Unprovoked DVT, the clot thickens

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ABSTRACT

Deep vein thrombosis (DVT) is a common presentation to acute medical services. This paper describes the investigation and subsequent treatment of a patient who presented with an extensive lower limb DVT and was found to have congenital inferior vena cava agenesis (IVCA).

Case

Ms A., a 28-year-old female, presented to the medical service at Middlemore Hospital (Auckland) with a 12-hour history of right leg swelling. She denied recent infective symptoms or trauma, aside from a dog-scratch 4 days previously on her right shin. She had no chronic illnesses, no recent surgery, and no air travel. Ms A smoked five cigarettes per day, and her only medication was an oral contraceptive pill (OCP), containing ethinyloestradiol 30 mcg. On examination, marked swelling of the right leg was noted from ankle to groin, with a circumference differential of 6 cm at the upper thigh, and 5 cm at the tibial tuberosity. D-dimer was 1,440 ug/L and lower limb ultrasound showed a large right deep vein thrombosis (DVT) from the popliteal to the external iliac vein. Thrombophilia screen was negative.

Therapeutic enoxaparin was commenced at 70 mg twice daily. Given the severe swelling, surgical thrombectomy with possible venous reconstruction was initially considered, and CT venogram was performed. This revealed agenesis of the inferior vena cava (IVCA) associated with the DVT, presumed to be congenital, as Ms A had no history of vascular intervention in childhood. Referral was therefore made to interventional radiology and catheter-directed thrombolysis with urokinase was undertaken, initially to the occluded popliteal vein, followed by right external iliac vein 2 hours later and common femoral vein the next day. Following this, Ms A underwent pharmacomechanical thrombectomy of the femoral and external iliac veins. This was achieved by an AngioJet catheter, which directs pulses of a thrombolytic agent into the clot. Fragments of clot are then actively aspirated by a vacuum formed within the catheter. This led to significant improvement in swelling and no residual stenosis. Warfarin was then started, with enoxaparin cover until therapeutic levels were reached. The OCP was stopped on admission, and after discussion about contraceptive options, Ms A chose the Depo-Provera injection. Smoking cessation advice and support was provided. At her 4-month follow-up appointment, Ms A was back to running, and was only having occasional pain in the right leg on strenuous exercise. Anticoagulation had been therapeutic since discharge, and no complications had arisen. Ms A was educated further at this stage about the need for lifelong warfarin, and enoxaparin cover during any future pregnancies.

Discussion

IVCA is a rare congenital vascular anomaly identified in approximately 5% of patients with DVT under 30 years of age. The diagnosis covers several anatomic variations including the absence of the suprarenal, infrarenal or entire IVC. IVCA is proposed to be a risk factor for DVT because the vena azygous system does not adequately drain the lower limbs, leading to venous stasis and subsequent clot formation.

The diagnosis of IVCA must be considered in DVT patients of younger age, with
Figure 1: CT venogram demonstrating lack of contrast uptake in the atresic IVC

Figure 2: Atresia of IVC parallel to the aorta
minimal risk factors, or with proximal DVT and extensive clot burden. Compressive ultrasonography is not sufficient to make the diagnosis of IVCA, and abdomino-pelvic CT, MRI or angiography is required. This can also guide treatment with catheter directed thrombolysis if required.

The diagnosis is important; IVCA is not a modifiable risk factor so there is significant risk for recurrent events. Treatment is with anticoagulation. There is no systematic follow-up data available regarding the rate of recurrence of DVT after stopping anticoagulation in patients with IVCA, although such cases have been reported. There are no guidelines for the duration of anticoagulation and most reported cases have been prescribed long-term vitamin K antagonists. Some authors report an association of IVCA with clotting disorders, although generally thrombophilia screening in these patients is not useful as it does not change the recommended duration of anticoagulation. In this case, the OCP was stopped and exchanged for the Depo-Provera injection. Evidence suggests that the risk of recurrent thrombus while anticoagulated is not increased by oestrogen containing contraceptives. However, given the teratogenicity of warfarin and the typical failure rate of the OCP (3%) compared with the Depo-Provera injection (0.3%), it makes sense to select a contraceptive method that minimises potential for unplanned pregnancy.

Long-term complications of DVT including oedema and post-thrombotic syndrome can lead to loss of mobility and inability to return to work. Recent trials have shown advantages of thrombolysis, particularly catheter-directed thrombolysis and pharmacomechanical techniques, over standard anticoagulation in terms of clot breakdown and venous patency. The long-term goal is to reduce the incidence of post-thrombotic syndrome (PTS). A recent Cochrane review of systemic and locoregional techniques demonstrated a number needed to treat of five to prevent one case of PTS, in patients who presented within 14–21 days of symptom onset. The newer pharmacomechanical techniques not included in the Cochrane review are proposed to have a lower bleeding risk through a reduced dose of thrombolytic, and improved venous patency by combining thrombolytic agent with mechanical techniques. These interventional procedures are particularly useful for patients with proximal iliofemoral DVT, a low bleeding risk, and good functional status who present within 3 weeks of symptom onset. Such techniques were therefore appropriate for Ms A, who fulfilled all of these criteria, and in whom post-thrombotic syndrome could have life-long implications.

IVCA is likely an under-diagnosed entity as CT is not a routine investigation for DVT, and IVCA is often found incidentally after imaging for suspected malignancy or occult sepsis. We need to consider IVCA in patients with DVT, especially young patients who have few risk factors, extensive clot burden and proximal location, such as Ms A. This could impact on both the duration of anticoagulation and the management in higher risk situations such as pregnancy. Further imaging also means that alternative acute treatments, such as thrombolysis or surgical thrombectomy, can be considered in appropriate patients.

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