

Case Report

Behcet's disease presenting as intracranial hypertension due to cerebral venous thrombosis



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Abstract

The non-parenchymal central nervous system's (CNS) involvement in Behcet's disease (BD) is considered rare. We herein report a case of BD complicated by intracranial hypertension (ICH) due to cerebral venous thrombosis (CVT) in a 25-year-old Saudi male. Our patient presented with a four-week history of increasingly severe headache, nausea and diplopia, which were preceded by previous recurrent intermittent oral and genital ulcers, history suggestive of acneiform lesions and arthralgia over the past two years. Ophthalmic examination disclosed normal visual acuity (20/20) in both eyes with bilateral 6th nerve palsy and papilledema. Both eyes showed no signs of anterior or posterior segment inflammation. Oral and genital ulcers were found on physical examination with no other lesions. Magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) of the brain showed lack of flow in the right transverse and sigmoid dural sinuses suggestive of venous thrombosis. On lumbar puncture, the opening pressure was greatly raised. After a comprehensive screening for prothrombotic conditions, a diagnosis of BD with ICH due to CVT was made. The patient was then treated by oral prednisolone, azathioprine, colchicine, cyclosporine, as well as anticoagulation, which resulted in significant clinical improvement.

Keywords: Behcet's disease (BD), Cerebral venous thrombosis (CVT), Intracranial hypertension (ICH), 6th nerve palsy, Papilledema

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Introduction

The first description of BD is attributed to Hulusi Behçet, who described the cases of oral and genital ulcers with hypopyon uveitis. The disease has since been recognized as a vasculitis with multiple disease manifestations.¹ BD has a distinct geographical distribution along the ancient trading route known as the 'Silk Route', extending from the Mediterranean countries to the Far East. This suggests that the etiological agent(s), including several genetic factors such as HLA-B51 had spread through this way.² It

has been reported, however, from most countries across the globe.

It is characterized by recurrent oral aphthae and any of several systemic manifestations including genital ulcers, ocular disease, skin lesions, neurological manifestations, vascular disease and arthritis.³

Central nervous system's involvement in BD includes parenchymal and non-parenchymal (i.e. cerebral venous thrombosis or arterial aneurysm) lesions.⁴ The clinical spectrum of CVT, its treatment modalities, response to treatment and its long-term outcome are still uncertain due to the small number of patients reported in the literature up till now.⁵

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Case report

We report a 25-year-old Saudi male, presented in November 2013 with a four-week history of increasingly severe headache, nausea and diplopia. A detailed medical history revealed that the patient had previous recurrent oral and genital ulcers, pimples on his back and arms suggestive of acneiform lesions and arthralgia in both knees and wrists over the past two years.

On physical examination, the vital signs were within normal. Ophthalmic exam showed a best corrected visual acuity (BCVA) of 20/20 in both eyes, and bilateral 6th nerve palsy with limitation of abduction (−3) OD and (−1) OS. The pupils were found to be regular and reactive with no afferent pupillary defect in both eyes. The intraocular pressure readings were 13 and 15 mmHg in the right and left eye, respectively. Anterior segment examination and vitreous showed no signs of inflammation. Fundoscopy revealed bilateral papilledema with no evidence of retinal vasculitis (Fig. 1). Visual field test using Humphrey perimeter showed bilateral enlarged blind spots (Fig. 2). Color vision was normal. Other aspects of the neurological examination were within normal. The remainder of physical examination was unremarkable except for multiple ulcers over the tongue and buccal mucosa, with a scrotal scar.

The initial non-contrast computerized tomography (CT) scan of the brain and orbit was normal. MRI of the brain with

and without contrast and a magnetic resonance venography MRV were done and showed lack of flow in the right transverse and sigmoid sinuses suggestive of CVT (Fig. 3). A lumbar puncture was performed and was remarkable for the opening pressure of 460 mm H₂O with normal cerebrospinal fluid (CSF) composition.

