CASE REPORT

Spontaneous multisystem deep venous thrombosis as an unusual presentation of Behçet's disease in a young Afro-Caribbean patient

Anuja Mitra

Royal Free Hospital, London, UK

Correspondence toDr Anuja Mitra,
anuja.mitra@doctors.org.uk

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SUMMARY

Behçet's disease is an autoimmune mediated multisystem vasculitis. It is most prevalent in Middle Eastern and Mediterranean patients and considered rare in Afro-Caribbean populations. The disease phenotype in Afro-Caribbean patients is more severe with systemic involvement, in particular lesions affecting the vascular system known as angio-Behçet's. The archetypal triad of disease in Behçet's includes oral stomatitis, genital ulceration and ocular lesions, however, the variety of symptoms patients experience is recognised by the revised International Criteria for Behçet's disease and is reflected in the clinical scoring criteria. The authors report an unusual case of Behçet's disease in a young Afro-Caribbean patient presenting with spontaneous bilateral renal, cerebral and pulmonary venous thrombosis as first presentation. Physicians should be aware of the aggressive and atypical manner in which Behçet's can present in Afro-Caribbean patients in order to avoid diagnostic delay and remain vigilant for thromboembolic lesions in this population.

BACKGROUND

This case is important as it provides a clinically valuable lesson on the importance of disease pattern recognition in Behçet's disease (BD).¹ It also increases the profile of Behçet's in Afro-Caribbean populations and highlights the atypical manner in which the disease can manifest in this ethnic group. The case illustrates the difficulties encountered in reaching a diagnosis in such cases of diagnostic uncertainty in young patients and therefore implementing management plans.

The multi-disciplinary team involvement in this case makes it relevant and of interest to numerous specialities across medicine and surgery, thus benefiting readers from a broad background.

CASE PRESENTATION

A previously fit, 18-year-old Afro-Caribbean (AC) man presented to the emergency department with acute onset non-traumatic left calf pain. There were no other remarkable features detected during history taking.

Positive findings on examination included an enlarged appearance of the left calf, restricted range of movement in all directions and pain that was maximally elicited on passive dorsiflexion of the left foot. The neurovascular status of the limb remained intact.

Of relevance, in his medical history the patient suffered from episodes of oral stomatitis. There was no other medical or surgical history and no history of familial coagulation disorders.

INVESTIGATIONS

Doppler ultrasound of the lower limb extremities proved negative for thrombus. The vascular surgical team reached a diagnosis of spontaneous compartment syndrome and the patient subsequently underwent emergency fasciotomies of the left calf. Intraoperative findings demonstrated healthy but grossly oedematous muscles in all lower limb compartments. Evaluation of blood test results proved unremarkable, apart from an expected post-operative rise in inflammatory markers. With no clear unifying diagnosis, the patient was discharged with medical and rheumatology follow-up.

The patient presented a week later with severe abdominal pain and acute onset of frank haematuria. Following initial resuscitative measures and insertion of a three-way catheter with bladder irrigation, a CT urogram was performed, which demonstrated left sided hydronephrosis. MR venogram (MRV) of the kidney and ultrasound Doppler examination demonstrated a large left-sided occlusive renal vein thrombus with extension into the inferior vena cava and non-occlusive right renal vein thrombus. There was no arterial involvement.

Cystoscopy for the investigation of haematuria demonstrated an inflamed posterior bladder with no active bleeding point and biopsies revealed haemorrhagic cystitis.

Extensive laboratory investigations with full haemophilia, coagulation, complement, rheumatology, cryoglobulin, lupus and virology screen were sent for. With the exception of a raised erythrocyte sedimentation rate at 44, all tests returned within the normal range. Platelet disorders were excluded through aggregation studies and nucleotide assays.

Despite continuing anti-thromboembolic treatment, the patient developed multiple peripheral right-sided pulmonary emboli and, shortly after, multifocal cerebral venous sinus thrombosis with left parietal venous ischaemic lesions were detected on MRI. An incidental pituitary mass, most likely to represent a macroadenoma compressing the optic chiasm, was also detected on MRV head.

Acute neurosurgical intervention was withheld considering the high risk of bleeding. Increasing the dosage of anticoagulation and initiating steroids optimised medical management.

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The following month, the patient reported arthralgia of elbow and knee joints and a prolonged episode of right-sided knee monoarthritis with thigh swelling. Investigation of affected joints with MRI demonstrated acute synovitis and inflammatory changes. Joint fluid culture and cytology proved negative, and thigh biopsies did not illustrate any abnormality. MRI of the thigh showed extensive oedema and swelling of subcutaneous fat and deep myofascial planes, and repeat vascular Doppler studies of the lower limb extremities were once again negative.

A diagnosis of BD was ultimately reached based on the clinical findings, evidence of oral stomatitis aided by a positive pathergy test and multidisciplinary team discussion aided by senior rheumatology input.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included ailments from the spectrum of coagulation disorders such as haemophilia, sarcoidosis, as well as rheumatological and various vasculitides. Underlying neoplasm was excluded with whole body positron emission tomography imaging.

