

## Behçet Syndrome and Headache

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**Abbreviation:** CNS central nervous system

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Behçet syndrome is named after Hulusi Behçet (1889-1948), a professor of dermatology in Istanbul, who reported 3 patients with orogenital ulcerations and eye inflammation in 1937. The many clinical aspects of Behçet syndrome include headache.

### CLINICAL HISTORY

A 37-year-old woman presented for evaluation of frequent headache. One year previously, she had a sudden severe pain (“like an axe”) in the back of the head, with maximum intensity at the onset and representing the worst headache of her life. Computed tomography of the brain and cerebrospinal fluid examination were normal. She subsequently experienced frequent headaches. She described a constant dull aching in the back and on both sides of her head, and 1 to 2 days per week she experienced occipital and bilateral retro-orbital throbbing with associated light and noise sensitivity, but no nausea or aura. Once every 2 weeks, she had a back-of-the-head and generalized throbbing headache with associated nausea, light sensitivity, and noise sensitivity, lasting up to 4 days. She had occasional mild headaches in the past more than a year ago. Her neurologic review of systems was notable for mild memory problems.

She reported having had recurrent oral and vaginal ulcers, aching of her knees and ankles, and a skin

rash “for a few years.” She denied any history of eye problems, and findings from a recent ophthalmologic examination had been normal. Blood studies for autoimmune disease were all normal. A pathergy skin test was positive. Her rheumatologist diagnosed Behçet syndrome, and 6 months before her neurologic presentation had placed her on corticosteroids, colchicine, and hydroxychloroquine. The headaches ceased for a few weeks after initiation of oral corticosteroids but then recurred.

Findings from the neurologic examination were normal. Results of magnetic resonance (MR) imaging and MR venography of the brain and MR arterial angiography of the brain and neck were normal. Her erythrocyte sedimentation rate was 16 mm/hr. Lumbar puncture produced an opening pressure of 16 cm with 3 white blood cells/mm<sup>3</sup>, 0 red blood cells, a glucose level of 88 mg/dL, and a protein level of 53 mg/dL. Neuropsychologic testing revealed mild difficulty with attention. An electroencephalogram showed no abnormalities.

**Questions.**—Could her headache be due to Behçet syndrome? What type of headache is associated with Behçet syndrome? Other than immune suppression, how do you treat headache associated with Behçet? Are triptans helpful for recurring migraine in patients with Behçet?

### EXPERT COMMENTARY

For those who are not very familiar with Behçet syndrome, it is a multisystemic, chronic, relapsing, inflammatory disease of unknown etiology. Diagnostic criteria require recurrent oral aphthae plus any

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2 of the following: genital ulcers or scars; uveitis or retinal vasculitis; skin lesions such as folliculitis, acneiform lesions, or erythema nodosa; and hyper-reactivity of skin to nonspecific physical insult such as pinprick (skin pathergy test).<sup>1</sup> Other organ systems also may be involved, including the gastrointestinal tract, blood vessels (mainly the venous side), and lungs. There is central nervous system (CNS) involvement in about 5% of cases.<sup>2</sup> In the majority of these, there is a meningoencephalitis involving mainly the brain stem and diencephalon. In a smaller group, occlusion of the major cerebral dural sinuses may lead to intracranial hypertension without any meningoencephalitic involvement.<sup>3</sup> Males are affected more commonly, and when there is any serious organ involvement (including the CNS), this gender predilection is further pronounced; among cases with neurologic involvement, the male to female ratio is nearly 4:1.

What pathophysiology underlies headache in cases of Behçet syndrome? Most commonly, patients describe tension-type headache or migraine, which does not differ symptomatically from that observed in the general population. There is a female predominance among cases of Behçet syndrome with such headaches. Some patients report recurrent, severe, bifrontal headaches resembling migraine after the onset of Behçet syndrome, but the significance of this is not clear.<sup>4</sup> In a study involving only short-term follow-up conducted in our department, the authors concluded that migraine or tension-type headache neither implies any CNS involvement nor indicates any risk for subsequent neurologic involvement.<sup>2</sup>

Another type of headache occurs in a minority of Behçet cases and is associated with eye inflammation or severe bouts of oral ulcerations. These headaches are rare, and usually respond to treatment of the systemic inflammation.

A third type of headache is associated with neurologic involvement, and this may occur in one of two ways. In cases involving meningoencephalitis, there is often progressively severe headache of subacute onset accompanying a florid neurologic picture with behavioral change, hemiparesis, ataxia, and brain stem signs. Fever occasionally may be present. Diagnosis is not difficult in such cases. Cranial MRI almost always

shows extensive involvement of the brain stem, diencephalon, and/or basal ganglia region. Cerebrospinal fluid shows neutrophilic or lymphocytic pleocytosis. Neuropsychological testing reveals memory impairment and frontal lobe findings.<sup>3</sup>

A final cause of headache in Behçet syndrome is intracranial hypertension due to dural sinus thrombosis.<sup>5</sup> Again, there is a subacute progressive headache, which may be worse upon wakening in the morning and partially resolve during the day as the patient remains upright. Presence of bilateral papilledema (and, occasionally, sixth cranial nerve palsies) should prompt MR venography or conventional angiography and lead to the diagnosis.

The patient described here clearly does not have Behçet meningoencephalitis; her clinical examination, MRI, and CSF are normal. Mild attention deficits do not indicate serious cognitive impairment and may be present in any chronic disease.<sup>6</sup> The diagnostic workup also excluded the possibility of dural sinus thrombosis. The patient does not have eye involvement, and we do not have any information about concurrence of the headaches with the bouts of oral ulcers. Although the headaches have started relatively late, and after the onset of Behçet symptoms in this case, I would suggest the diagnosis to be simple migraine perhaps with some overlapping tension-type headache. Steroid responsiveness is not uncommon in migraine.

When there is CNS involvement, treatment of Behçet syndrome consists of high-dose corticosteroids and other immunosuppressants such as azathioprine or cyclophosphamide. If there is no CNS involvement or any other serious organ involvement, immunosuppression is not indicated for the treatment of headache. There are no controlled studies for the treatment of headache in cases with Behçet syndrome, but my own clinical experience suggests that tricyclic antidepressants or valproate are effective for prophylaxis and that nonsteroidal analgesic drugs combined with metoclopramide are effective for acute attacks. I do not have any experience with the triptans in cases of Behçet. Since Behçet syndrome is a chronic disease with a predilection for inducing vascular occlusion, I would be reluctant to prescribe triptans or, at least, would reserve them for the most unresponsive patients.

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