Inferior Vena Cava Thrombosis attributable to Hyperhomocysteinemia: A Case Report from Nepal

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Abstract

Inferior vena cava thrombosis (IVCT) is a rare occurrence and is a result of leg deep vein thrombosis (DVT). The etiology of IVC thrombosis can be divided into congenital versus acquired etiological factors found in Virchow's triad of stasis, injury, and hypercoagulability. Hyperhomocysteinemia is a rare risk factor for thromboembolism.

Introduction

Inferior vena cava thrombosis (IVCT) is a rarely seen clinical condition. It is an under-recognized entity which is associated with significant morbidity and mortality.[1] It is estimated about 2.6 to 4.0 percent of patients with lower extremity deep vein thrombosis (DVT) have IVCT.[2-5] Our patient here was a congenitally normal person who didn't have any etiology of prothrombotic factors or abdominal pathology. The only peculiar observation was that he had an elevated serum homocysteine level. Although, previous study has shown elevated homocysteine concentration found in 40 percent of patient with vascular disease and 35 percent of patient with venous thromboembolism.[6] However, high levels of homocysteine in the absence of any other etiology is a rare phenomenon.

We describe a case of a congenitally normal 78-year-old male with hyperhomocysteinemia with a left leg DVT extended towards the IVC. The patient was treated with an anticoagulant and was supportively discharged.

Case report

A 78-year-old Nepalese male was admitted to our Grande International Hospital with a history of a sudden onset of pain and swelling over his left leg. He didn't complain of fever, chest pain, shortness of breath, cough, or syncope. A family history of thrombophilia, autoimmune diseases, and hematological malignancies were absent. His personal history included 15 years of alcohol abuse, which he ceased 10 years ago. Medical history included hypertension under anti-hypertensive medications since 5 years, and had open angle glaucoma for 8 years. He denied any history of recent trauma or surgical intervention or any immobilization. On examination, his vital signs and systemic examinations were unremarkable. Besides his general appearance, he looked well-nourished and had a body mass index (BMI) of 26.03. Local examination showed ecchymosis, raised temperature, with pitting edema around the left knee with multiple blisters. There was no compromise in the perfusion or motor functions of the leg; deep tendon reflexes were preserved; and muscle power was 4/5. In addition, his mid-thigh circumference and mid-calf circumference measured 22 inches and 12 inches, respectively, as shown in Figure 1.

The patient's history and physical findings pointed towards a likely diagnosis of deep vein thrombosis (DVT) with a modified Wells criteria score of 4 points.[7] An urgent venous Doppler ultrasound of the left leg vein

was performed, which revealed acute DVT involving the left superficial femoral, common femoral, external iliac, common iliac veins, and lower part of the inferior vena cava (IVC). Minimal re-canalization of the mid and distal superficial femoral veins with slow flow was noted. Partially occlusive thrombus was also found in the popliteal and proximal posterior tibial veins with diffuse subcutaneous edema. Following that, he was immediately started on low molecular weight heparin 120 mg/day subcutaneous route and oral warfarin 5 mg/7.5 mg on alternate days. The laboratory results are discussed separately in Table 1. The complete blood count (CBC), kidney, and liver functions were all normal. Meanwhile, serum homocysteine levels was $>$ 50 mol/L(normal 5-15mmol/L), D-dimer was 2.15 mg/l (normal range,$<$ 0.5 mg/l), and Fibrin degradation product (FDP) was 200 ng/ml. The thrombophilia profile (factor V Leiden, anti-thrombin III, protein C, and protein S) were negative.

During his stay in our ward on the second day, we observed the patient developed a sudden onset of cough, resting tachycardia, tachypnea, disorientation status, and mild cognitive impairment. He had bilateral decreased air entry and oxygen saturation was maintained at 0.5 liters of oxygen via nasal cannula. We had to shift him to the intensive care unit (ICU) as a pulmonary embolism was suspected. Computed tomography (CT) -pulmonary angiography was done, which ruled out pulmonary embolism. However, extensive images of the abdomen showed IVC thrombosis as shown in Figure 2 and Figure 3. He received monitoring, chest physiotherapy, and mobilization in the ICU. His echocardiography showed normal right atrium and right ventricle, normal left ventricular systolic function with grade I left ventricular diastolic dysfunction. Mild tricuspid regurgitation (TR) with an estimated pulmonary artery systemic pressure of 30 mm of mercury was noted. Low molecular weight heparin injection and oral warfarin were stopped and was started on the novel oral anticoagulant rivoraxaban at 30 mg/day for 2 weeks, then 20 mg/day as a maintenance dose. He was then shifted to ward for further treatment. The patient was started on methylcobalamin and folic acid treatment and responded well to our treatment during his stay in the ward. As his symptoms started to subside, he was then discharged. On the day of discharge, his mid-thigh and mid-calf circumference were 21 inches and 10.5 inches, respectively, as shown in Figure 1. We advised him to continue oral rivaroxaban and anti-hypertensive medications and come for follow-up after a week.

