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Case Report

CASE REPORT

An unusual case of deep venous thrombosis in a young patient: congenital absence of the infrarenal portion of the inferior vena cava

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Abstract

Deep venous thrombosis (DVT) is a commonly encountered diagnosis in clinical practice with a variety of well-established risk factors. Congenital absence of the inferior vena cava (IVC) is an extremely rare but established risk factor for DVT. Patients who develop DVTs are at high risk of long-term complications, including DVT recurrence and post-thrombotic syndrome. Here we report a rare case of a 27-year-old female who presented with an extensive DVT of the right lower extremity secondary to complete absence of the infrarenal portion of the IVC, confirmed on computed tomography. There is little consensus regarding the appropriate management of this patient population, and a brief review of the current evidence follows.

INTRODUCTION

Congenital absence of the inferior vena cava (IVC) is a rare but established risk factor for deep venous thrombosis (DVT). The precise underlying pathophysiology remains unknown; however, defective embryonic development and thrombosis of the IVC during the intrauterine/perinatal period may both play a role.

Patients who develop DVTs (particularly proximal iliofemoral DVTs) are at high risk of long-term complications, including DVT recurrence and post-thrombotic syndrome (PTS). IVC anomalies with associated DVTs in young patients, although rare, do present an important clinical problem. Furthermore, debilitating PTS in a young population can have significant socioeconomic implications.

While much is understood regarding the epidemiology of DVT in the context of IVC anomalies, there is little consensus regarding appropriate management of these patients. A case description and review of the current evidence follows.

CASE REPORT

A 27-year-old Caucasian female of English and Italian descent presented to the Emergency Department with an acutely swollen and painful right leg but no associated systemic or cardiorespiratory symptoms.

She had no known risk factors for DVT, and there was no history of trauma. She had a past medical history of psoriasis and a family history of breast cancer in two second-degree relatives (maternal aunt and grandmother), who were both BRCA gene mutation carriers. She was a non-smoker and consumed alcohol occasionally.

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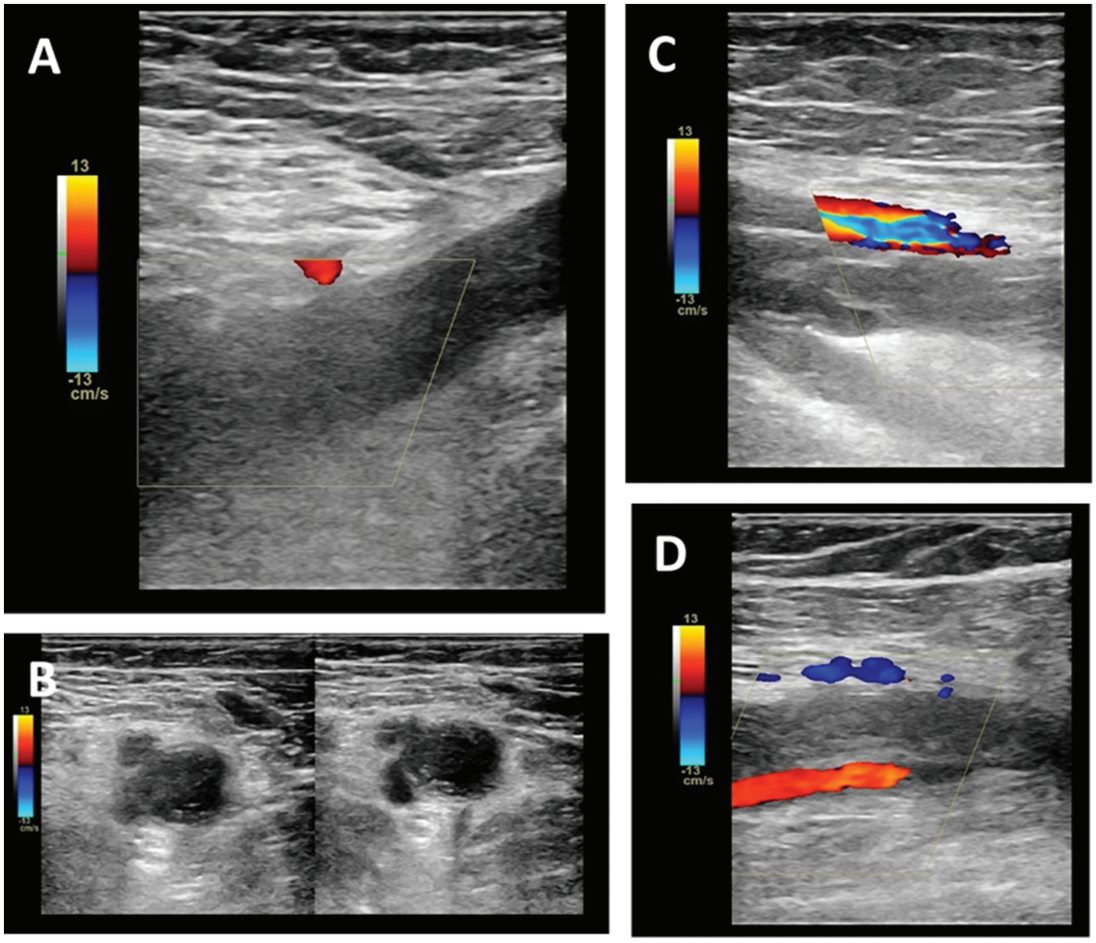

