Cerebral Venous Sinus Thrombosis in Behcet's Disease: A Case Report

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Behcet's disease (BD) is a systemic inflammatory vascular disease with variable clinical manifestations and numerous clinical masquerades. The venous involvement may affect veins of different size with tendency for thrombosis. BD is the commonest cause of cerebral venous thrombosis in some Middle Eastern countries. However, in Thailand, this clinical entity has been rarely described as a cause of cerebral venous sinus thrombosis. A 38 year-old man presented with recurrent attacks of transient ischemic attack (TIA) for 9 months. Two months after the TIA, he developed right hemiparesis and persistent diffuse headache. He had a 10 year history of recurrent oral and genital ulcers. Physical examination revealed bilateral uveitis, right hemiparesis, bilateral sixth cranial nerve paresis and bilateral papilloedema. Pathergy skin test showed positive result. Neuroimaging demonstrated empty delta sign on CT-scan and thrombosis of the posterior part of superior saggital sinus, transverse sinus, straight sinus and internal jugular vein on magnetic resonance venography (MRV). Cerebrospinal fluid (CSF) analysis revealed increased intracranial pressure and aseptic CSF profiles. Prednisolone, chlorambucil and anticoagulant had been prescribed. The clinical course improved gradually.

Keywords : *Behcet's disease, Cerebral venous sinus thrombosis*

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Behcet's disease (BD) was first described by a Turkish dermatologist, as a three symptom complex comprising uveitis, oral aphtae and genital ulcerations[1]. BD is a multisystemic, recurrent, inflammatory disorder affecting the eyes, skin, mucosa, joints, vascular system, lungs, gastrointestinal tract and nervous system[2]. The latest diagnostic criteria for the diagnosis of BD consist of recurrent oral aphtae accompanied by any two out of the following features: genital ulcerations, skin lesions, eye involvement and skin pathergy reaction[3]. Although not included in the diagnostic criteria, some other features are commonly seen in patients with BD. These are thrombophlebitis, oligoarthritis, gastrointestinal ulcerations and neurological involvement[4,5]. Central nervous system (CNS) involvement is a serious complication in BD and its most frequent presentation is meningoencephalomyelitic syndrome[6]. Occasionally, it presents as dural venous sinus thrombosis[7-9].To illustrate this manifestation, we report a case with magnetic resonance venography (MRV) proven venous sinus thrombosis, affecting superficial and deep venous sinus system.This patient also had other features of neuro-BD included meningoencephalitic and vasculitic syndrome.

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Case Report

A 38-year-old man presented with a 9-month history of transient ischemic attack, characterized by recurrent right leg weakness. He developed right arm weakness 2 months later which progressed to right hemiparesis. At the same time, persistent generalized headache occurred. It was characterized by dull aching pain which was progressive. He also had horizontal diplopia 6 months later. Past history revealed recurrent oral ulcer twice per year for 5 years and genital ulcer had occurred 10 years ago. Physical examination showed afebrile, healthy male patient with normal pulsation, respiration and blood pressure. Neither orogenital ulcer nor skin lesion had been observed on admission. No other systemic

abnormality had been detected. The neurological examination revealed mild right hemiparesis with increased muscle tone of the right leg and right facial paresis of upper motor neuron type. Deep tendon reflexes were hyperactive on the right. Absent plantar response and positive ankle clonus bilaterally were observed. There were bilateral sixth cranial nerve paresis and bilateral papilloedema. Neurological examination was otherwise normal. During hospitalization, he had visual impairment. Ophthalmologic examination revealed a visual acuity of 20/200 on the left and 20/50 on the right, panuveitis and peripheral retinal vasculitis in both eyes. Skin pathergy test was positive.