TREATMENT

During the acute presentation of the disease, the patient was started on twice-daily treatment dose low molecular weight heparin injections with daily antifactor Xa level monitoring to achieve the therapeutic balance between anti-coagulation in the face of on-going haematuria. Management difficulties were overcome by using a multidisciplinary team approach to reach consensus regarding therapeutic anticoagulation in the face of active bleeding.

The patient was maintained on oral anticoagulation, steroids and colchicine for symptom control. Repeat imaging at 2 months demonstrated resolution of bilateral renal vein thrombosis and partial resolution of the cerebral venous thrombosis with no evidence of new clot, negating the need for invasive thrombolytic therapy.

Non pharmacological treatment included regular physiotherapy sessions and social support.

OUTCOME AND FOLLOW-UP

The patient is undergoing regular monthly rheumatology review and, up to date at 9 months follow-up, the clinical course has been favourable.

DISCUSSION

It is unusual for BD to affect AC or African-American populations. The atypical manner of disease manifestation has been further observed. In particular, there is an association with more aggressive involvement of the vasculature, known as angio-Behçet's syndrome, with a particular predilection for the venous system.

Geographical variability of clinical disease expression is a reported phenomenon of BD. Positive pathergy and cutaneous reactions are more sensitive and specific for BD in Turkish patients; Mediterranean populations have localised disease involvement with lower rates of angio-Behçet and neuro-Behçet's, and Japanese populations are reported to have a high prevalence of gastrointestinal symptoms,² whereas vascular lesions with thrombosis have been an associated phenomenon in BD in AC patients.^{3 4}

Angio-Behçet's has a varied prevalence of 7–32% and represents the main cause of mortality from the disease.⁵ Classically involving the vasculature of the lower extremities and the inferior vena cava, angio-Behçet's also affects major abdominal, thoracic and intra-axial vessels causing inflammation, thrombosis and development of venous aneurysms.³

One case reported thrombosis of the common iliac veins and inferior vena cava requiring catheter directed thrombolysis,⁶ and another has described complete thrombosis of the superior vena cava, right and left brachiocephalic veins and right internal jugular vein.⁷ Both cases occurred in paediatric AC patients with a known diagnosis of BD. In such scenarios, when the diagnosis is established, the detection of venous thrombosis occurred 3 years after initial diagnosis.⁸

In both reports, thrombosis developed despite a normal coagulation profile. Although BD has been associated with a hypercoagulable tendency, the precise mechanism behind this is unclear. No abnormalities in coagulation profile or platelets have been identified. Central large vessel thrombosis occurs at an earlier age than the non-vascular BD manifestations, with a mean age of presentation being 28.1 years.⁷ The disease course in these patients is also more severe. As far as we are aware, there is no other case of bilateral renal vein thrombosis due to Behçet's described in any population.

Central nervous system involvement is considered to be the most severe sequelae of BD. The prevalence of cerebral vein sinus thrombosis (CVST) in all populations with Behçet's is reported to be between 10% and 20%.⁹ CVST is strongly associated with extra-axial major vessel disease, which is attributable for the high mortality in this cohort of patients, rather than the specific neurological problems it causes. Interestingly, Siva and Saip report it as unusual for CVST to cause venous infarction, focal parenchymal lesions on MRI, or neurological deficits and seizures, alluding to the possibility that the majority of thrombus in BD are subacute and non-occlusive.¹⁰

Although uncommon, BD can also manifest in the arterial system, causing fatality through rupture of aneurysm and pseudoaneurysm. BD was diagnosed solely on the characteristic appearances of multiple pulmonary artery aneurysms and pulmonary thrombosis in an AC patient.¹¹ Rao *et al*¹² report a case of bilateral vertebral artery pseudoaneurysms requiring endovascular treatment in a young African American patient, and there are also cases of lower limb arterial aneurysms due to BD.¹³

Other non-vascular clinical presentations of confirmed BD in AC patients include ocular lesions and neurological disease such as meningoencephalitis.¹⁴ There has been morbidity and mortality from Behçet's in patients developing acute abdomen as a result of caecal perforation and significant cerebrovascular events with long-term neurological damage.^{13 15} Furthermore, Behçet's syndrome patients from the African continent are noted to have a greater disease severity score. A study by Krause *et al*² reported higher rates of ocular disease, neuro-Behçet's and vascular thrombosis in patients of North African origin than in those in Mediterranean or Middle Eastern populations, resulting in a significantly greater disease severity score.

Learning points

- ▶ Behçet's disease (BD) can present in Afro-Caribbean patients in a more aggressive and systemic manner.
- ▶ Afro-Caribbean patients with Behçet's are more likely to suffer from angio-Behçet's at an earlier age.
- ▶ To avoid diagnostic delays and initiate timely appropriate treatment, physicians should acknowledge the association of major vessel thrombotic lesions in Afro-Caribbean patients with BD and should be vigilant for detection and monitoring of its fatal complications.

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