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Case Report

Behçet's Disease with Severe Arterial Involvement in a Child

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Abstract: Behçet's disease is a vasculitis characterised by its thrombotic tendency. In some patients, manifestations of vascular lesions may dominate the clinical picture instead of the classic triad. We describe a 13-year-old boy with a 1.5-year history of Behçet's disease presenting with complaints of acute abdominal pain, severe headache and decreased vision. His work-up revealed a saccular aneurysm of the distal abdominal aorta, thrombosis in the right common iliac, external iliac and femoral arteries, and thrombosis of the superior sagittal sinus. Aortoiliac bypass with a Dacron graft was performed with success. He also received cyclosporin A and anticoagulant therapy.

Severe vasculitis may become overt at any age in patients with Behçet's disease. Early diagnosis and management is important to prevent morbidity and mortality.

Keywords: Arterial involvement; Behçet's disease

Introduction

Behçet's disease (BD) is a vasculitis with a chronic and relapsing course. According to international criteria for BD, diagnosis requires the presence of oral ulceration plus any two of genital ulceration, typical defined eye lesions, typical defined skin lesions, or a positive pathergy test. The vasculitis of BD affects arteries and veins of various sizes, ranging from small to large [1–3]. Aneurysm formation, arterial or venous occlusive diseases and varices are the commonly defined vascular lesions. In the literature, vascular disease is rather common in adult patients with BD [3–7]. However, only a few cases of vascular involvement in children with BD have been reported [8,9].

We describe a 13-year-old boy with BD presenting with abdominal aortic aneurysm and arterial thrombosis of the right iliofemoral artery, together with superior sagittal sinus thrombosis leading to severe neurological manifestations.

Case Report

A 13-year-old boy presented to our department with acute abdominal pain and a history of severe headache with decreased vision. He complained of oral aphthous lesions, and migratory arthritis of the ankles and knees for the last 1.5 years. On physical examination his weight and height were below the third percentile. His blood pressure was 120/80 mmHg. There were multiple painful aphthous lesions on the buccal mucosa and tongue. Fundoscopic examination revealed fibrotic band formation over the papilla, which was interpreted to be the sequelae of recent uveitis. The papilla and maculae were bilaterally pale. His abdomen was tender and a bruit was heard over the periumbilical region. His right leg was pale and cold, and all the pulses of the right leg, including of the femoral artery, were absent. The pathergy test was negative.

Laboratory investigations were as follows: haemoglobin 11.2 g/dl, WBC 9600/mm^3 with a normal differential count. Urinalysis, renal and liver function tests were normal. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were 85 mm/h and 18 mg/dl (normal ranges: 0–8 mg/dl), respectively. Rheumatoid factor, ANA and ANCA were all negative. Other laboratory findings were as follows: complement levels

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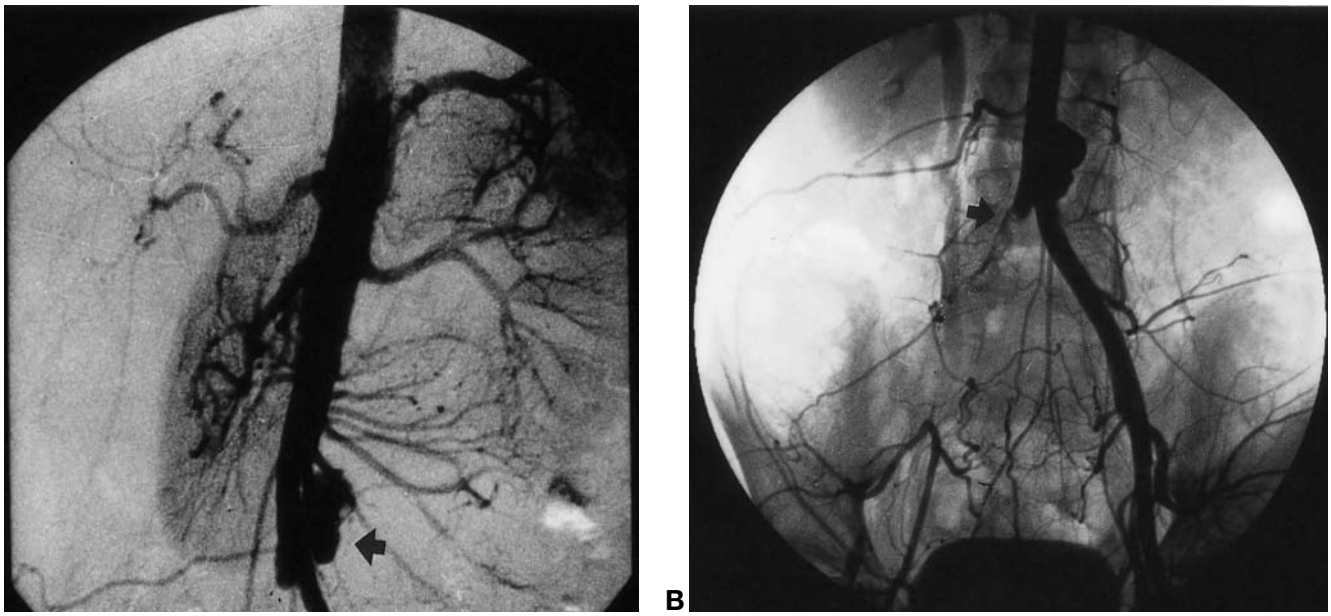

