Behçet's disease

Behçet's disease is an inflammatory disorder involving multiple organs.

Etiology

Its cause is still unknown, but vasculitis is the major pathologic characteristic. The common vascular lesions associated with Behçet's disease are aneurysm formation, arterial or venous occlusive diseases, and varices. Arterial aneurysms mostly occur in large arteries. Intracranial aneurysms hardly occur with Behçet's disease [1].

Interleukin 1 (IL)-1 plays a key role in the pathogenesis and thereafter in the search for specific treatments of different inflammatory and degenerative eye diseases. Indeed, an overactivity of IL-1 might be an initiating factor for many immunopathologic sceneries in the eye, as proven by the efficacy of the specific IL-1 blockade in different ocular diseases. For instance, the uveitis in monogenic autoinflammatory disorders, such as Blau syndrome and cryopyrin-associated periodic syndrome, or in complex polygenic autoinflammatory disorders, such as Behçet's disease, has been successfully treated with IL-1 blockers. Similarly, therapy with the IL-1 receptor antagonist anakinra has proven successful also in scleritis and episcleritis in the context of different rheumatic conditions. Moreover, interesting findings deriving from animal models of ocular disease have set a rational basis from a therapeutic viewpoint to manage patients also with dry eye disease and a broadening number of ocular inflammatory and degenerative conditions, which start from an imbalance between IL-1 and its receptor antagonist [2].

Pathology

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Clinical features

Relapsing ocular lesions and recurrent oral and genital ulcers, with occasional skin lesions, thrombophlebitis, and arthritis [3].

H/A occur in > 50%. Neurologic involvement includes pseudotumor, cerebellar ataxia, paraplegia, seizures, and dural sinus thrombosis. Only 5% have neurologic symptoms as the presenting complaint.

Diagnosis

86% have CSF pleocytosis and protein elevation. Cerebral angiography is usually normal. CT may show focal areas of enhancing low density.

Treatment

Steroids usually ameliorate ocular and cerebral symptoms, but usually have no effect on skin and genital lesions. Uncontrolled trials of cytotoxic agents → some benefit. Thalidomide may be effective (uncontrolled studies), but carries risk of serious adverse effects (teratogenicity, peripheral neuropathy…).31 Although painful, the disease is usually benign. Neurologic involvement portends a worse prognosis.

For oral and genital ulcerations, topical steroids or sucralfate solution are first-line therapy for mild isolated ulcerations. Colchicine has also been used to prevent mucocutaneous relapse.

For severe mucocutaneous lesions, systemic corticosteroids, azathioprine, pentoxifylline, dapsone, interferon-alfa, colchicine, and thalidomide have demonstrated benefit.

For ocular disease, azathioprine is widely accepted as the initial agent. For severe eye disease (significant drop in visual acuity, retinal vasculitis, or macular involvement), either cyclosporine A or infliximab may be used in combination with azathioprine and corticosteroids.

Interferon-alfa, alone or in combination with corticosteroids, appears to be a second choice in eye disease.

For GI lesions, based on expert opinion, 5-ASA derivatives, including sulfasalazine or mesalamine; systemic corticosteroids, azathioprine, tumor necrosis factor–α (TNF-α) antagonists, and thalidomide can be used.

Arthritis may respond to prednisone, local corticosteroid injections, and nonsteroidal anti-inflammatory drugs (NSAIDs), and colchicine. Interferon-alfa, azathioprine, and TNF-α blockers may be tried in rare cases of patients with resistant, prolonged, and disabling attacks.

Cutaneous disease with erythema nodosum is a special circumstance and may be treated with colchicine or dapsone.

CNS disease is usually treated with systemic corticosteroids, interferon-alfa, azathioprine, cyclophosphamide, methotrexate, and TNF-α antagonists.

Major-vessel disease with thrombotic events are treated with systemic anticoagulation in addition to corticosteroids, azathioprine, cyclophosphamide, or cyclosporine A. Pulmonary arterial aneurysms are treated with cyclophosphamide and corticosteroids.

TNF-α antagonists are increasingly used and have become standard treatment of Behçet disease that is inadequately controlled by standard immunosuppressive regimens. Infliximab has been most widely studied, but adalimumab has proved successful in cases refractory to both conventional therapy and infliximab. [45] . Etanercept is the only TNF inhibitor with data from a short term randomized controlled study with proven efficacy in suppressing most of the mucocutaneous manifestations of Behcet disease.

Treatment with IL-1 inhibitors is effective in the management of BD-related uveitis and provides a long-term control of ocular inflammation in refractory and long-lasting cases [4].

Thalidomide may be effective , but carries risk of serious adverse effects [5].

Outcome

Although painful, the disease is usually benign. Neurological involvement portens a worse prognosis.

Case series

2016

Since the prevalence of Behcet's disease is relatively high in Iran, this study was carried out to compare the features of headache between an acceptable number of patients with this rare disease and a control group.

The current case-control study was performed to compare the features of headache between 312 patients with definite Behcet's disease who referred to a Behcet's clinic and healthy individuals. Patients with Behcet's disease were randomly selected. Controls were matched for age and sex. They were personally examined and interviewed meticulously using a questionnaire that met the standards of the International Headache Society classification for different types of headache.

The incidence of headache in the case and control groups was 28.3 % (n = 120) and 18.6 % (n = 59), respectively ($p < 0.05$; OR 2.73). Tension-type headache was observed in 12.2 % (n = 38) of cases which was significantly higher than control group (n = 6.3 %) ($p = 0.011$; OR 2.05). The most frequent type of headache in the case group was tension-type headache (12.2 %). In the control group, however, migraine without aura was the most common type (9.1 %). A correlation between ophthalmological involvement and headache was observed in 11 patients in the case group. In addition, a significantly higher systolic blood pressure was found in the case group compared to the controls (125.1 vs. 121.7 mmHg; $p = 0.007$). There was no major correlation between prednisolone consumption in patients with Behcet's disease and the type and frequency of headache.

Headache, especially tension-type headache, is more common in patients with Behcet's disease. This might be the result of specific types of uveitis-related and non-structural headaches seen in Behcet's disease [6].

Case report

2016

A 41-year-old female patient with Behçet's disease who showed symptoms of severe headache due to

subarachnoid hemorrhage. Brain computed tomography revealed multiple aneurysms [7].

A 35-year-old woman referred to the Imam Ali Hospital, Kermanshah, Iran, in July 2014 for evaluation of postoperative dyspnoea after neurosurgery performed seven days previously for a ruptured cerebral artery aneurysm. She was known to have Behçet's disease with a history of recurrent oral and genital aphthous ulcers and uveitis. At referral, her symptoms included vertigo, dysarthria, palpitations and chest pain. Transthoracic echocardiography (TTE) revealed a large thrombus in her right ventricle outflow tract and open-heart surgery was performed eight days after the previous surgery to remove the clot. The postoperative period was complicated by transient acute renal failure, which resolved spontaneously. The patient was discharged 13 days after the cardiac surgery on warfarin, prednisolone, azathioprine and cyclophosphamide. Cyclophosphamide and azathioprine were discontinued after three months as the symptoms had completely resolved; however, prednisolone was continued due to recurrent uveitis. A 10-month follow-up TTE scan revealed no thrombus recurrence and treatment with warfarin and prednisolone was continued [8].

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