Juvenile angio-Behçet's disease: report and brain MRI findings of 3 cases

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Abstract

Background: Behçet's Disease (BD) is a vasculitis of unknown origin; it is characterized by recurrent mouth and genital ulcerations, uveitis and diverse systemic manifestations. It is very rare in children. Vascular tropism is mainly characterized by phlebothrombosis; arterial involvement is less frequent.

Case presentations: We report here three cases of juvenile angio-Behçet in two boys aged 11 and 16 years-old and a 14 year-old girl. All three children were admitted for a newly-diagnosed BD characterized by multiple, migrating and recurring phlebothromboses, treated with anticoagulants and corticosteroids and requiring cyclophosphamide pulses, along with a severe uveitis in one patient, having required the addition of azathioprine, with favorable outcome. Complications such as pulmonary embolism and Budd-Chiari syndrome were present in case 3, which improved under immunosuppressants. In order to prevent future thrombosis, anticoagulants were maintained for long periods as well as imunosuppressants. Magnetic Resonance Imaging (MRI) of the brain revealed subclinical findings in the 3 cases.

Conclusions: Development of venous thrombosis in juvenile BD cases should not be overlooked and special attention is required for these cases in order to improve their disease outcome. Performing advanced radiologic investigations is useful to detect subclinical cases and delineate the extent of affection. Prognosis remains variable but often bad, depending on the presence of vascular, ocular and neurological complications.

Keywords: Juvenile angio-Behçet, Phlebothrombosis, MRI brain, Rare disease, Immunosuppressants

Introduction

Behçet Disease (BD) is a vasculitis of unknown origin. It is a chronic, complex multisystem disease characterized clinically by oral aphthae, genital aphthae, cutaneous lesions, and ophthalmic, neurologic, or rheumatologic manifestations. The first description of Behçet's disease was probably by Hippocrates in the fifth century BC[1], and the first modern account was presented in 1937 by the Turkish dermatologist Hulusi Behçet, who reported on a patient with recurrent oral and genital aphthae and uveitis[2].

It is rare in children. Arterial and venous vessels can be involved, with phlebothrombosis as the main vascular manifestation, arterial involvement being less frequent[3].

New criteria for BD[4] are represented by mouth ulcerations (1 point, compulsory criterion), genital ulcerations (2 points), cutaneous lesions (1 point), ocular involvement (2 points) and a positive pathergy reaction (1 point); diagnosis is made when 3 or more criteria are present. There is no specific criteria, either clinical, laboratory or histological, for the diagnosis. We report here three cases of juvenile angio-Behçet.

Case 1

D. Mourad, aged 16 years was admitted to the Department of Rheumatology, Ben Aknoun Hospital for the management of a Behçet disease evolving since he was 12 years, with multiple deep and recurrent phlebothromboses, having affected the sural veins, the right brachiocephalic vein, the lateral sinus on the brain Magnetic Resonance Imaging (MRI) (Figure 1), associated with bucogenital ulcerations and posterior uveitis. Clinical examination revealed a small stature, truncal and facial obesity (cushingoid aspect), mouth ulcerations, a swollen left leg, negative for Homans' sign, collateral venous circulation on the chest (Figure 2) and skin lesions, mainly represented by cicatrized pseudo-folliculitis. Laboratory findings: Erythrocyte Sedimentation Rate (ESR) 45mm, C-Reactive Protein (CRP) 12 mg/L, high White Blood Cells (WBCs) count (17,100/mm^3), positive antiphospholipid antibodies. Ophthalmologic evaluation has shown posterior uveitis of the left eye. The patient was treated with anticoagulants

and glucocorticoid pulses, followed by monthly pulses of cyclophosphamide for 6 months (500 mg/m^2) and colchicine (1 mg/day). Evolution was characterized by stabilization and improvement of skin lesions as well as of antiphospholipid antibodies (APL); however, two episodes of uveitis have been noted, improved later by azathioprine and glucocorticoids (0.6 mg/kg/day).

Figure 1: Brain MRI angiography of case 1: Thromboses of the sagittal and lateral sinus (arrows on the left image)

