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An uncommon cause of deep venous thrombosis

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ABSTRACT

We present the case of a 23-year-old Turkish man who developed extensive deep venous thrombosis as a first presentation of Behçet's disease. We describe the work-up of his condition and discuss the potential for Behçet's disease to cause deep venous thrombosis as a presenting finding.

KEYWORDS: Behçet's syndrome, deep venous thrombosis

Case presentation

A 23-year-old Turkish man presented to the emergency department with a 9-month history of worsening left leg swelling, erythema and pain. His symptoms started with a widespread erythematous rash affecting his legs and associated bilateral ankle swelling. He was seen by his GP and given a course of prednisolone, which led to resolution of the rash. He travelled to Turkey shortly afterwards, where he developed left leg swelling. He was treated with aspirin and returned to the UK 1 month later. He persevered with his symptoms for some months before the pain and swelling became so intense that he attended the emergency department. Doppler ultrasonography confirmed the presence of a deep venous thrombosis (DVT) involving the left external iliac vein, and he was commenced on low molecular weight heparin (LMWH) as an outpatient. Despite being compliant with treatment for 6 weeks, his symptoms worsened, prompting his presentation to hospital.

On further questioning, he also reported a 2-week history of unintentional weight loss of 7 kg, pyrexia and night sweats. He denied any contact with tuberculosis or unprotected sexual intercourse. There was no cough, sputum, haemoptysis, urinary symptoms, gastrointestinal disturbance, chest pains or breathlessness. Past medical history included severe post-adolescent acne treated with isotretinoin. No risk factors for venous thrombosis were identified. The only relevant family history was that his mother had recently been diagnosed with renal cell carcinoma.

On examination, the positive clinical findings were temperature 38°C, pulse rate 110 beats per minute, oxygen saturations 100% on room air, and extensively swollen and erythematous left leg with painful inguinal lymphadenopathy. Femoral, popliteal and pedal pulses were present. There were marked acneiform lesions and post-acne scarring on his back as well as some mild scalp folliculitis. Baseline admission investigations are shown in Table 1.

What is the differential diagnosis and likely diagnosis?

The most likely diagnosis here is DVT, with possible clot extension. Large, unexplained DVT in a young otherwise healthy man should prompt further investigation; congenital venous malformations (for example May-Thurner syndrome), thrombophilia or occult malignancy should all be considered. His other symptoms, such as fever, weight loss and night sweats, also require further investigation to exclude haematological malignancy, infections such as tuberculosis, or an autoimmune or inflammatory process.

What is the initial management?

Blood cultures were sent and the patient was commenced on intravenous antibiotics for a presumed overlying cellulitis. Thrombophilia screen was requested. Magnetic resonance venography (MRV) of his legs was arranged to establish the extent of the thrombus. Therapeutic anticoagulation was commenced and anti-factor Xa levels were requested to ensure the patient was adequately anticoagulated. Chest radiograph was normal. Additional investigations requested included HIV serology, autoantibodies, creatinine kinase (CK), lactate dehydrogenase (LDH), testes ultrasonography and cross-sectional imaging to look for an underlying neoplasm.

Case progression

Despite antibiotics, the patient remained pyrexial. Blood and urine cultures were persistently sterile, and thrombophilia screen was negative. HIV serology was negative, and CK, LDH and blood film were normal. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were significantly elevated at 108 mm/h [1–10 mm/h] and 99 mg/L [0–5 mg/L], respectively. Autoantibody screen was negative and anti-factor Xa levels were within the normal range. Ultrasonography, although negative for testicular lesions, did identify benign looking 1 cm left-sided inguinal lymph nodes. Computed tomography did not demonstrate any malignancies, cavities, collections or lymphadenopathy in the chest or abdomen.

MRV of his lower limbs demonstrated distal extension of the clot, which was now also implicating the common femoral and superficial femoral veins. Additionally, the iliac vein was noted to have marked surrounding inflammatory change, not typical of a

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Table 1. Baseline admission investigations.

