Case report

Neuro Behcet's disease

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Summary

Behcet's disease is a multisystem vasculitis of unknown aetiology, in which neurologic involvement has been reported in the range of 5% to 10%. We report a young patient, who presented with orogenital ulcers, brainstem dysfunction and positive pathergy reaction where the diagnosis of Neuro Behcet's disease (parenchymal type) was made. His magnetic resonance imaging (MRI) showed bilateral lesions, mainly in brainstem, thalami and periventricular regions. He was successfully treated with immunosuppressive agents.

Index words: Neuro Behcet's disease, vasculitis, brainstem syndrome

Introduction

Behcet's disease was originally described by a Turkish dermatologist, Hulusi Behcet in 1937 as a triad of oral and genital ulcerations with uveitis[1]. Now we know that it is a multisystem vasculitis of unknown origin, in which neurologic involvement has been reported in the range of 5% to 10%[2].

According to the widely accepted International Study Group (ISG) criteria, for the diagnosis of Behcet's disease recurrent oral aphthae (at least three times in one year) are a prerequisite. It should be accompanied by any two out of the following: recurrent genital ulcerations; skin lesions such as erythema nodosum, papulopustular lesions, pseudofoliculitis and acneform lesions; eye involvement such as anterior or posterior uveitis; skin pathergy reaction[1].

Case report

A 28-year-old male presented with a one week history of unsteady gait, slurred speech, vertigo, diplopia in both directions, mouth deviation to right and right hemiplegia. He had developed painful oral and genital ulcers one week prior to the onset of neurological symptoms. Past history was remarkable for recurrent painful oral ulcers (3-4 episodes per year) and one episode of genital ulcers which had developed few years back. There was no fever, headache, rashes, joint pain, abdominal pain or loose stools. On examination, there were multiple oral ulcers, where each had a well defined border, yellowish base and a diameter of less than one centimetre. Moreover, there were multiple scrotal ulcers. There were no other skin lesions. Neurological examination revealed bilateral lateral rectus palsy, bidirectional horizontal nystagmus, left sided lower motor neuron type facial nerve palsy, bilateral cerebellar signs with scanning dysarthria and mild right sided hemiplegia with anupgoing plantar response. He had normal cognitive functions, pupillary and fundoscopic findings.

Initial haematological and biochemical parameters were within normal range except for moderately raised inflammatory markers. Erythrocyte sedimentation rate (ESR) was 40 mm after one hour and C reactive protein (CRP) was 12 mg/l (<6)). Magnetic resonance imaging (MRI) of brain demonstrated multiple focal hyperintensities in T2 weighted and fluid attenuated inversion recovery (FLAIR) images in bilateral pons, midbrain, periventricular regions, cerebral and middle cerebellar peduncles and thalami with restricted diffusion in diffusion weighted images (DWI) (Figure 1). MRA, MRV and digital subtraction angiogram (DSA) were normal.

Cerebrospinal fluid (CSF) analysis showed marginally high protein levels of 48 mg/dl (ref. range: 15 - 45 mg/dl), lymphocytic pleocytosis (30 lymphocytes / mm^3) and two polymor phonuclear leukocytes / mm^3) and normal glucose (glucose of 5.1 mmol/l in CSF with a plasma value of 5.9 mmol/l). Workup for infective causes including tests for tuberculosis (TB), viral and fungal pathogens, HIV and syphilis were negative. ANA, c and p ANCA were not detected. As the patient had recurrent oral and genital ulcers with neurological symptoms, pathergy test was done, which became positive after 48 hours (Figure 2).

Based on ISG criteria and by excluding other infective and inflammatory causes, diagnosis of Behcet's disease was made. He fulfilled the required criteria (recurrent oral ulcerations) and two of the four minor criteria (recurrent genital ulcerations and positive pathergy test).