Complete blood count showed normochromic normocytic anemia (Hb 10.7 mg/dl), mild leucocytosis (11,000/ml with 58.9% neutrophils, 18.7% lymphocytes, 7.7% monocytes, 14.7% eosinophils) and mild thrombocythemia (496,000 / ml). Screeening coagulogram was normal. Renal function test, liver function test and complement activity were within normal ranges.Antinuclear antibody and antiphospholipid antibodies were negative. Erythrocyte sedimentation rate was 102 mm/hr. CSF analysis demonstrated an open pressure of 370 mmH2O, WBC count of 50/ml with 100% mononuclear cells, glucose of 60 mg/dl, protein of 51 mg/dl. Gram stain for bacteria, India ink preparation for cryptococcus, VDRL and cytological study were negative. No organism was isolated from CSF culture .

Plain CT scan with contrast enhancement revealed an empty delta sign. MRI showed multiple hyposignal intensity lesions on T1WI, hypersignal intensity on T2WI and FLAIR, at right pons, left cerebral peduncle, bilateral basal ganglia and right periventricular deep white matter (Fig. 1A,B). MRV showed thrombosis of the straight sinus, posterior part of the superior saggital sinus and torcular herophili, both transverse sinus and internal jugular vein (Fig. 2). MRA showed irregularity of branches of both anterior cerebral, middle cerebral, and posterior cerebral arteries.

This patient fullfilled the diagnostic criteria for BD i.e. recurrent oral aphtae plus genital ulcer, panuveitis and positive pathergy test. The neurological abnormalities were cerebral venous sinus thrombosis, aseptic meningitis, cerebral vasculitis and multifocal lesion in the brain parenchyma.

He was treated with high dose prednisolone (60 mg/day), chlorambucil (2 mg/day). Since most of his clinical syndromes were caused by venous sinus thrombosis i.e. progressive stroke and increased intracranial pressure, anticoagulant in the form of low molecular weight heparin (nadroparin Ca) was started followed by oral anticoagulant in the form of warfarin

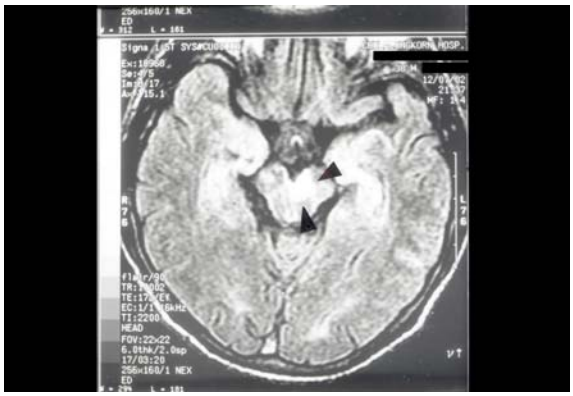

Fig. 1A FLAIR MRI showed hypersignal intensity within left cerebral peduncle

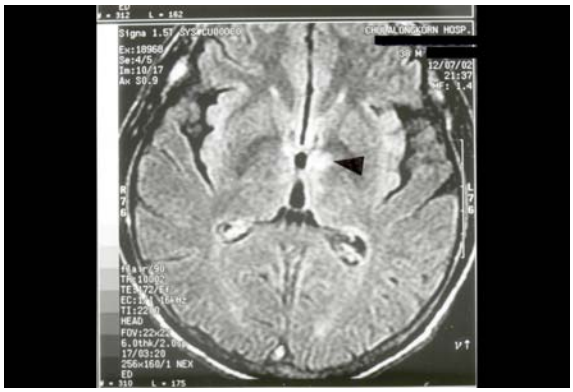

Fig. 1B FLAIR MRI showed hypersignal intensity within periventricular deep white matter