Fig. 1. Non-selective aortography and pelvic arteriography. Left oblique (A) and AP (B) projections showing saccular aneurysm of the terminal aorta extending posterolaterally to left (A) (arrow) and occlusion of the right common and external iliac arteries (B) (arrow).

and immunoglobulin levels were within normal ranges. Anti-DNA, anticardiolipin antibodies, PT and PTT were normal. Protein C was 62.9 % (normal range: 66–175), protein S 76.5 % (normal range: 73–210), antithrombin III 30.7 mg/dl (range: 18–28). Activated protein C resistance and Factor V Leiden mutation were absent. He was HLA-B51 positive.

Intra-arterial digital subtraction angiography (DSA) revealed the presence of a saccular aneurysm in the distal abdominal aorta and thrombosis in the right iliofemoral artery (Fig. 1).

Cranial magnetic resonance imaging (MRI) showed obliteration of the superior sagittal sinus and sinus rectus (Fig. 2).

Aortoiliac bypass with a Dacron graft was performed successfully, and the patient was anticoagulated with low-molecular weight heparin. Physical examination showed that his right lower extremity had returned to normal after the bypass operation. The patient was then discharged on 5 mg/kg/day cyclosporin A, warfarin and dipyridamole. After 6 months he was well, albeit with some decreased vision.

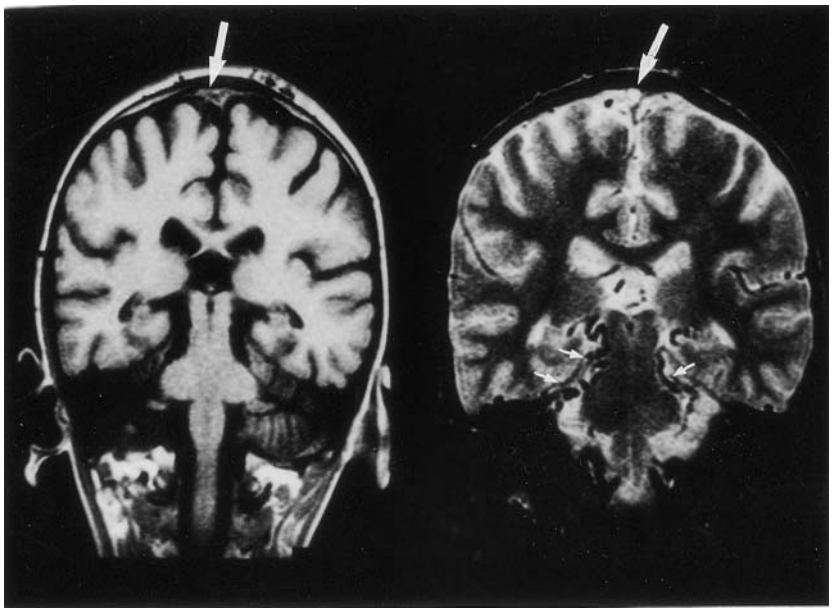

Fig. 2: T_1- (left) and T_2- (right) weighted coronal MR images demonstrating absence of signal void in the superior sagittal sinus with iso- and hyperintensity, respectively (large arrows). Also note the increased vascular structures around the brainstem, at the tentorium (Fig. 2, right) possibly representing collateral flow due to sinus rectus involvement (small arrows).