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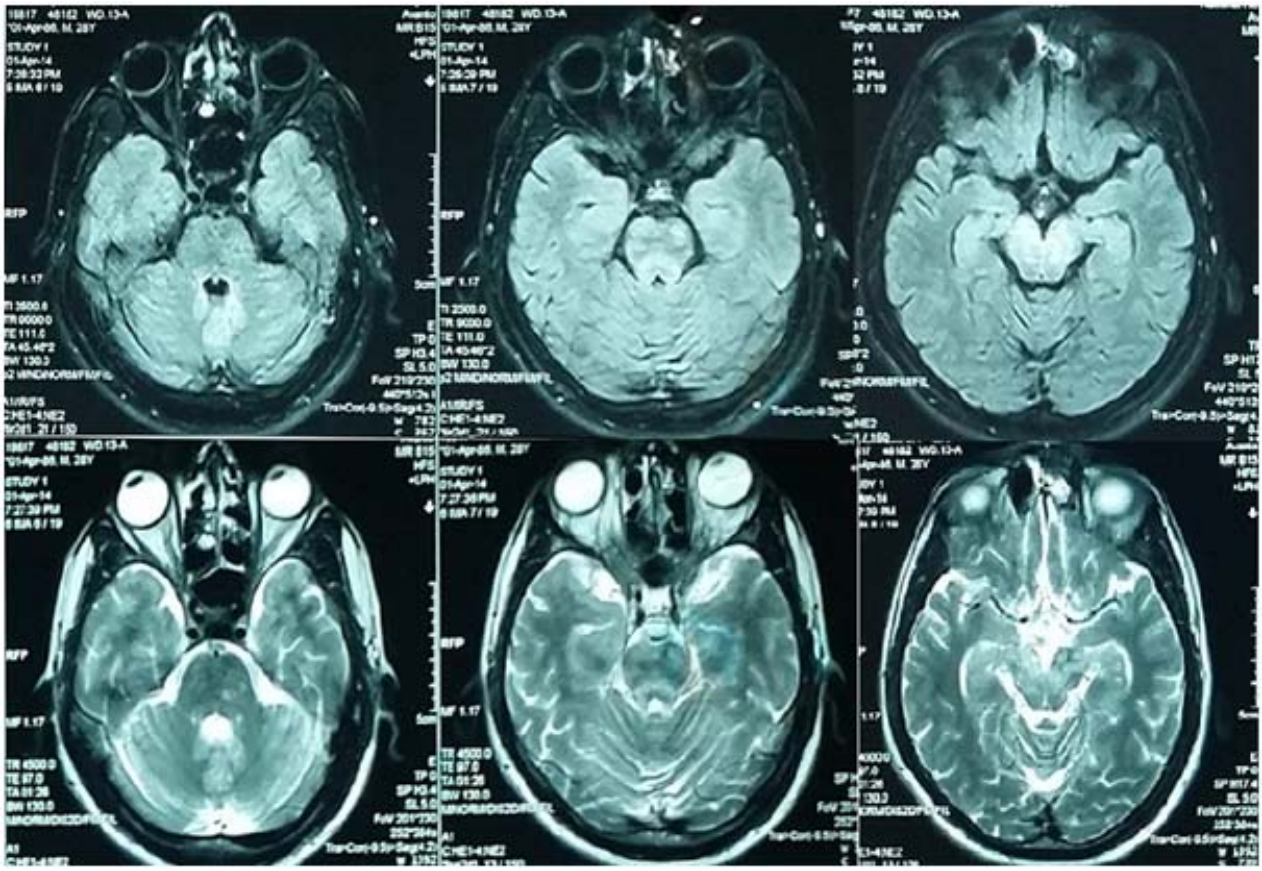

Figure 1. MRI. Multiple focal hyperintensities in fluid attenuated inversion recovery (FLAIR) (top row) and T2 weighted (bottom row) images.