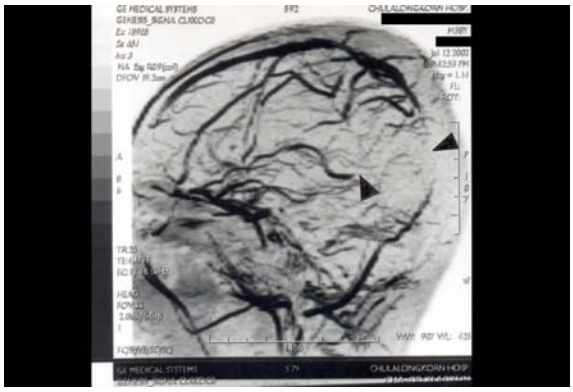

Fig. 2 MRV showed thrombosis of the straight sinus, posterior part of the superior saggital sinus and torcular herophili, both transverse sinus and internal jugular vein

which was maintained for life. He gradually improved. Headache disappeared in a few days after anticoagulant therapy and weakness improved within 2 weeks but his visual acuity deteriorated and he was finally blind in the left eye due to severe panuveitis.

Discussion

Pallis and Fudge classified the neurological syndrome in BD into three forms: 1) brainstem disturbance, 2) meningomyelitis, 3) meningoencephalitis[10]. Epidemiological study of neuro-BD has not extensively been done in various clinical series. However, in an autopsy series, 20% of 170 cases of patients with BD showed pathological evidence of neurological involvement[11]. In general, non-neurological involvement precedes the neurological manifestations. The non-neurological involvement may be unrecognized in some cases or it may appear late in the patient's course, thus posing diagnostic difficulty. One of the most common non-neurological involvements is recurrent oral ulceration which has been detected in 97-100 % of cases[12]. Oral ulcers are the initial symptom in most cases but not necessarily the presenting symptom[13,14], however they can occur in mild form and thus escape clinical detection. This patient presented predominantly with a neurological syndrome. The non-neurological involvement such as recurrent oral and genital ulcers which occurred at the beginning of the disease were mild and was unrecognized. Severe uveitis followed the neurological involvement and caused permanent visual impairment.

The predominant clinical manifestation of neuro-BD is a parenchymal central nervous system involvement, particularly brainstem involvement. The less common manifestation is dural venous sinus thrombosis[15]. The patient presented with clinical signs and symptoms of dural venous sinus thrombosis. He had a recurrent TIA-like episode at the beginning and developed progressive focal neurological deficit. The radiological findings in this patient confirmed the diagnosis of dural venous sinus thrombosis . BD is common in the Middle East, Mediterranean and some Asian countries[16]. In some Middle Eastern countries, BD is a common cause of cerebral venous sinus thrombosis especially in man[17]. However, in Thailand, venous sinus thrombosis is common in females and is usually associated with contraceptive pill users, nephrotic syndrome and systemic lupus erythematosus[18].

MRA in this case showed arteritis of anterior, middle and posterior cerebral arteries. MRI also showed parenchymal involvement, at the right side of the pons, left cerebral peduncle, both basal ganglia and right periventricular deep white matter. These parenchymal findings are common in neuro-BD and might be secondary to the small vessel disease either venulitis or arteritis[19-21]. CSF examination in sinovenous thrombosis is usually normal except for high CSF pressure[15]. The CSF profile in this case showed lymphocytic pleocytosis and elevated protein content, which indicated associated meningitic syndrome. In conclusion, the clinical features in this patient included venous sinus thrombosis, vasculitis, meningoencephalitis, but the main clinical manifestation was venous sinus thrombosis.

Current pathogenesis of BD is a vasculitic condition of unknown etiology. It is not a typical autoimmune disease and having no female preponderance. BD is not associated with other autoimmune diseases, and is usually not associated with HLA antigens (A1, B8, DR3, DR4) or autoantibodies. However, some studies have confirmed a strong association with HLA-B51 particularly in patients from Japan[22], the Mediterranean, and Middle Eastern countries[23,24]. Behcet's disease runs a chronic course with unpredictable exacerbations and remissions. The frequency and severity of the disease usually diminish with time[25]. Rupture of arterial aneurysms particularly in young males, extensive thrombotic events, and perforated intestinal ulcers can be the causes of death[26]. Morbidity is high for ocular and neurological involvement.