Figure 1: US imaging of the proximal right thigh demonstrates echogenic non-compressive material filling the lumens of the (**A**) external iliac, (**B**) common femoral, (**C**) femoral and (**D**) popliteal veins consistent with an extensive occlusive thrombus.

On clinical examination she was haemodynamically stable and apyrexial. Her right lower extremity was swollen and tender on palpation. The remaining physical examination was unremarkable.

Laboratory investigations revealed a raised C-reactive protein at 80 mg/L (range 0–10), a normal white cell count at 7.8 10^9/L (range 4–11), normal biochemical markers and a normal coagulation screen. A point of care D-dimer assay was found to be elevated at > 1000 ng/ml (normal range 0–500).

A colour Doppler ultrasound (USA) of the right lower limb demonstrated an extensive, occlusive DVT extending from the popliteal vein to the level of the right external iliac vein (Fig. 1).

Given her family history of cancer and young age of presentation, a contrast-enhanced computed tomography (CT) of the abdomen and pelvis was performed to investigate for an underlying malignancy as a possible cause of her unprovoked DVT. Fortunately, no features of malignancy were found; however, incidental note was made of complete absence of the infrarenal portion of her IVC with compensatory dilatation of extensive venous collaterals facilitating venous drainage of the lower extremities (Fig. 2).

Following discussion with the vascular surgeons, no interventional procedures were considered necessary. She was discharged on treatment dose low molecular weight heparin and was subsequently followed up by the haematology team who switched her anticoagulation to warfarin, with an international normalized ratio (INR) target of 2.75 (range 2.5–3.0). Warfarin was selected over novel oral anti-coagulants due to limited experience with these newer agents in the context of IVC anomalies. A thrombophilia screen was negative.

She re-presented a fortnight later with a swollen and painful left lower extremity. Doppler US confirmed the presence of an occlusive left-sided iliofemoral thrombus. Unfortunately, her left leg was not scanned at the time of her original presentation as it was asymptomatic; therefore, it is not certain whether this DVT was present at the time when her right-sided DVT was diagnosed. This is an important observation, as patients who develop further DVTs despite being on adequate therapeutic anticoagulation will thereafter require more aggressive anticoagulation therapy. Given the significantly increased risk of bleeding in these circumstances, this strategy should not be adopted unless absolutely necessary. Thus, given the uncertainty surrounding the time of onset of the left-sided DVT, it was decided to continue with a target INR of 2.75 (range 2.5–3.0), rather than a high-risk target INR of 3.5 (range 3.0–4.0).

DISCUSSION

DVTs occur with a prevalence of 1 in 1000 in the general population and are associated with congenital and/or acquired established risk factors in 80% cases. In the younger population,