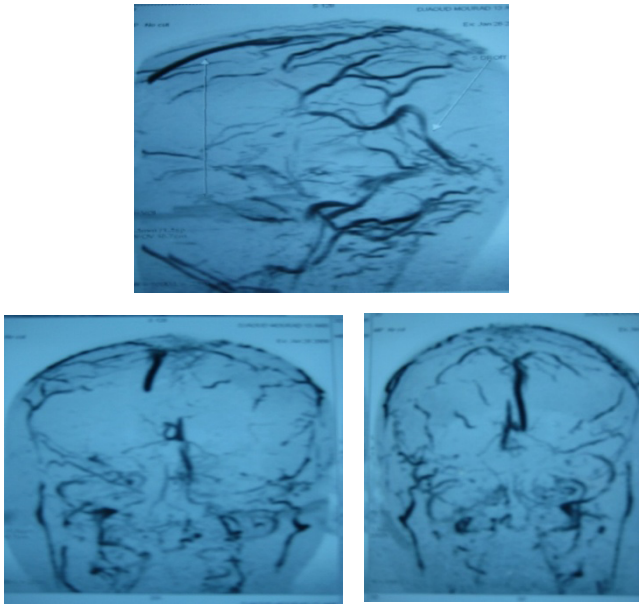
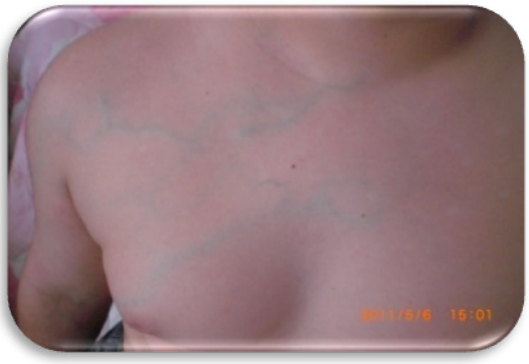


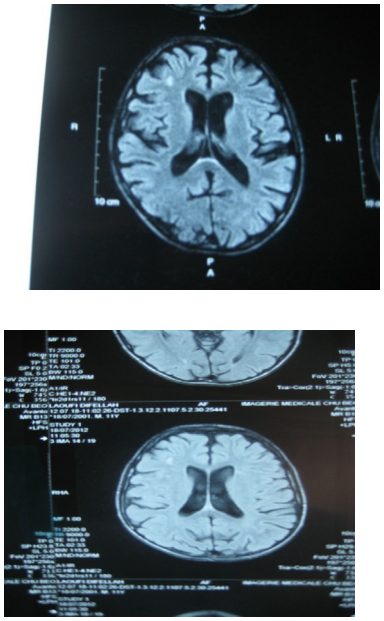
Figure 2: Collateral venous circulation on the chest wall of case 1



Case 2

An 11 year old boy, presenting with a history of recurrent sural and femoral phlobothromboses, at the age of 8 and 9 years, treated with anti-vitamin K, presented with bilateral panuveitis, mouth ulcerations as well as erythema of the upper and lower limbs and poor general condition. At admission, the child was pale, wasting (BMI 11kg/m^2), with arthralgia of the large joints. Clinical examination found spinal stiffness, pain on the left clavicle, and stiffness of both shoulders and a limitation in the opening of the oral cavity, with glossitis. Skin examination revealed erythema nodosum on the dorsal side of the left MCP 1. Ophthalmological examination revealed right side blindness. Laboratory findings revealed hypochromic anaemia (7.7g/dL), high (WBC) count (leucocytosis) (19,700 /mm^3), thrombocytosis (745,000/mm^3), elevated ESR (80 mm/1st hour) and high CRP at 231 mg/L. There was also low serum albumin (24 g/L) and positive antiphospholipid antibodies (IgM anticardiolipin). Cervical ultrasonography found a thickening of the left carotid artery and the left jugular vein, associated with cervical and sub-mandibular lymphadenopathy. Brain MRI revealed cortical and cerebellar atrophy and zones of demyelinization of the white substance (Figure 3), testifying vasculitis. The patient was treated with colchicine (1 mg/day), aspirine (100mg/day), methylprednisolone (4 mg/day) along with 6 courses of cyclophosphamide (500mg/m^2) and calcium/vitamin D supplementation. Six months later, the patient was well, and gained 4 kg of weight.

Figure 3: Brain MRI of case 2: Multiple nodular lesions of the periventricular white substance



Case 3

A young girl aged 14 years was admitted to the Department of Rheumatology, Ben Aknoun Hospital for angio-Behçet beginning at the age of 12 years, with inflammatory arthralgia and recurrent buco-genital ulcerations. One year later, appearance of headache, unhalted with analgesics, followed by phlebothrombosis of the left lower leg and then by a massive pulmonary embolism, treated with anticoagulants. Clinical examination noted lingual ulcerations, a positive pathergy reaction, an abdominal collateral venous circulation (Figure 4), as well as painful knees and ankles. Laboratory findings revealed normal values for ESR, complete blood count, rheumatoid factor, Anti-Nuclear Antibodies (ANA), Anti-Neutrophil Cytoplasmic Antibodies (ANCA) and APL antibodies. Brain MRI revealed multiple thromboses of the sagittal and the right lateral sinus (Figure 5).

