

## Cerebral Venous Thrombosis as the Initial Presentation of Behcet's Disease

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Neurological symptoms are rare manifestations of Behcet's disease. In this paper, we report cerebral venous thrombosis as the initial presentation of Behcet's disease in a 40 year-old man. Our patient presented with a six-week history of headache, progressive loss of vision in the right eye and recurrent oral ulcers. Physical examination revealed oral ulcers and posterior synechia in the right eye with loss of light perception. Fundoscopic examination showed evidence of retinal vasculitis. Magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) of the brain showed superior sagittal, left transverse, and left sigmoid sinus venous thrombosis. A diagnosis of Behcet's disease was made based on clinical criteria. Treatment with methylprednisolone, cyclophosphamide, and azathioprine as well as anticoagulation was done with significant clinical improvement. (*Chang Gung Med J* 2009;32:220-3)

**Key words:** Behcet's disease, cerebral venous thrombosis

Behcet's disease is a chronic relapsing inflammatory disease that was first described by the Turkish dermatologist Hulusi Behcet in 1936. However, the disease might have been recognized earlier by Hippocrates.<sup>(1,2)</sup> Behcet's disease is characterized by recurrent oral aphthae and any of several systemic manifestations including genital aphthae, ocular disease, skin lesions, neurological manifestations, vascular disease and arthritis. The etiology is not known and the diagnosis is mainly clinical.

### CASE REPORT

A 40 year-old Sudanese man presented with a six-week history of headache and progressive loss of vision in the right eye. He also reported an intermittent low grade fever and insignificant weight loss. Other medical history was non-contributory. Physical examination disclosed multiple ulcers over

the tongue and soft palate, and evidence of posterior synechia in the right eye with loss of light perception. Fundus examination showed bilateral papilledema along with retinal hemorrhage and exudates. The remainder of the physical examination was unremarkable.

Initial laboratory tests showed hemoglobin 8.2 gm/dl, white blood cells (WBC) 26,000/ $\mu$ L, (mainly neutrophils), and platelets 484,000/ $\mu$ l. A peripheral blood smear showed normocytic normochromic anemia with target cells and neutophilic leukocytosis. Biochemical data showed alkaline phosphatase 210 U/L (Normal: 40-129), alanine transaminase (ALT) 56 U/L (Normal: 0-40), albumin 30 gm/l (Normal: 35-50), and C-reactive protein (CRP)  $\geq$  96 mg/l. Urine microscopy results were WBC 51-100/ $\mu$ L, and red blood cells (RBC) 9/ $\mu$ L, with leukocyte casts. The urine culture grew no organisms. Serology for viral hepatitis B and C was negative. The blood cul-

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Received: Aug. 8, 2007; Accepted: Jan. 30, 2008

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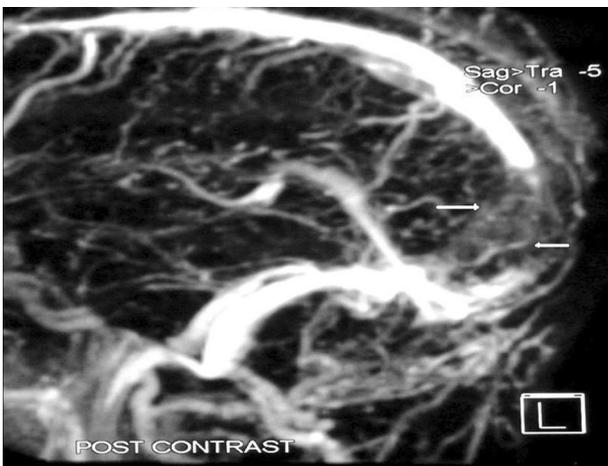
ture grew no organisms.

The initial non-contrast computerized tomography (CT) scan of the brain was normal. Magnetic resonance imaging (MRI) of the brain showed a hyperintense thrombus within the posterior part of the superior sagittal sinus (Fig. 1), and a magnetic resonance venography (MRV) scan of the brain revealed a thrombosed non-opacified area in the posterior part of the superior sagittal sinus (Fig. 2).