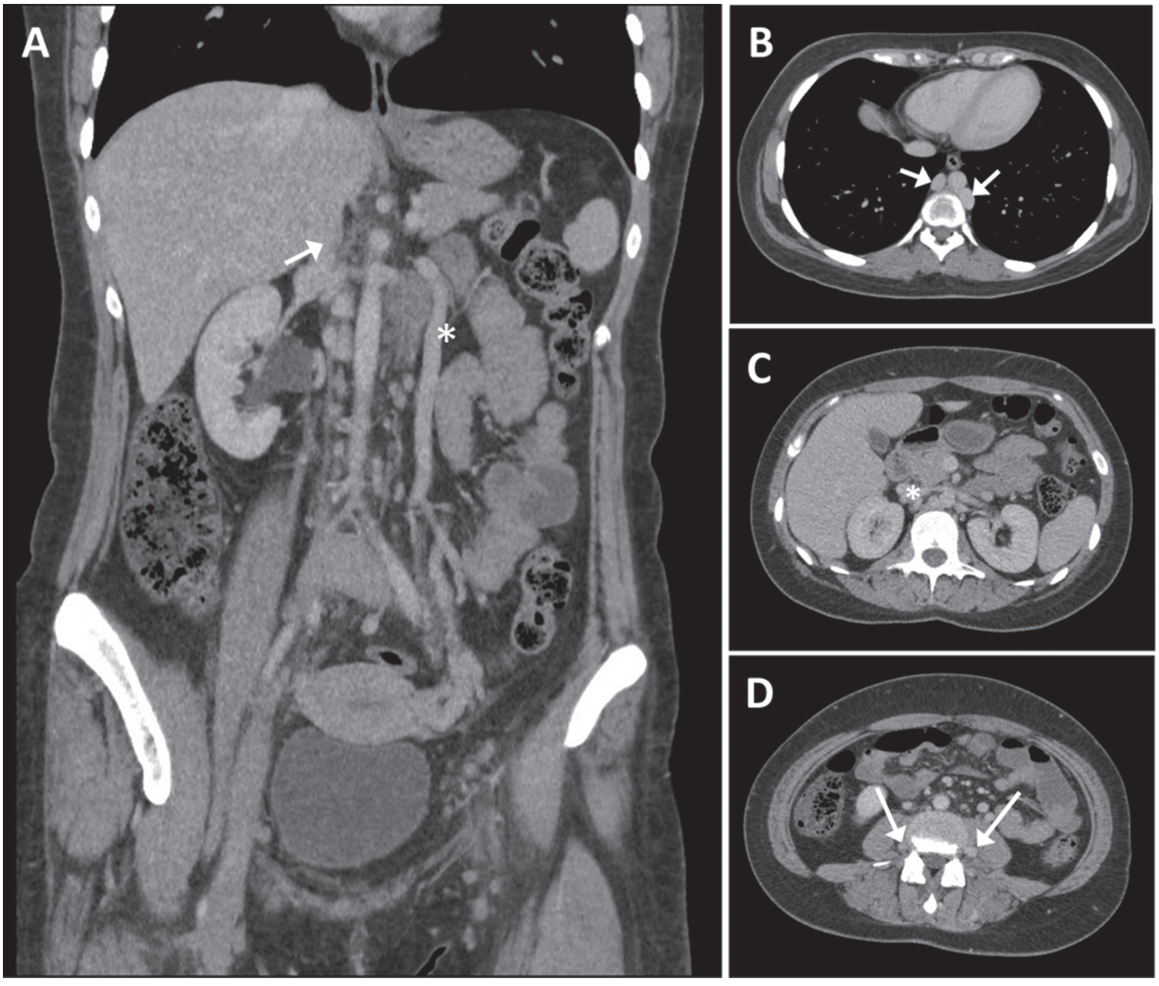

Figure 2: (**A**) Coronal CT image obtained at the level of convergence of the common iliac veins demonstrating absence of the infrarenal portion of the IVC. The suprarenal portion of the IVC is noted (arrow). There are multiple small calibre paraspinal venous collateral vessels, and compensatory distension of the left gonadal vein (star) is seen. (**B**) Axial CT image showing compensatory distension of the azygos and hemiazygous veins (arrows), providing an alternative route for venous drainage of the lower extremities. (**C**) Axial CT image at the level of the kidneys demonstrating drainage of the left and right renal veins into the suprarenal portion of the IVC (star). (**D**) Axial CT image inferior to the level of the right kidney showing absence of the infrarenal portion of the IVC. Note is made of distension of both lumbar veins deep to the psoas muscles (arrows).

the prevalence is much less, estimated to be approximately 1 in 10 000.

The IVC is the main conduit of venous return from the lower extremities and abdominal viscera, alongside the azygous and hemiazygous systems. The mature IVC has four segments—the intrahepatic, suprarenal, renal and infrarenal. It is formed in a complex process of anastomosis and regression of embryonic veins, principally the paired posterior cardinal, subcardinal and supracardinal veins, that occurs between the fourth and eighth week of gestation. Abnormal regression or persistence of these various embryonic veins can lead to congenital anomalies of the IVC, believed to occur in between 0.3% and 0.5% of the general population. IVC anomalies are an established risk factor for DVT [1], especially in younger patients. They are observed in up to 5% of young adults less than 30 years of age with a confirmed DVT diagnosis.

