Medical Underwriting of Behçet's Disease

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We recently evaluated an applicant with a diagnosis of Behçet's disease, which prompted a review of this unusual and rare clinical disorder and the formulation of an approach to its medical underwriting.

CLINICAL FEATURES

Diagnosis/Definition

In 1937 a Turkish dermatologist named Hulusi Behçet described patients who were afflicted with oral aphthous ulcers, genital lesions, and uveitis. The existence of this disorder perhaps was noted centuries ago by Hippocrates, but Behçet's reports established this as a separate disease entity characterized as a triple symptom complex. Later studies clarified the multi-systemic nature of this illness, and its classification as a vasculitis.

Diagnosis of Behçet's disease is based on an accumulation of clinical features, aided by biopsy demonstration of vasculitis of venules and other small vessels. There are no specific laboratory or radiographic features. Several sets of clinical criteria for diagnosis have been proposed. Major criteria most usually include oral, ocular, skin, and genital lesions, and diagnosis of this disease is uncertain without these features. Minor criteria, which occur infrequently, include arthritis, gastrointestinal lesions, rarely lung and renal disease, venous and arterial thromboses, and a multitude of neurologic dysfunctions.

Not all clinical features occur simultaneously, and it may be months or years before sufficient criteria accumulate for a firm diagnosis. Many types of inflammatory and vasculitic syndromes have similar non-specific symptoms early in the course of the illness, and observation over time helps to differentiate Behçet's disease from Reiter's disease, Stevens-Johnson syndrome, inflammatory bowel disease, systemic lupus erythematosus, or necrotizing vasculitidies such as polyarteritis nodosa.

Epidemiology and Etiology

The number of known affected individuals worldwide is not large, although increasing as diagnostic criteria are clearer and interest keener. Most reported cases have been in countries along the historic silk-trading route between the Far East and the eastern Mediterranean; the significance of this is not clearly known. Many cases have been described in Japan (prevalence estimated as 10/100,000 persons) and in the Middle East. Prevalence figures in Europe and the United States are less than half those in Japan. Those affected are usually young, with average age of onset of the disease between 24 and 35 years. Patients are more often male in Eastern studies, but a female preponderance is noted in Western reports. There is an association with HLA-B5 in some studies, and an immunogenetic predisposition is postulated. The underlying cause of this disorder, however, has not been clearly identified.

Clinical Involvement

The most common initial manifestation of Behçet's disease is aphthous stomatitis, and these lesions are multiple, painful, and recurrent. Systemic symptoms may accompany the acute attack. Genital ulcers often appear later. Several kinds of skin lesions (erythema nodosum, sterile pustules, superficial thrombophlebitis, acneiform rashes) occur. Other early manifestations include nonspecific abdominal symptoms, and intermittent attacks of an inflammatory arthritis in large joints.

Typically, the major features appear within the first five years, and the minor diagnostic features occur with a more variable range.

The majority of Behçet's patients have ocular involvement. Inflammatory lesions occur within a few years of the onset of the disease and can affect any part of the eye. Less troublesome is recurrent iritis, episcleritis or conjunctivitis. More serious is posterior uveitis or retinal vasculitis, which has a poor prognosis. Blindness occurs in 30 to 60% of Behçet's patients with poorly controlled posterior uveitis, and usually within 5-10 years of the onset of the eye disease. Behçet's disease is the leading cause of acquired blindness in Japan, but ocular morbidity is less severe in North American studies.

Vascular disease is present in up to 30% of Behçet's patients. The most frequent vascular complication is recurrent thrombophlebitis. Large vein occlusive thromboses also occur and while they may recannulize or improve with collateral circulation, chronic venous impairment may remain. More worrisome, but fortunately rarer, are large vessel arterial thromboses. These can present as claudication or gangrene in the extremities, renovascular hypertension, or strokes. Even more serious are aneurysms of large vessels; these frequently recur even after surgical repair, and sudden rupture is disastrous. Most of the patients who die of the vascular complications of Behçet's disease have had aneurysmal rupture, usually of the aorta.

