Neuro-Behçet’s Disease: A Multisystemic Neurological Disorder from Silk Road to Turkey

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“Über residivierende, aphthöse, durch ein virus verursachte Geschwüre am Mund, am Auge und an den Genitalien”*(1)

Behçet’s disease (BD) is a recurrent systemic autoinflammatory disorder of unknown etiology (2). It was first described in 1937 by the Turkish dermatologist Hulusi Behçet, featuring a triad of recurrent oral aphthae, genital ulcerations, and uveitis (1). Currently, criteria established in 1990 are being used for the diagnosis (3). However, other than those cited in these criteria, many other organ systems may be involved in BD such as the vascular system, mainly the veins and pulmonary arteries, gastrointestinal system, joints, and the nervous system (4). Males are more commonly and more severely affected, and the usual onset is around the third decade. BD is more prevalent in Japan, mid-Asia, Middle East, and Mediterranean basin, therefore called “the Silk Road disease” by some authors.

Neurological involvement which is seen in about 5 to 10% of the cases is almost always confined to the central nervous system (CNS) with occasional reports on peripheral neuropathy or myopathy (4). Two main types of neurological involvement can be seen in BD as parenchymal CNS involvement, which is characterized by a brainstem-diencephalic meningoencephalitis; and non-parenchymal CNS involvement, mainly due to dural sinus thrombosis (5).

Parenchymal CNS involvement is commonly presented with a brainstem syndrome evolving over a few days or weeks. Common features of this brainstem syndrome are ataxia, dysarthria, hemiparesis and bilateral pyramidal signs usually accompanied by severe headache. Sphincter problems or cognitive-behavioral changes may accompany or precede other symptoms. Interestingly cranial nerve palsies are rarely seen, as well as sensory symptoms (5). The best method of investigation is a cranial magnetic resonance imaging (MRI). The usual and characteristic MRI finding is a large T2 hyperintense lesion in the brainstem or basal ganglia region extending to diencephalon resembling a waterfall (Figure 1), with a small central enhancement. It may be bilateral or may have a slight mass effect. After the treatment of the patient, this lesion usually becomes smaller, which is then seen as scattered hyperintense spots in the same region (6). In progressive cases severe brainstem/diencephalic atrophy may be seen. Clinical course is usually with attacks and remissions, usually with sequelae; the more the number of attacks, the poorer the prognosis (5,7). Occasionally spinal cord is predominantly involved either alone or more commonly with additional CNS findings, usually associated with a longitudinally extensive spinal cord lesion and progressive course (4). In the chronic phase an atrophic cord may be seen on spinal MRI. A minority of the cases (about 10%) may present with a multiple sclerosis (MS)-like clinical and MRI picture resembling MS. Cerebrospinal fluid (CSF) examination is also a useful tool in cases with neuro-Behçet’s disease. It may occasionally be normal, but usually reveals a mild to moderate pleocytosis consisting of lymphocytes and polymorphic cells, and a mild protein elevation. Oligoclonal bands are usually negative while IgG index may be elevated. Interleukin 6 levels may be elevated in the CSF of acute and chronic neuro-Behçet patients (8). Besides verifying an inflammatory neurological involvement, abnormal CSF indicates a poorer prognosis (5).

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*Editorial*
Non-parenchymal CNS involvement mainly presents with intracranial hypertension due to dural sinus thrombosis. These cases usually have a predilection to other types of vascular involvement elsewhere in the body; usually deep vein thromboses or occasionally pulmonary aneurysms (4).

Clinical presentation of the dural sinus thrombosis due to BD is different from that of other causes (9). Subacute slow evolution of a severe headache worsening during reclining is common. Infrequently unilateral or bilateral V1th nerve palsies may be seen. Other than this and papilledema, neurological and cognitive evaluations are usually normal; epileptic seizures or cortical venous infarction are rare. Cranial MRI may reveal the occluded dural sinus but is otherwise normal. Conventional angiography or MR-venography may be of further help. CSF is almost always normal other than high pressure. Interestingly, these cases very rarely develop parenchymal neurological involvement (5,7). Cases with non-parenchymal CNS involvement have a significantly better prognosis than those with parenchymal involvement (5,7). Rarely arterial involvement of the CNS may be seen (less than 5% of all cases) resulting in either a stroke-like syndrome or complications of an aneurysm.

If the patient only has episodic headaches without any other neurological findings, the complaints should not be attributed to neuro-Behçet, since primary headache disorders are commonly seen in patients with BD (4).

There is no Class 1 evidence for the treatment of neuro-Behçet’s disease, due to lack of randomized controlled trials. However, patients with neuro-Behçet’s disease should receive immediate immunosuppressive treatment in order to prevent disability and progressive disease (10). Acute parenchymal CNS involvement attacks should be treated with high dose intravenous methylprednisolone (IVMP), followed with a prolonged oral or pulsed taper. After the attack long term maintenance treatment should be initiated; the drug of first choice is azathioprine at a dose of 2.5 mg/kg/day. Other alternatives include cyclophosphamide, methotrexate, mycophenolate mofetil, and newer biological agents such as interferon alpha, anti-TNF agents, or anti-interleukin 1 agents. Cyclosporine should not be used in neuro-Behçet’s disease, since it may worsen the disease. Dural sinus thrombosis due to BD should be treated similarly. Unlike those with other causes, the use of anticoagulants in BD is debatable. A short course of fractionated heparin could be added, but the mainstay of the treatment is steroids and immunosuppressants. Moreover, long term anticoagulation seems to be unnecessary. Any aneurysms should be meticulously excluded in a patient with BD, before starting anticoagulant medication.

Neuro-Behçet’s disease a potentially fatal and debilitating disease. However, if treatment is started early, there is usually very good response, rendering neuro-Behçet a “preventable” disorder. It should be kept in mind that steroids should never be stopped abruptly, and long term immunosuppression should be maintained in order to keep the patients out of the risks of long term steroid use.

*On relapsing aphthous ulcers of the mouth, eyes and genitalia caused by a virus

References