	Measurement	Normal range
Haemoglobin	10.9 g/L	13–17 g/L
Mean cell volume	79.0 fL	83–101 fL
Platelets	329 x 10^9/L	150–410 x 10^9/L
White cell count	13.7 x 10^9/L	4–10 x 10^9/L
Neutrophils	8.8 x 10^9/L	2–7 x 10^9/L
Lymphocytes	3.7 x 10^9/L	1–3 x 10^9/L
Sodium	139 mmol/L	133–146 mmol/L
Potassium	4.2 mmol/L	3.5–5.3 mmol/L
Urea	5.2 mmol/L	2.5–7.8 mmol/L
Creatinine	52 µmol/L	62–106 µmol/L
Bilirubin	4 µmol/L	1–21 µmol/L
Alanine aminotransferase	34 unit/L	10–40 unit/L
Alkaline phosphatase	78 unit/L	30–130 unit/L
Urinalysis	Normal	
Chest radiograph	Normal	
Electrocardiogram	Sinus tachycardia; normal axis	

straightforward thrombosis. There was no sign of May–Thurner syndrome.

While on the ward, the patient complained of a sore throat, and examination of his oral cavity revealed multiple aphthous ulcers and associated cervical lymphadenopathy. On further questioning, he admitted having oral ulceration 3–4 times a year for many years. There was no current evidence or past history of genital ulceration. Positron emission tomography (PET) confirmed an inflammatory process within both pharyngeal tonsils and metabolically active bilateral cervical lymphadenopathy.

What is the likely diagnosis and how should this be managed?

The patient's ethnicity, thrombosis and oral ulceration raised the suspicion of Behçet's syndrome. An opinion was sought from an oral medicine specialist, who agreed that this was the likely diagnosis. Pathergy skin testing was positive. HLA-B51 antigen testing was requested and later found to be positive. The patient was commenced on azathioprine and high-dose oral prednisolone, and anticoagulation was continued. His clinical symptoms improved.

Discussion

Behçet's disease is a multisystem inflammatory condition most commonly seen in those of Mediterranean and Eastern origin; the highest incidence is in Turkey. [1] Our patient satisfies the International Study Group criteria for the diagnosis of Behcet's disease (Box 1).[2] Recurrent aphthous ulceration is a cardinal feature and might precede the development of systemic symptoms by many years – as seen in our patient. Vascular involvement is not limited to any vessel size, affects veins more than arteries and, when present, can be associated with constitutional symptoms.[1] Patients might develop venous thrombosis affecting the lower limbs, vena cava or hepatic veins. Occasionally, haemoptysis as a result of pulmonary artery aneurysms occurs, and is associated with worse outcomes.[1] Venous thrombosis in Behçet's disease is caused by phlebitis and not thrombophilia: hence the thrombus remains attached to the inflamed vessel wall and tends not to metastasise. Venous thrombosis responds well to treatment with immunosuppression.

Box 1. International study group criteria for the diagnosis of Behçet's disease.[2]

Recurrent oral ulceration

Minor aphthous, major aphthous or herpetiform ulceration observed by physician or patient, which recurred at least 3 times in a 12-month period

And two of the following

Recurrent genital ulceration

Aphthous ulceration or scarring, observed by physician or patient

Eye lesions

Anterior uveitis, posterior uveitis, or cells in vitreous on slit lamp examination, or retinal vasculitis observed by ophthalmologist

Skin lesions

Erythema nodosum observed by physician or patient, pseudofolliculitis or papulopustular lesions, or acneiform nodules observed by the physician in post-adolescent patients not on corticosteroid treatment

Positive pathergy test

Read by physician at 24–48 hours

The beneficial role of anticoagulation is unclear, and can lead to adverse events in patients with coexistent pulmonary aneurysms.[4]

Although DVT is a common clinical presentation, this case emphasises the importance of identifying the cause of unprovoked venous thromboses and that clinicians should consider Behçet's disease in appropriate ethnic groups, particularly in patients with a history of recurrent oral or genital ulceration and negative thrombophilia screening.

Key learning points

- An underlying cause for deep vein thrombosis should always be sought for in patients without any identifiable risk factors.
- A multisystem vasculitis, like Behçet's disease, should be considered in all patients presenting with venous thrombosis, aphthous ulcers and constitutional symptoms.
- The use of anticoagulation in Behçet's should be carefully balanced with the risk of major haemorrhage in patients with coexisting arterial aneurysms.
- Immunosuppressive therapy may cause overwhelming infections and patients should be counselled about this before the initiation of treatment. ■

Conflicts of interests

The authors declare no conflicts of interests.

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