there is little or no evidence of inflammation in the eyes. In one third of cases, the front of the eye may be involved alone, presenting as severe anterior uveitis with hypopyon. Disease affecting the back of the eye, which is often sight threatening, may produce macular edema, retinal swelling and hemorrhage (bleeding), and inflammation of the blood vessels and optic nerve. Examination of the back of the eye may be difficult due to intense inflammation in the vitreous. In its most severe form, Behçet's retinitis may be confused with a viral infection. Untreated, Behçet's may lead to retinal detachment, vitreous hemorrhage, neovascularization and glaucoma.

Diagnosis and Testing

There is no single diagnostic test for Behçet's disease. Several laboratory tests have been studied, but none have been found to be specific for disease activity. In patients with Behçet's disease affecting the brain, increased cerebrospinal fluid protein and cell count may be detected. A genetic predisposition with a strong association with the HLA-B51 gene appears to play an important role in the cause of Behçet's.

The diagnosis of Behçet's disease is therefore based on findings present during history-taking and careful examination. Five different sets of criteria for the diagnosis of Behçet's disease have been used, with the differences in these criteria hindering interpretation of different studies. An international study group was formed in 1990 to develop new internationally agreed upon diagnostic criteria for Behçet's disease. These criteria require the presence of oral ulceration (sores) **plus** any two of the following: genital ulceration; typical eye lesions; typical skin lesions; or a positive skin test for pathergy.

Treatment

Colchicine, non-steroidal anti-inflammatory drugs, corticosteroids and immunosuppressants may be used in the treatment of Behçet's disease. Therapy is tailored to the individual patient. Acute anterior uveitis generally responds to corticosteroid eye drops. Inflammation involving the back of the eye requires treatment that is more aggressive with corticosteroids given by injection and/or pill (systemic therapy). Systemic corticosteroids are helpful in treating acute manifestations. Corticosteroids alone are neither sufficient nor safe for long-term management and prevention of blindness. Immunosuppressive drugs, such as cyclosporine, azathioprine, and chlorambucil may be considered. Cyclosporine, either alone or in combination with corticosteroids, is effective for the ocular lesions, but its nephrotoxicity, occurring in 20-30% of patients, restricts usage. Chlorambucil—also often in combination with corticosteroids—has been shown to be effective.

Similar to other ocular inflammatory diseases, surgery may be required to deal with the complications of Behçet's disease. The heightened inflammatory response of patients with Behçet's disease to trauma, including surgery, should be considered but should not be regarded as an absolute contraindication to surgery.

Cause of Condition
The cause of Behçet's disease is unknown. Numerous causes have been proposed including exposure to toxins, infections, or genetic factors. No virus has been satisfactorily isolated to date. An autoimmune basis has gained increasing acceptance. A genetic predisposition coupled with a triggering event seems to lead to alterations in the immune system.

Prognosis
Male gender, early development of the disease, and HLA-B51 gene positivity are markers of poor prognosis. Eye disease, the most frequent cause of serious morbidity, may lead to blindness in 20% of those affected. The disease may occasionally be fatal, with a mortality rate of up to 6%, due to vasculitis leading to arterial occlusion, ruptured arterial aneurysms, pulmonary vasculitis or involvement of the central nervous system.

Research and Future Outlook
Studies are underway to find reliable indicators for disease activity and newer and better treatment protocols to prevent blindness from Behçet's disease.

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