IVC anomalies have been extensively described in the literature. The most commonly reported examples include the left-sided IVC, double IVC, circumaortic left renal vein, retroaortic left renal vein, retrocaval ureter and interruption of the IVC, usually constituting absence of the intrahepatic/suprarenal segment with azygous or hemiazygous continuation. Multiple anomalies can co-exist, and combinations of the above are also noted to occur—particularly double IVC with retroaortic right renal vein and hemiazygous continuation and double IVC with retroaortic left renal vein and azygous continuation [2]. They may also be associated with additional malformations in the kidneys, spleen, liver, heart and lungs.

Congenital IVC 'absence' is considered one of the rarest forms of IVC malformation, with an estimated prevalence of 0.0005–1% in the general population. It most often occurs as either absence of the infrarenal IVC with preservation of the suprarenal segment or absence of the entire IVC. There has been a suggestion in the literature about whether these types of malformation are truly attributable to defective embryonic development or whether thrombosis of the IVC in the intrauterine/perinatal period plays a role [3].

In cases where venous return via the anomalous IVC is deficient, the early development of collaterals (via the gonadal venous system, the paravertebral venous plexus, the haemorrhoidal plexus and the superficial pathway via superficial abdominal veins) provides a degree of compensation.

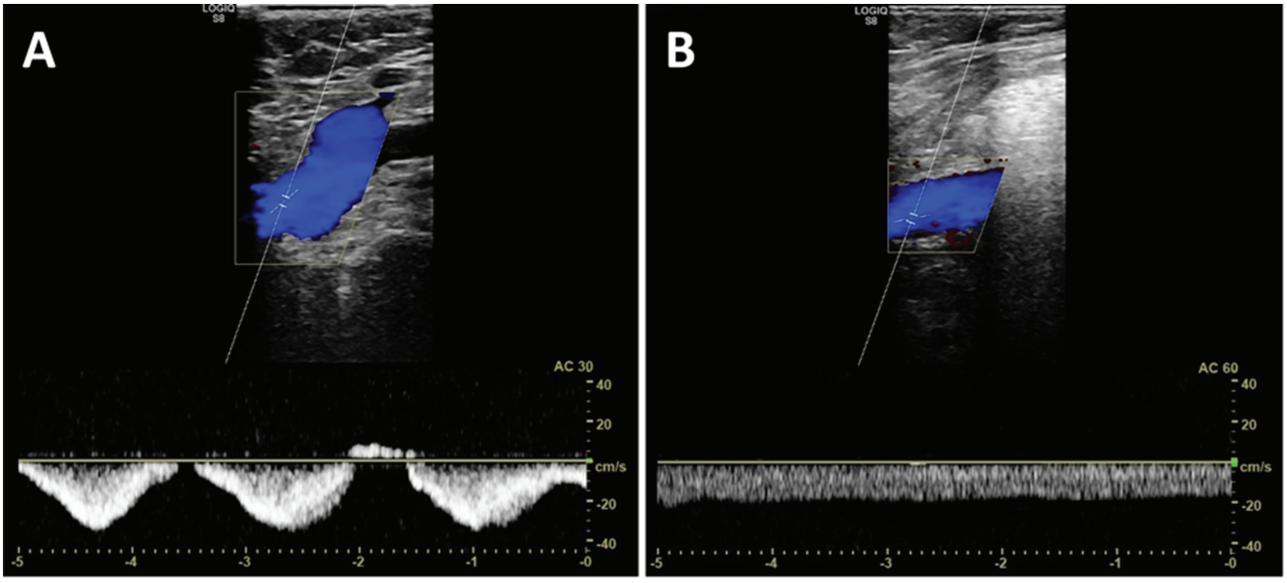

Figure 3: (**A**) US image of the common femoral vein demonstrating normal respirophasic variation consistent with patency of the proximal venous system. (**B**) US image of the common femoral vein demonstrating loss of normal respirophasic variation consistent with obstruction of the proximal venous system.

Thus, most IVC anomalies are asymptomatic and are discovered incidentally on imaging. Occasionally, they may provoke non-specific symptoms such as lower back or abdominal pain; however, the most frequently associated clinical manifestation, particularly where all or part of the IVC is absent, is DVT. Where compensation provided by the collateral circulation fails, the resulting lower extremity venous hypertension and stasis predisposes to thrombosis. This is commonly bilateral and usually involves the femoral and iliac veins.