Initial laboratory tests showed hemoglobin 11.1 g/dl, ESR 120 mm/hr and C-reactive protein 0.4 mg/dl. Normal or negative investigations included WBC, platelets, prothrombin time, antithrombin III, factor V, factor IX, factor XI, factor VIII, protein C, protein S, homocysteine, anticardiolipin, anti-double-stranded DNA, ANA, rheumatoid factor, liver function tests, renal function tests, lipid profile, urine analysis, sickle cell screening test, chest X-ray, CT scan of the chest, electrocardiogram (ECG) and echocardiogram.

After neurological and rheumatological consultations, a diagnosis of BD with intracranial hypertension secondary to CVT was made. The patient was started on prednisolone 60 mg/day, warfarin 5 mg/day, azathioprine 100 mg/day, and colchicine 0.5 mg twice daily with improvement of the headache during the first 2 weeks. Diplopia was managed by 25D (OD) and 10D (OS) Fresnel prisms. Cyclosporine 100 mg/day was added subsequently and the patient was maintained on 10 mg prednisolone daily. HLA-B51 typing was done and found to be positive.

After a nine-month follow up, the 6th nerve palsy and papilledema have resolved, with no recurrence of the oral

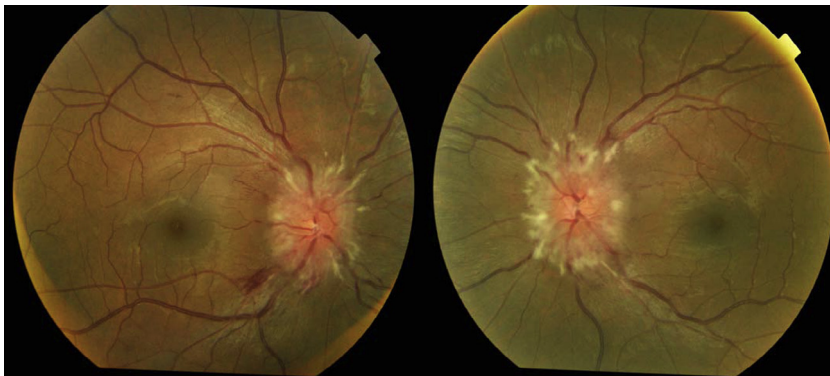


Figure 1. Papilledema without the evidence of posterior uveitis or vasculitis in the initial presentation.

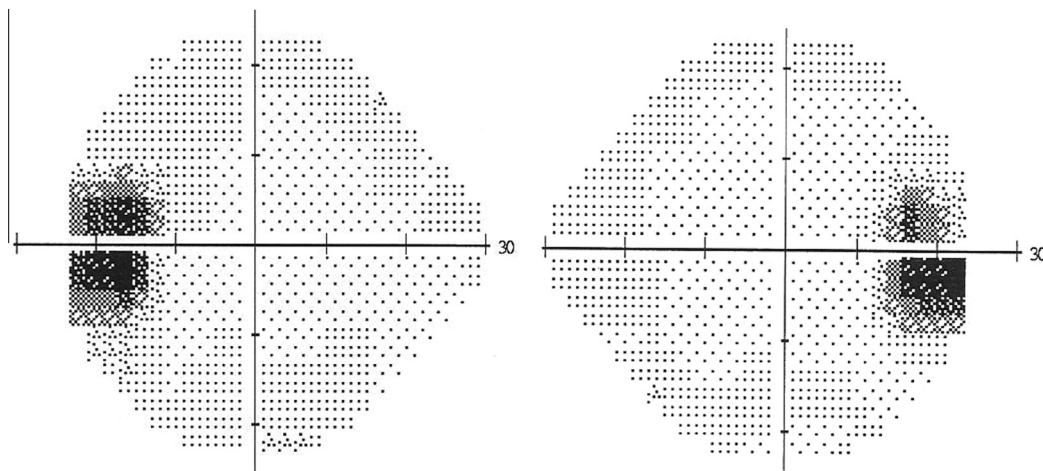


Figure 2. Humphrey visual field showing enlarged blind spot in both eyes.