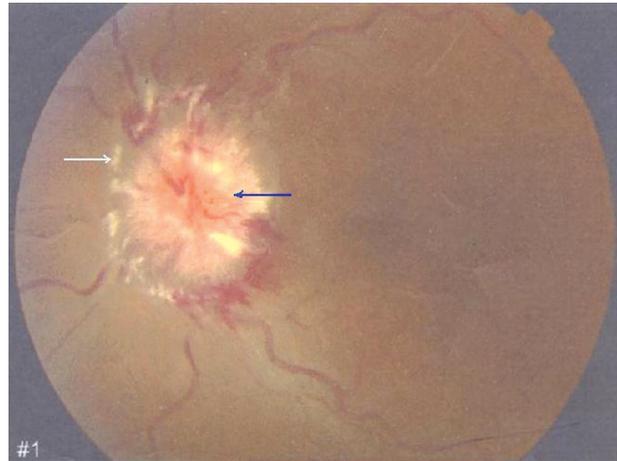
Ophthalmologic examination disclosed evidence of retinal vasculitis (papilloedema and retinal infarcts) in both eyes (Fig. 3), with panuveitis in the



**Fig. 1** Magnetic resonance imaging (MRI) of the brain shows a hyperintense thrombus within the posterior part of the superior sagittal sinus (arrows).



**Fig. 2** Post contrast magnetic resonance venography shows a thrombosed non-opacified area in the posterior part of the superior sagittal sinus (arrows).



**Fig. 3** A photograph of the fundus of the left eye shows papilloedema (blue arrow) with retinal infarcts (white arrow).

right eye. Thrombophilia screening for protein C and S, antithrombin-III, factor V leiden, antiphospholipids and homocysteine was negative.

The patient was diagnosed with Behcet's disease based on clinical criteria. Treatment was begun with intravenous methylprednisolone 1 gm daily for three days and then changed to oral prednisolone 60 mg/day. Intravenous cyclophosphamide 1 gm was then added three days later along with oral azathioprine at 2 mg/kg/day. Symptomatic improvement, with resolution of headache was noted two weeks after beginning treatment.

## DISCUSSION

Behcet's disease is a chronic relapsing inflammatory condition which many experts consider a multisystem vasculitis. Although neurologic involvement occurs less frequently than other major manifestations, it is important because it produces severe disability and is associated with a grave prognosis.

The disease is more common along the ancient Silk Road which extends from eastern Asia to the Mediterranean, with Turkey being the most commonly affected country (80-730 cases/100,000)<sup>(3)</sup> The exact incidence in the state of Qatar is not known. Young men are at particular risk from the disease and its complications.

The disease is characterized by recurrent oral and genital ulcers (in about 100% and 75% of cases,

respectively). Other manifestations include cutaneous lesions and ocular disease (typically manifested in our patient by panuveitis and retinal vasculitis); patients with acute attacks of retinal vasculitis often have retinal hemorrhage and edema which may lead to visual loss, however, uveitis is usually the dominant feature of the disease. Neurological involvement occurs in fewer than one-fifth of patients;<sup>(4-6)</sup> it may occur concurrently (7.5%) or precede non-neurological findings (3%). An Italian study reported that the onset of neuro-Behcet is usually characterized by an acute attack with motor symptoms in 2/3 of patients and behavioral/cognitive changes in more than 40% of patients, whereas headache is mainly seen in the remission phase.<sup>(7)</sup> Focal parenchymal lesions and complications of vascular thrombosis are the most common abnormalities. Behcet's disease is the most common cause of cerebral venous thrombosis in some Middle Eastern countries. Cerebral vein thrombosis is the main cause of intracranial hypertension,<sup>(8-10)</sup> and patients usually present with headache, as in our patient; its main mechanism is not completely understood, however, vasculitis may partially explain the thrombosis.<sup>(11,12)</sup> Hyperhomocysteinemia has also been assumed to be an independent factor for venous thrombosis in Behcet's disease.<sup>(12,13)</sup> Other neurological manifestations include aseptic meningitis, encephalitis, personality changes and dementia. Diagnostic criteria according to the International Study Group include oral ulcerations which recur at least three times in one year, plus any two of the following: recurrent genital ulceration, eye lesions (anterior or posterior uveitis or cells in vitrous on slit lamp examination or retinal vasculitis observed by an ophthalmologist), skin lesions (erythema nodosum, pseudo folliculitis, papulopustular lesions, or acneform nodules observed in post-adolescent patients not on corticosteroid treatment).