Patients who develop iliofemoral DVTs are at high risk of developing long-term complications. Despite adequate anticoagulation, risk of recurrence is high [4], and within 2 years, 40% will develop a PTS, where the presence of thrombus induces an inflammatory response, leading to valvular scarring and incompetence. This promotes venous reflux and chronic venous hypertension, which presents as limb swelling, pain, stasis dermatitis and ulceration. The probability of pulmonary embolus is relatively low, as thrombus migration to the pulmonary arteries is inhibited by the extensive compensatory network of collaterals.

Appropriate and timely management of this patient population is important in order to reduce the risk of DVT recurrence and reduce the risk of patients developing debilitating PTS. The published literature describing DVTs in the context of IVC anomalies universally recommends oral anticoagulation and regular outpatient follow up for ongoing re-assessment of haemorrhagic risk, with concurrent use of anti-thromboembolic stockings, and avoidance of modifiable risk factors (oral contraceptive, prolonged immobilization and smoking). The optimal duration of anticoagulant treatment is subject to debate. Lifelong anticoagulation has been advocated on the basis that IVC anomalies represent a 'permanent' risk factor, and associated thromboembolic events can result in significant acute and chronic morbidity [5]. However, it has been demonstrated that the risk of DVT recurrence and PTS in patients with isolated IVC anomalies and no additional risk factors are no higher than in the general population [6]. Thus, many authors are now suggesting that, in the absence of other risk factors, a shorter treatment with a duration of 3–6 months is sufficient. Lifelong anticoagulation is generally favoured in the presence of additional risk factors, particularly thrombophilia, as several studies have noted a higher incidence of DVT and DVT recurrence in patients with co-existing IVC anomalies and thrombophilia [7]. Thrombophilia and autoimmune screening should therefore be performed in all patients found to have IVC anomalies presenting with acute DVT.

Endovascular thrombolytic therapy for acute DVT can be performed in selected patients following careful assessment of bleeding risk. The overall goals are to reduce the thrombotic burden and restore venous patency, thus easing venous congestion and reducing the risk of DVT recurrence and PTS. Urgent thrombolysis is indicated to prevent the life-, limb- or organ-threatening complications of acute DVT, and non-urgent thrombolysis can be considered for patients with severe persistent symptoms despite adequate anticoagulation. Catheter-directed methods are considered superior to systemic thrombolysis, which has fallen out of favour due to an intolerably high bleeding risk. Options include drug-only catheter-directed thrombolysis (CDT), device-only percutaneous mechanical thrombectomy and drug-plus-device pharmacomechanical CDT (PCDT). Of these, PCDT demonstrates the best safety and efficacy profile [8] and is the preferred treatment option for patients presenting with acute iliofemoral DVT [9]. A number of studies have described successful outcomes with CDT methods in the context of IVC anomalies, both with and without concurrent venoplasty and stenting [10–13]. PCDT can also be performed in conjunction with the catheter-directed delivery of US energy into the thrombus, which is postulated to augment the penetration of thrombolytic agents into the clot and facilitate disaggregation of uncrosslinked fibrinogen. Success has been demonstrated with the EkoSonic Endovascular System in the context of IVC anomalies [14, 15].

Surgery can be considered as an alternative to endovascular therapy in cases of iliofemoral DVT with associated IVC anomalies. It is most often performed in cases of severe chronic venous congestion that have failed to respond to conservative or endovascular measures, rather than in the acute phase.

