CASE REPORT

Unprovoked deep venous thrombosis in a young adult associated with membranous obstruction of inferior vena cava

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SUMMARY

Unprovoked deep venous thrombosis (DVT) in young adults is an unusual phenomenon, but it is associated with significant morbidity. Developmental anomalies of the inferior vena cava (IVC) should be considered as a possible aetiological factor, and appropriate investigations should be performed to determine the conclusive diagnosis and necessary treatment plan. We report a case of spontaneous thrombosis of the IVC and bilateral iliac venous system in a young man, associated with membranous obstruction of the IVC. He was diagnosed using several different investigational techniques, and successfully treated with mechanical thrombectomy, thrombolysis therapy and anticoagulation.

BACKGROUND

Though the lifetime incidence for unprovoked deep venous thrombosis (DVT) is low, it is even rarer in young adults, especially under the age of 30 years. In young adults who present with unprovoked DVT, it is important to consider developmental anomalies of the inferior vena cava (IVC) as an important aetiological factor. In addition, testing for thrombophilic disorders should be performed, as it is still unclear whether the anomalous IVC by itself or the interaction between an anatomical abnormality and thrombophilia tendency is responsible for IVC thrombosis.¹

We present the case of a 21-year-old man who developed spontaneous thrombosis of the IVC and bilateral iliac venous system associated with membranous obstruction of the IVC. A detailed discussion regarding the investigations and therapeutic options for unprovoked DVT in young adults is undertaken. This case serves as an important clinical reminder for physicians taking care of venous thrombotic disorders.

CASE PRESENTATION

A 21-year-old otherwise healthy Caucasian man, who works as a carpenter, presented to the hospital with concerns of bilateral lower extremity (thigh) pain and swelling of 1 week duration. Four days previous to this, he had seen his family physician with thigh pain, which was attributed to his very strenuous and physically demanding carpentry job. Apparently, there was no swelling noted at that time. He was reassured and discharged home. However, the pain continued to worsen with associated tightness and swelling of both thighs, limiting his activities of daily living, and prompting him to seek further medical attention. He also reported easy

fatigability with minimal exertion, but no shortness of breath or chest pain. There was no history of recent surgery, trauma, long distance travel or prolonged immobilisation, and there was no personal or family history of venous or arterial thrombotic disorders. He denied any history of perinatal insult such as sepsis, trauma or surgery.

INVESTIGATIONS

On physical examination, both lower extremities appeared symmetrically swollen and tender, especially in the thighs, with intact neurovascularity. Doppler sonography of the lower extremities revealed extensive thrombus in both iliofemoral veins, extending up to the IVC. He also underwent a CT pulmonary angiogram, which was negative for pulmonary embolism.

Hence, in view of unprovoked extensive DVT, the patient underwent a thrombophilia work up and CT scan of the abdomen and pelvis. The thrombophilia work up came back positive for heterozygous prothrombin gene 20210 mutation, positive lupus anticoagulant and elevated factor VIII level (227, normal 60–135). The CT of the abdomen and pelvis redemonstrated the venous thrombosis involving the lower IVC and iliac vessels ([figure 1](#)). In addition, the CT scan revealed associated collateral circulation and soft tissue oedema. No masses or lymphadenopathy was identified.

TREATMENT

The patient was initiated on anticoagulation with intravenous heparin, and interventional radiology was consulted. Contrast venography confirmed extensive thrombosis in the iliac venous system and infrarenal IVC with high-grade, web-like stenosis ([figure 2](#)). The patient underwent catheter-directed thrombolysis with tissue plasminogen activator. The thrombotic burden was decreased over 2 days by a combination of mechanical thrombectomy and thrombolysis therapy. The IVC was recanalised by balloon angioplasty ([figure 3](#)). He had improvement in his symptoms postprocedure and was discharged home on therapeutic enoxaparin (80 mg subcutaneous (s/q) twice daily) and with the recommendation to wear compression stockings all the time. His antifactor Xa level at the time of discharge was 0.63 IU/mL (normal 0.3–0.7 IU/mL).