Figure 4: Patient 3: Abdominal collateral venous circulation

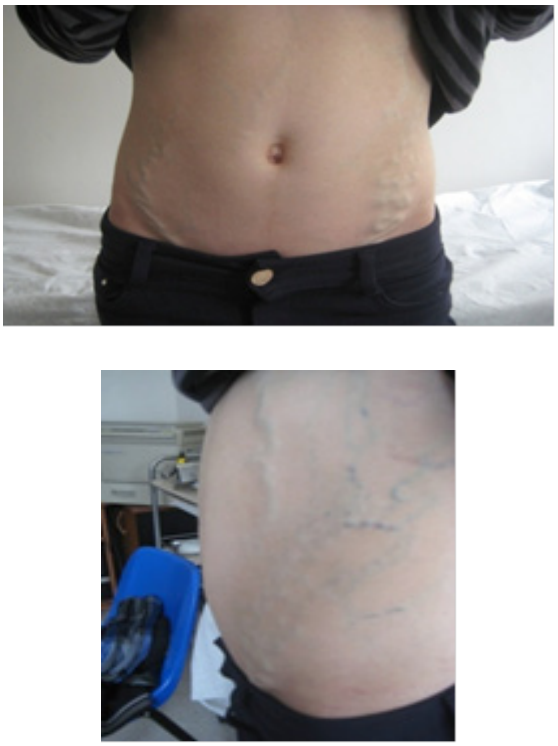
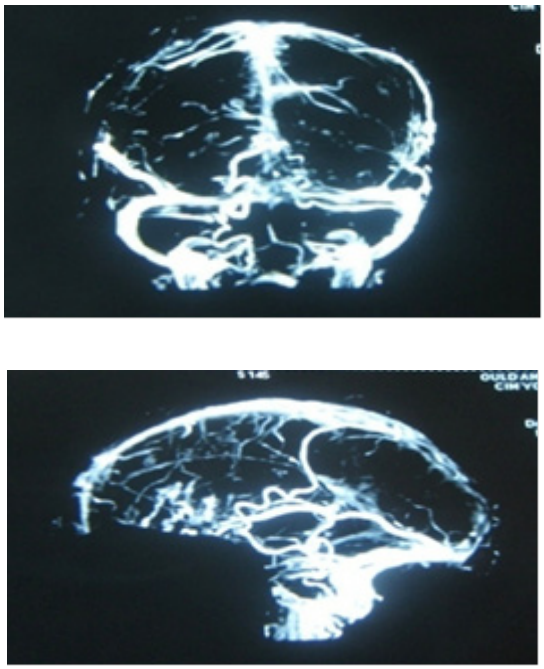


Figure 5: Brain MRI of case 3: thrombosis of the right sagittal sinus



Angio-CT of the chest revealed thromboembolic scars on the left inferior pulmonary artery, with focal infarction, associated with an expansion of the right atrium. Abdominal ultrasound found a heterogeneous hepatomegaly associated with multiple thromboses: lower vena cava and right supra hepatic vein. Ophthalmological examination was normal. Anticoagulants were associated with glucocorticoids (1 mg/day) and the patient was treated with cyclophosphamide (6 infusions) and colchicine (1 mg/day), with good outcome, ulcerations disappeared as well as arthralgia. The patient did not experience thrombo-embolic episodes since the start of the treatment, with a follow-up period of 12 months.

Discussion

Behçet's disease is rare in children and often under-diagnosed. It may be severe, and be responsible for vascular involvement, mainly venous thrombosis, associated with the presence of antiphospholipid antibodies, like in cases 1 and 2. Clinical presentation in children seems as rich and variable as in adults; however, some particularities have been noted, such as an equal involvement of boys and girls, a more frequent bowel and vascular involvement. Like in adults, there are no pathognomonic laboratory findings[5,6]. The Phlebothrombosis seems frequently associated with cutaneous manifestations such as erythema nodosum, pseudo-folliculitis and uveitis[7,8]. Phlebothromboses are mainly seen on lower limbs. Arterial involvement is rare, as was seen in case 3. It is more easily diagnosed nowadays thanks to modern imaging techniques. Budd-Chiari syndrome is rare and severe; it was seen in case 3; its frequency seems very low (< 1%)[9]. The diagnosis of Behçet disease is difficult in children because of the delay between the first symptoms and the complete presentation, allowing diagnosis.

In order to prevent future development of thrombosis, anticoagulants should be maintained for long periods, associated with immunosuppressants[10], in order to reduce systemic inflammation which is responsible for the endothelial activation. Prognosis is still severe, depending on the evolution of the vascular, ophthalmological and neurological involvement, which seems more severe than in adults[8-10]. An aggressive management may limit the consequences.

Behçet's disease is under-diagnosed in children and vascular involvement is a life threatening condition that should be seriously considered. It could be concluded that subclinical vascular involvement is overlooked in juvenile BD patients and performing advanced radiologic investigations is useful to delineate the extent of affection. In order to avoid the development of thrombosis, anticoagulants are maintained, associated with immunosuppressants.

Conflicts of interest: The authors have no conflict of interest to declare.

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