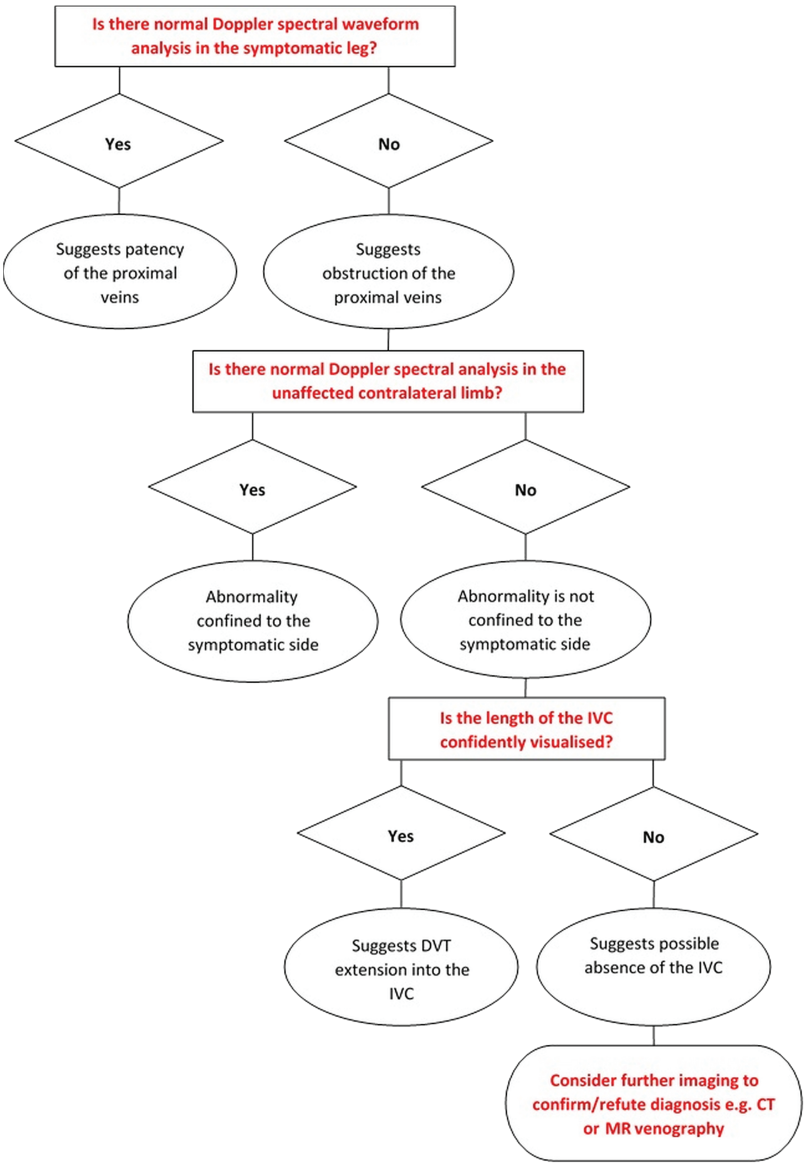

Figure 4: Flow diagram illlustrating a systematic approach that can be used during US assessment to help determine either the degree of DVT extension or whether IVC absence is a possibility.

Approaches typically involve reconstruction of the absent IVC via placement of polytetrafluoroethylene bypass grafts, thus permitting decompression of venous outflow and resulting in significant symptomatic relief [16–20].

As an additional point, performing US Doppler spectral analysis of the common femoral vein during the routine investigation of DVTs can help with assessing the patency of proximal venous structures. Loss of the normal phasic response in the common femoral vein during respiration results when the transmission of respiratory pressure is dampened by extrinsic compression or intrinsic luminal narrowing of a more proximal vein (Fig. 3) [21]. In this case, occlusive thrombus was seen within the right external iliac vein, and a Doppler spectral waveform could not be obtained on the symptomatic side. On reflection, it would have been beneficial to perform Doppler spectral analysis in the contralateral lower limb as additional loss of phasicity on the asymptomatic left side would have signified involvement of the IVC in the underlying pathologic process. The degree of loss of phasicity is dependent on the extent of the draining venous collaterals. Although it does not differentiate between IVC thrombus and IVC absence, it does prompt a focussed interrogation of the IVC. Provided good ultrasonographic views can be obtained, lack of visualization of the IVC alerts the operator to its possible absence. By following a systematic approach (Fig. 4), the operator can select the next most suitable imaging modality to help determine the underlying cause (e.g. CT or magnetic resonance venography).

In summary, an underlying vascular anomaly should be considered in young patients presenting with an unprovoked DVT, especially if bilateral—in which case, determining the exact time of onset is crucial in order to guide optimal anticoagulant therapy. Lifelong anticoagulation may no longer be required in patients with isolated IVC anomalies for whom there are no additional DVT risk factors. Endovascular methods have proven to be successful in the acute-phase management of patients with congenital absence of the IVC presenting with iliofemoral

DVTs, thus interventional strategies can assist with reducing the thrombotic burden, easing venous congestion and reducing the risk of DVT recurrence and PTS.

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CONFLICT OF INTEREST STATEMENT

No conflicts of interest exist in association with this case report.

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ETHICAL APPROVAL

Ethical approval was not required.

CONSENT

Written consent from the patient involved has been duly obtained.

GUARANTOR

Dr Thomas Osborne assumes the role of guarantor for this case report.

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