OUTCOME AND FOLLOW-UP

The patient returned for a 1-month follow-up with his haematologist. He was noted to be

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Figure 1 Coronal section of the abdomen/pelvis; CT showing venous thrombosis involving the lower inferior vena cava and iliac vessels as depicted by the filling defects (yellow arrows).

asymptomatic, but still had an elevated factor VIII (150) level and positive lupus anticoagulant, as well as an elevated D-dimer (0.71 mg/L, normal 0.19–0.49 mg/L) level. A repeat contrast venography demonstrated complete reocclusion of the infrarenal IVC with numerous unnamed collaterals at the groins providing return of blood to the central circulation. His antifactor Xa level was 1.09 IU/mL, so he was advised to continue anticoagulation with enoxaparin (120 mg s/q once daily).

Three months later, when he was again seen in the haematology clinic, his factor VIII (123) and D-dimer (0.28 mg/L) levels

were normal, while lupus anticoagulant was undetectable. Doppler venous study of his lower extremities did not show any new thrombosis. He was switched to rivaroxaban (20 mg once daily) for anticoagulation. The patient continued to remain stable on rivaroxaban and comply with compression stockings at his 6-month follow-up visit.

DISCUSSION

It is well known that Virchow's triad (ie, alterations in blood flow (stasis), injury to the vascular endothelium and blood hypercoagulability) predisposes to DVT. However, unprovoked DVT, especially in patients younger than 30 years of age, is rare. The development of DVT in young adults is linked to developmental abnormalities of the IVC.^{2 3} As with any anomaly of the IVC, there is inadequate blood return despite prominent collaterals. This stasis increases blood pressure in the veins of the lower extremities and predisposes to thrombus development.¹

Though some studies suggest that an anomalous IVC may be a sufficient cause for development of DVT, others suggest an interaction between an anomaly of the IVC and thrombophilia in the pathogenesis of DVT.^{1 4 5} Also, it is important to remember that in a young adult, despite the presence of thrombophilia, an IVC anomaly should still be suspected, as studies have shown that thrombophilia may be present in approximately 30% of patients with IVC anomaly/absence.^{1 6} Factor V Leiden, prothrombin 20210 and methylenetetrahydrofolate reductase (MTHFR) gene mutation, low protein S levels, high homocysteine concentration and antiphospholipid antibodies represent the thrombophilia subtypes commonly associated with DVT.^{4–7} As illustrated in our case, the patient had an elevated factor VIII level with heterozygous mutation of prothrombin gene and positive lupus anticoagulant.

The IVC is a complex structure created by the formation, regression and fusion of three sets of paired veins, specifically the posterior cardinal, subcardinal and supracardinal veins, during weeks 6–8 of embryonic development.¹ A normal IVC is composed of five main segments in a caudocranial direction (figure 4): posterior cardinal veins (iliac segment), right supracardinal vein (subrenal segment), anastomosis between the right supracardinal and subcardinal veins (renal segment), right subcardinal vein (suprarenal segment) and hepatocardiac canal

Figure 2 Contrast venography demonstrating occlusion of the bilateral iliac venous system; (A) demonstrates no filling beyond right common femoral vein (blue arrow), while (B) shows occlusion of the left external iliac veins (red arrow) with multiple collaterals (yellow arrows).

Figure 3 Contrast venography showing recanalisation of the inferior vena cava.

(hepatic segment).⁸ The failure of these paired veins to fuse into a unilateral, right-sided venous system leads to an anomalous IVC.⁴ Also, the areas of IVC development near the liver and diaphragm (infrarenal IVC in adult) are more prone to anomalies such as webs and strictures. There are three types of developmental IVC obstruction. In type I, a thin membrane is present. Type II represents the fibrous cord structure. Type III is a type I or II pathology associated with thrombosis.⁹ Of note, many of the published cases of IVC anomalies associated with DVT involve complete absence of the IVC (AIVC) and not just IVC obstruction. Absence of the suprarenal IVC is the more common abnormality. Absence of the infrarenal or entire infrahepatic accounts for only 6% of all cases of AIVC.¹⁰

Collateral networks (azygos, hemiazygos, accessory hemiazygos and thoracolumbar veins) play an important role in drainage in case of a developmental abnormality of the IVC. The patency of these collateral veins is crucial because they receive drainage directly from the common iliac veins. If there is a combined iliac/IVC obstruction, collateral compensation is likely to be inefficient.¹¹ Our patient also had a clinically significant bilateral common iliac vein occlusion with IVC obstruction and failure of collateral veins to function properly.