Neurologic involvement in Behçet's disease has a poor prognosis. The reported incidence of this complication varies from 10 to 40%. Onset of neurologic complications is early, usually

in the second to the fifth year, and rarely after ten years from the presentation of other Behçet's manifestations. Almost any part of the nervous system can be involved. Some of the central nervous system impairments include brain stem syndromes with cranial nerve palsies and ataxia, confusional and psychiatric disturbances, cognitive dysfunction with memory loss or dementia, meningomyelitic states, and CVA's with hemiplegia. Recovery often occurs but chronic neurologic sequelae can remain. Mortality from CNS disease is high, up to 40%. Most of these deaths occur within a few years of the onset of the neurologic complication.

Treatment

A universally effective treatment program is not established for Behçet's disease, and cure is not often accomplished, although remissions or improvements occur spontaneously or with medication. Treatments similar to that of other kinds of vasculitis are used. Mild and benign features respond to non-steroidal anti-inflammatory medications, and topical or ocular steroids. Systemic corticosteroids are used for more serious involvement, but response to them is variable. A variety of immunosuppressive drugs, such as chlorambucil, azothiaprine, and cyclophosphamide are felt to be more effective than steroids for significant organ or life threatening disease, such as uveitis, retinal vasculitis or meningoencephalitis. Recently use of cyclosporine has shown some promise.

INSURANCE IMPLICATIONS

The course of Behçet's disease, like many chronic relapsing rheumatic disorders, is not uniform. The majority of patients will initially have frequent attacks of the less severe manifestations, with exacerbations and remissions, but then the overall course will improve and stabilize at a low level of benign activity. New disease activity is unlikely after the age of 40 or 45, or after 10 or 15 years of illness. A small percent of patients have a similar intermittent course, but develop troublesome impairments which increase the risk of mortality or chronic morbidity. Prognosis then depends on the systems involved and the severity of that involvement.

Life Underwriting

There are very few data regarding mortality in Behçet's disease, and these data are extracted from clinical studies of small numbers of patients followed for variable lengths of time. Life expectancy in this disease is nearly normal; overall mortality is estimated as 3-4%. Mortality is much lower in those cases with predominately ocular and mucocutaneous lesions. Deaths from Behçet's disease are caused mostly by CNS disease, less frequently by vascular rupture, or rarely from colonic perforation. Adverse effects of medications account for some mortality.

The following guidelines for rating are inferred from the limited data available at this time, and assume a firm diagnosis of Behçet's disease. The applicants with CNS disease or severe arterial vascular disease should be postponed for two years. After two years, ratings which reflect total anticipated mortality of 200-400%, depending on severity of disease, are reasonable. After 5 years from diagnosis of these complications, most of the mortality will have occurred and a mild to moderate (150 to 250%) substandard rating depends on the extent of remission. The other group, without CNS or vascular disease, but with ocular and mucocutaneous features, has a better prognosis, warranting mild ratings of up to 200% during the first 5 years and perhaps standard subsequently.

Those older than 40-45 years, or with disease duration more than 10-15 years, are usually in a better rating group, given no chronic impairments exist. Even with otherwise favorable features, medication use mildly increases baseline mortality. Superinfection from corticosteroids adds to early mortality, and malignancies from cytotoxic therapy may add to late mortality.

Life underwriting of Behçet's disease reflects the wide range of its clinical spectrum. Using parallels to other connective tissue disorders, mild and stable disease warrants ratings similar to those of mild rheumatoid arthritis or Reiter's disease. On the other hand, severe and active disease justifies ratings similar to moderate to severe systemic lupus erythematosus or polyarteritis.

Health and Disability Insurance Considerations

Since there are recurrent acute attacks of disease flares, work absence may be necessary until symptoms abate. These periods of short-term disability may be frequent and unpredictable, and require periodic reevaluations. Long term disability is unusual, and when it occurs is due most frequently to blindness and less often to nervous system or vascular impairments. Since the majority of individuals affected with Behçet's disease are younger than 40, any chronic impairment causing long term disability will produce many years of work loss. Health costs include the usual services for outpatient care of a chronic illness; rarely is hospitalization necessary other than for the severe disease subsets previously noted. Joint disease is not destructive. Renal impairment, unlike more worrisome types of vasculitis, is less frequently seen.

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