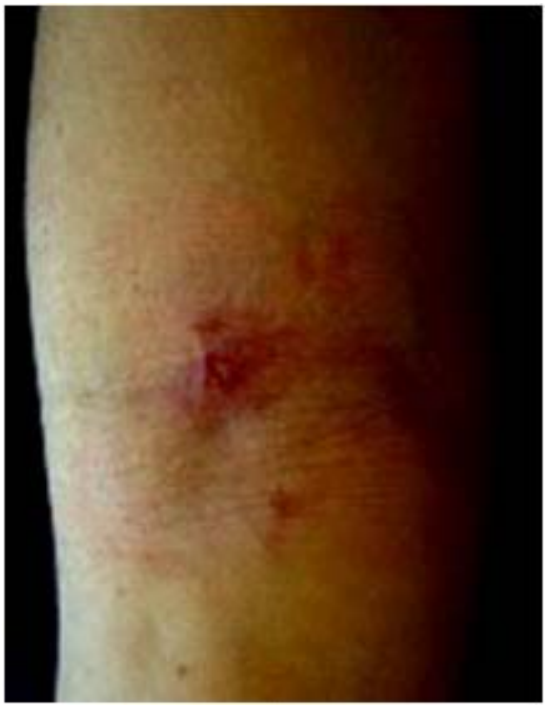

Figure 2. Positive pathergy reaction.

Eye involvement was excluded by ophthalmological examination. He was started on IV methylprednisolone followed by oral prednisolone 1 mg/kg. In the mean time he was started on azathioprine. Oral prednisolone was tailed off and azathioprine is to be continued for 18 to 24 months. With the immunosuppressive therapy, the patient improved clinically, and interval MRI done 3 months later demonstrated near complete resolution of the brain lesions.

Discussion

Behcet's disease is a chronic, relapsing, occlusive vasculitis of unknown etiology, affecting almost every organ system in the body. Theories behind the pathogenesis of Behçet disease currently suggest an autoimmune aetiology. It has been observed that there is an increase in the risk of HLA-B51/B5 carriers to develop Behçet's disease[3]. Among the systemic vasculitides, Behçet's disease is remarkable for its ability to involve blood vessels of all sizes (small, medium, and large) and in both the arterial and venous sides of the circulation[2].

In 1999, Akman Demir and colleagues reported the evaluation of 200 patients with Behcet's disease who had neurological manifestations. They found out two patterns of neurological involvement: parenchymal and nonparenchymal[3]. Parenchymal involvement is due to lesions in the corticospinal tracts, brainstem, cerebellum, periventricular white matter, spinal cord and basal ganglia. Pathology reveals local perivenular lymphocytic cuffing, inflammatory cell infiltration, gliosis, necrosis and neuronal loss. Frank vasculitis is not always observed in parenchymal lesions. Common presentations of parenchymal involvement are brainstem syndrome with cranial nerve palsy, cerebellar dysfunction and corticospinal tract signs, similar to above described patient. Nonparenchymal type, also known as vasculo-Behcet's disease, mainly results from vascular involvement and commonly presents as venous occlusion such as dural sinus thrombosis, arterial occlusion and arterial vasculitis[3,4]. Arteritis may lead to ischemic strokes, dissection, aneurysmal dilatation, and subarachnoid hemorrhage[1,3]. Other manifestations include aseptic meningitis and epileptic seizures[1].

Neuro Behcet's disease (NBD) can be mistaken for other diseases with multi focal presentations, such as multiple sclerosis (MS) and systemic lupus erythematosus (SLE), especially in the absence of systemic manifestations. In the acute phase of NBD, large confluent lesions in the brainstem-thalamic-basalganglia region are highly suggestive of the disease. In SLE, the lesions predominantly involve the subcortical white matter, and in MS, the lesions are predominantly periventricular, with less frequent basalganglia or brainstem involvement[3]. Our patient had MRI lesions in brainstem-thalamic region with normal MRA/V, which favors the diagnosis of parenchymal Neuro Behcet's disease. One notable feature in our patient was the lack of eye involvement, as 66% of the patients in the case series by Akman Demir and colleagues had ophthalmological manifestations[1].

Parenchymal involvement, especially of the brainstem, and high CSF cellular and/or protein content, is significantly associated with a worse prognosis[1,3]. Management of neurological manifestations of Behcet's disease involves high dose steroids combined with a second immunosuppressive agent[3]. Venous sinus thrombosis requires immunosuppressive therapy simultaneous to anticoagulation. Hence identifying the type of neurological involvement is important for the management and prognosis.

Competing interests

The authors declare that they have no competing interests.

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