The prognosis varies with the type of neurologic process; those with dural sinus thrombosis or other non-parenchymal processes are less likely to have recurrent disease, disability, or premature death.

Treatment of Behcet's disease is focused on the inflammatory mechanism. Glucocorticoids, and immunosuppressive agents such as azathioprine and cyclophosphamide, as well as immunomodulatory agents are the most commonly used drugs.<sup>(14)</sup> Management of cerebral venous thrombosis is directed towards 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 and thrombophilia is still problematic.<sup>(15)</sup>

Our patient responded well to the treatment with significant clinical improvement, however, radiological improvement could not be ascertained due to loss of follow up as the patient returned to his home country.

This case report emphasizes the importance of Behcet disease as a cause of cerebral venous thrombosis. Furthermore, it can increase awareness among physicians of the neurological manifestations of this disease.

#### Acknowledgements

We would like to thank Dr. Fahmi Yousef Khan and Dr. Wanis H Ibrahim for their valuable comments.

#### REFERENCES

1. Feigenbaum A. Description of Behcet's syndrome in Hippocratic third book of endemic diseases. *Br J Ophthalmol* 1956;40:355.
2. Mutlu S, Scully C. The person behind the eponym: Hulusi Behcet (1889-1948). *J Oral Pathol Med* 1994;23:289-90.
3. Sakane T, Takeno M, Suzuki N, Inaba G. Behcet's disease. *N Engl J Med* 1999;341:1284.
4. Akman-Demir G, Serdaroglu P, Tasci B; The Neuro-Behcet's Study Group. Clinical patterns of neurological involvement in Behcet's disease: evaluation of 200 patients. *Brain* 1999;122:2171-81.
5. Serdaroglu P. Behcet's disease and the nervous system. *J Neurol* 1998;245:197-205.
6. Lee SH, Yoon PH, Park SJ, Kim DI. MRI findings in neuro-Behcet's disease. *Clin Radiol* 2001;56:485-94.
7. Lo Monaco A, La Corte R, Caniatti L, Borrelli M, Trotta F. Neurological involvement in North Italian patients with Behcet's disease. *Rheumatol Int* 2006;26:1113-9.
8. Wechsler B, Vidailhet M, Piette JC, Bousser MG, Dell Isola B, Beltry O, Godeau P. Cerebral venous thrombosis in Behcet's disease: clinical study and long-term follow up of 25 cases. *Neurology* 1992;42:614-8.
9. Bank I, Weart C. Dural sinus thrombosis in Behcet's disease. *Arthritis Rheum* 1984;27:816-8.
10. Swerdlow RH, Hanna GR. Behcet's disease presentation with sagittal sinus thrombosis diagnosed non-invasively. *Headache* 1996;36:115-8.
11. Er H, Evereklioglu C, Cumurcu T, Turkoz Y, Ozerol E,

- Sahin K, Doganay S. Serum homocysteine level is increased and correlated with endothelin-1 and nitric oxide in Behcet's disease. *Br J Ophthalmol* 2002;86:653-7.
12. Leiba M, Seligsohn U, Sidi Y, Harats D, Sela BA, Griffin JH, Livneh A, Rosenberg N, Gelernter I, Gur H, Ehrenfeld M. Thrombotic factors are not the leading cause of thrombosis in Behcet's disease. *Ann Rheumatic Dis* 2004;63:1445-9.
  13. Aksu K, Turgan N, Oksel F, Keser G, Ozmen D, Kitapcioglu G, Gumusdis G, Bayindir O, Doganavsargil E. Hyperhomocysteinaemia in Behcet's disease. *Rheumatology (Oxford)* 2001;40:687-90.
  14. Yesudian PD, Edirisinghe DN, O'Mahony C. Behcet's disease. *Int J STD AIDS* 2007;18:221-7.
  15. Yazici H, Fresko I, Yurdakul S. Behcet's syndrome: disease manifestations, management and advances in treatment. *Nat Clin Pract Rheumatol* 2007;3:148-55.