Management of an aphthous lesion in BD consists of topical or intralesional corticosteroid[27]. Colchicine, thalidomide and methotrexate are used in the treatment of mucocutaneous disease[5,28,29]. Azathioprine has a beneficial effect on the development and progression of ocular disease, mucosal ulcers, arthritis, deep vein thrombosis, and it may improve the long-term prognosis in BD[30,31]. Cyclosporine has a role in the management of uveitis[32,33]. Chlorambucil or cyclophosphamide may be useful for uncontrolled ocular diseases, central nervous system diseases, and large vessel vasculitis including deep venous thrombosis[34,35]. Corticosteroids are useful for suppressing inflammation in acute phases of the disease, but have a limited role in chronic management of the central nervous system or ocular complications[36]. Cerebral venous thrombosis has a good response to heparin, colchicine and corticosteroid. However, venous thrombosis may be progressive or recurrent in spite

of anticoagulant treatment, if the inflammation underlies the thrombosis has not been controlled[27]. In these cases corticosteroids and immunosuppressive agents should be considered. Surgical treatment is usually indicated in systemic arterial aneurysm[37]. The presented patient was treated with high dose corticosteroid, combined with chlorambucil for uveitis, and anticoagulant was given for dural venous sinus thrombosis. His clinical state gradually improved except for permanent blindness of the left eye from severe panuveitis.

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หลอดเลือดดำสมองอุดตันในผู้ป่วยโรคเบเช็ท: รายงานผู้ป่วย

ชูศักดิ์ ลิโมทัย, กัมมันต์ พันธุมจินดา

โรคเบเช็ทเป็นโรคที่มีหลอดเลือดทั่วร่างกายอักเสบ ทำให้เกิดอาการแสดงได้หลายรูปแบบ โดยสามารถทำให้เกิดหลอดเลือดดำทุกขนาดอักเสบ อาการแสดงที่สำคัญอย่างหนึ่งก็คือ หลอดเลือดดำในสมองอุดตัน ซึ่งพบได้น้อยในผู้ป่วยไทย แต่พบได้บ่อยในประเทศกลุ่มตะวันออกกลางบางประเทศ ผู้ป่วยชายไทย อายุ 38 ปี มีอาการสมองขาดเลือดชั่วครู่เป็นพัก ๆ และในที่สุด เกิดแขนขาอ่อนแรงซีกขวาและมีอาการปวดศีรษะ เมื่อ 9 เดือนก่อนมาโรงพยาบาล ผู้ป่วยรายนี้เคยมีประวัติมีแผลในปากและที่อวัยวะเพศเป็นๆหายๆตั้งแต่ 10 ปีก่อน การตรวจร่างกายพบว่า มีเยื่อบุตาขั้นกลางอักเสบ, แขนขาด้านขวาอ่อนแรง, การทำงานของเส้นประสาทสมองคู่ที่ 6 เสียไป และจอประสาทตาบวมทั้งสองข้าง นอกจากนี้ ผลการตรวจ พาเทอร์จีที่ผิวหนังให้ผลบวก การตรวจคอมพิวเตอร์สมองพบลักษณะที่น่าจะเป็นการอุดตันที่หลอดเลือดดำในสมอง และผลตรวจคลื่นแม่เหล็กไฟฟ้าสมองในส่วนของหลอดเลือดดำพบว่าหลอดเลือดดำในสมองบริเวณส่วนหน้าสุพีเรียซากิตตัลไซนัส, ทรานสเวอสร์ไซนัส, สเตรตไซนัส และจุกกุลาเวนด้านในอุดตัน การตรวจน้ำไขสันหลังพบความดันภายในโพรงกะโหลกศีรษะสูง และการวิเคราะห์น้ำหล่อสมองและไขสันหลังเข้าได้กับลักษณะการอักเสบชนิดปลอดเชื้อ ผู้ป่วยรายนี้ ได้รับการรักษาโดยการให้ เพร็ดนิโซโลน, คลอแรมบูซิล และ ยาต้านลิ่มเลือดแข็งตัว อาการผู้ป่วยดีขึ้นตามลำดับ