The recent increase in detection of IVC anomalies is due to better utilisation of diagnostic procedures such as sonography, CT and MRI.^{2–4} Sonography is usually the first line imaging modality, especially in the evaluation of DVT in young patients, but anomalies of the IVC may be missed on sonography due to operator error, body habitus or the presence of bowel gas. CT is a rapid, non-invasive method that can accurately diagnose thrombosis of the IVC associated with IVC anomalies, and it may potentially diagnose the abdominal or pelvic processes that contribute to the development of DVT. However, MRI is now considered a better investigation tool compared to CT, since there is no radiation exposure. Although contrast venography is

Figure 4 Structure of the inferior vena cava and its embryological origin. *Iliac segment* arises from the posterior cardinal veins; (1) *Subrenal segment* arises from the right supracardinal vein; (2) *Renal segment* arises from the anastomosis between the right supracardinal and subcardinal veins; (3) *Suprarenal segment* arises from the right subcardinal vein; (4) *Hepatic segment* arises from the hepatocardiac canal.

the gold standard for diagnosis, it should be solely reserved for therapeutic intervention and should not be used for diagnosis when CT/MRI is available. This is because venography is an invasive procedure and is associated with thrombus formation in 2–10% of patients. In our case, the patient was young with bilateral extensive thrombosis, which warranted CT as the initial study of choice. Contrast venography was later used for therapeutic purposes.

Treatment options of IVC thrombosis include anticoagulation, systemic or regional (transcatheter) thrombolytic therapy and mechanical thrombectomy. The type of anatomical defect of the IVC guides the options for a surgical approach. Balloon angioplasty needs to be performed if membrane is present, while stent placement or graft surgery may be necessary in a case of fibrous cord.^{4–12} Though very rarely done but still an available option, venous bypass/prosthetic graft bypass is a last ditch effort in the event of DVT recurrence.¹³ Oral anticoagulation is recommended in all patients with IVC anomaly. The duration of anticoagulation therapy should be individualised; however, case evidence suggests life-long treatment with the detection of a thrombophilia disorder(s).^{4–12} Currently, there is no evidence

regarding the optimal duration of anticoagulation treatment in patients with isolated IVC anomalies. Patients were treated anywhere ranging from 6 months to 2 years without recurrence after 2 years of follow-up.^{13 14} The data on long-term recurrence is unclear, barring a couple of case reports,^{15 16} as there have been no studies with long-term follow-up of these patients on or off treatment. All these patients need to wear compression stockings for least 1 year to reduce the risk of post-thrombotic syndrome.

Learning points

- ▶ Deep venous thrombosis (DVT) of the inferior vena cava (IVC), iliac veins and femoral veins in young adults is rare, but it is associated with significant morbidity.
- ▶ Understanding the embryological IVC development and pathophysiology of thrombus formation is critical to suspecting congenital anomalies of the IVC, especially with bilateral DVT.
- ▶ The initial diagnostic procedure should be ultrasound of the lower extremities. Further investigation modalities are mandatory with the detection of iliofemoral thrombosis. CT or MRI is required to identify the extension of the thrombus and IVC anatomy. For the complete evaluation, thrombophilia work up should be performed.^{1 5 6}
- ▶ Treatment options include anticoagulation, thrombolytic therapy and mechanical thrombectomy. In a case of IVC development abnormalities, the location and type of the defect determine the surgical approach. Even with extensive therapeutic modalities, long-term or even life-long anticoagulation is often required.^{4 5}

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