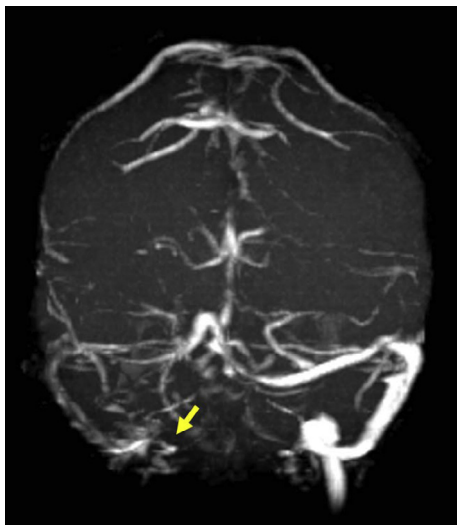


Figure 3. Magnetic resonance venogram (MRV) demonstrating lack of flow in the right transverse and sigmoid sinuses suggestive of CVT. (Yellow arrowhead depicts lack of flow in the sinuses).

Table 1. Diagnostic criteria for Behcet's disease (International Study Group for Behcet's Disease, 1990).

Recurrent oral aphtae: Plus any two of	At least three times in a year
Genital ulcerations: Skin lesions:	Active lesion or scar Erythema nodosum, folliculitis, other ulcerations
Eye involvement:	Anterior or posterior uveitis, or retinal vasculitis
Positive pathergy test:	Skin hyper-reactivity to pinprick (sterile pustule formed in 24–48 h)

or genital ulcers, skin lesions or arthralgia using the above regimen.

Discussion

BD is a clinical diagnosis based on the presence of characteristic manifestations.⁶ The International Study Group (ISG) published "diagnostic" criteria for BD (Table 1) in 1990,⁷ though these are actual classification criteria used to assure the similarity of patient groups in studies. As such, they lack sensitivity for the diagnosis in some patients. CNS manifestations are not considered in these criteria, but should be considered in securing the diagnosis.⁸

During a 2-year period, our patient suffered from recurrent intermittent oral and genital ulcers, acneiform eruptions, and arthralgia. These manifestations met the ISG criteria for BD. The neurological findings in our patient including 6th nerve palsy and papilledema with symptoms of headache and nausea were attributed to the raised intracranial pressure. The MRI/MRV results confirmed our diagnosis of CVT, which was the cause of ICH.

There are two major types of neurologic involvement in BD: parenchymal and non-parenchymal. These two types rarely occur in the same individual.⁹

In the parenchymal type, the brain stem, hemispheres, meninges, and spinal cord can be affected either individually

or in combination.¹⁰ Clinical presentations include bilateral pyramidal symptoms, mental changes, hemiparesis, cranial nerve palsies, sphincter disturbances, and brain stem symptoms. Isolated psychiatric symptoms and peripheral nerve involvement are rare.¹¹

Neurological involvement in BD may also occur as a non-parenchymal form, which includes CVT. In this form, patients may present with symptoms and signs of increased intracranial pressure including headache and papilledema, or with an acute meningeal syndrome. Less commonly, patients can present with an acute stroke resulting from arterial thrombosis, dissection or aneurysm. MRV is the imaging modality of choice when CVT is suspected. Lumbar puncture demonstrates a high CSF opening pressure, but fluid analysis is normal.¹²

Although neurological manifestations typically appear with or following other systemic symptoms of BD, they may present initially, posing a diagnostic challenge.¹

Treatment of BD is focused on the inflammatory mechanism. Glucocorticoids, immunosuppressive agents such as azathioprine and cyclophosphamide, as well as immunomodulatory agents are the most commonly used drugs.¹³ Management of cerebral venous thrombosis is directed toward the underlying inflammatory process and the use of anticoagulation. Although treatment of skin-mucosa manifestations, eye disease and pulmonary artery aneurysm has improved significantly in the past decades, the treatment of central nervous system lesions is still problematic.¹⁴ Our protocol was to use both oral prednisolone and immunosuppressive agents (azathioprine and cyclosporine) in addition to warfarin. The patient responded well to the treatment with significant clinical improvement.

In conclusion, we have reported this case to highlight the importance of including BD as a cause of CVT, especially in a young patient where there is a high index of clinical suspicion. We also aimed to increase the awareness of neurological manifestations of BD among physicians.

Conflict of interest

The authors declared that there is no conflict of interest.

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