Discussion

Behçet's disease is a multisystem disorder that is classified among the vasculitic syndromes. Because the disease affects blood vessels of different types and sizes, manifestations may occur in many sites of the body. Occlusions and ruptured aneurysms of arteries involving large systemic vessels, the pulmonary bed and the CNS may result in severe disabling sequelae and death [1–7]. Vascular involvement in BD is reported to range between 7.7% and 60.0 % in adult series [4]. In paediatric patients vascular complications are less frequent than in adults. In a collaborative study of 86 paediatric BD patients eight were reported to have arterial complications [8]. However, none had aneurysm in the aorta, as defined in this patient. However, Tuzuner et al. reported a boy with an aneurysm of the abdominal aorta and two others in the common carotid artery [9]. Although venous thrombosis predominates in Behçet's disease and arterial lesions are less frequent, a recent review of the literature revealed that the combined occurrence of arterial and venous thrombosis is far more frequent than venous or arterial involvement alone [4].

The pathogenesis of the vascular lesions in BD patients is multifactorial. In BD, serum levels of cytokines have been studied extensively and increased TNF-α and soluble IL-2 receptor levels have been found [10]. Abnormalities in neutrophils, enhanced adherence to endothelial cells and increased adhesion molecules have all been suggested to be responsible in the pathophysiology of vascular involvement [11]. Genetic factors may also be operative. It has been suggested that presence of HLA-B51 antigen is associated with the severe manifestations of BD [2].

Apart from the vascular inflammation due to the disease per se, a number of coagulation factors have been studied to investigate the prothrombotic tendency in BD. In one study elevated levels of IgG anticardiolipin antibodies (ACL) were detected in 40% of patients with BD, but they were not associated with thrombosis [12]. A small number of patients were studied with regard to protein C and no consistent abnormality was detected. Congenital protein S deficiency was reported to be associated with BD in a family (a man and three of his children) by Chafa et al. [13]. On the other hand, Oner et al. [14] have suggested that Factor V Leiden mutation may be a contributing risk factor for thromboembolic events in Behçet's disease. Thus, in BD, when there are thrombotic events, haemostatic investigations have to be performed to exclude an additional cause of thrombosis. In our patient we found no such additional risk factor.

The signs of arterial involvement are various, depending on the location and the type of arterial lesion. Arterial wall lesions may result either in the development of a true aneurysm or in perforation leading to a false aneurysm. Aneurysms involving large arteries are usually associated with occlusive lesions. Occlusive lesions involve predominantly lower limbs. In all series reported to date most arterial lesions have been found in the large vessels, followed by the pulmonary and femoral arteries [4–7]. For the development of vascular complications, 3–16 years elapsed after the disease onset [4,5]. In addition, vascular disease is well known to occur in adult male patients. The patient described here is younger than 16 years, and the onset of symptoms was only a year before the development of vascular manifestations, which was shorter than in the cases described in the literature.

Neurologic involvement in BD has prevalence rates of 10%–49% in retrospective studies [15]. In childhood BD, 26% have been found to have neuro-Behçet features [8]. Non-parenchymal lesions, including dural sinus thrombosis, have a better prognosis than the parenchymal type of cerebral involvement [16]. Headache has been reported to be of no clinical importance unless accompanied by other neurological findings [15]. The decreased vision in this patient may also be partially related to the uveitis sequelae.

Occlusive lesions have had better prognosis than aneurysms. Because aneurysms expose the patient to the risk of rupture, surgery should be considered. After surgery, corticosteroids (CS) alone may not be sufficient to obtain clinical remission and radiologic resolution. In recent years, new therapeutic approaches with drugs such as cyclosporin, cyclophosphamide, azathiopurine, methotrexate, thalidomide, high-dose corticosteroids, acyclovir and FK506 have been introduced for BD [2,5,17]. Cyclosporin has been recently the drug of choice in ocular disease and for the vascular complications of Behçet's disease [17]. Vasoactive drugs such as antiaggregants or anticoagulants may be indicated in the case of thrombosis.

The patient presented here was a 13-year-old boy with a serious arterial vasculitis who was treated successfully. Predicting the patients who will develop serious complications (such as uveitis, large vessel aneurysm, neuro-Behçet) is the major concern of recent investigations. Long-term follow-up is essential in BD patients because of the relapsing nature of the disease. Currently there are no serological markers that reliably assess disease activity and severity. Patients may present with life-threatening complications at any time during their disease course. Early diagnosis of these complications is helpful to plan effective management and save the child from sequelae.

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