On follow-up, repeat venous Doppler ultrasound showed good recanalization of the left common femoral, superficial femoral, and popliteal veins, with slow flow in the lumen of these veins. No obvious thrombus was observed inside the calf veins. Very minimal to no recanalization of the left common iliac and external iliac veins. Our patient reported decreased swelling without any other complications. Since then, he has been on anticoagulant and was further advised to follow up after 3 months.

Discussion

Inferior vena cava thrombosis (IVCT) in a congenitally normal patient is rare and is usually a result of a predisposing hypercoagulable state along with an acquired pathology in the IVC or one of its adjacent structures.[8-11] Etiologically, there are prothrombotic factors such as thrombophilia, malignancy, oral contraceptives, smoking, obesity, pregnancy, hormonal replacement therapy, and nephrotic syndrome. Besides these, there are abdominal pathologies such as renal cell tumor, abdominal masses producing extrinsic compression such as a very large uterine fibroid, Budd-Chiari syndrome, abdominal trauma/surgery, May-Thurner syndrome, and thrombotic occlusion of an IVC filter. Meanwhile, a recent study has shown local problems such as IVC anomalies contribute 11.3 percent, external venous compression contributes 11.3 percent, malignancy contributes 17.0 percent, and the presence of lupus anticoagulants contributes 10.9 percent to the risk of IVCT.[12] There are some interesting clinical aspects in our case report. He was a congenitally normal IVCT patient who didn't relate to the aforementioned etiologies and differed from them in all aspects. He had a sudden onset of symptoms related to venous thromboembolism. The only medical history he had was of hypertension, which was well managed by anti-hypertensive medication. We observed a high level of serum homocysteine, which was a new observation for us.

The association between deep vein thrombosis and hyperhomocystinemia was first reported in 1991, and since then a large number of prospective and retrospective trials have established a relation between hyperhomocysteinemia and deep vein thrombosis.[13] Mild hyperhomocysteinemia appears to be an indepen-

dent risk factor for arterial vascular disease and thromboembolic risk factors.[14] Homocysteine levels can be raised by altered methionine metabolism, which can occur as a result of genetic defects affecting transcription of enzymes responsible for homocysteine metabolism. Many other factors, such as age, smoking, renal impairment, diabetes mellitus, hypothyroidism, and other nutritional deficiencies of folic acid, vitamin B6, and vitamin B12, and drugs such as phenytoin, carbamazepine, and methotrexate, may be linked to hyperhomocystinemia.[13,15]Interestingly, we describe a rare case of IVCT with no identifiable risk factors contributing to IVCT except hyperhomocysteinemia, which captures the attention.

Conclusion

Our case emphasizes the importance of performing a complete hypercoagulable workup on any patient who presents with DVT. Furthermore, our findings underline the importance of homocysteine levels in the diagnosis of venous thrombosis. IVC thrombosis is a less prevalent and less well-known condition than lower extremity thrombosis, and early intervention is indeed essential well before development of pulmonary embolism.

Ethics statement

The study protocol was approved by the Ethical Review Committee of Grande International Hospital. The reporting of this study conforms to CARE Guidelines (Check list in supplementary materials).[16]

Consent

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Declaration of conflicting interests

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Figure Legends

FIGURE 1: Visible swelling was noted in the left lower limb area at the time of admission

Swelling markedly decreased in the left lower limb at the time of follow-up.

FIGURE 2: Axial and Coronal CT pulmonary angiogram images show a hypodense filling defect in the sub-segmental branch of the right lower lobe pulmonary artery (blue and white arrows).

FIGURE 3: Coronal and axial CT images of the abdomen in the venous phase show hypodense filling defects in the inferior vena cava (blue arrow), right common iliac vein (green arrow) and left common iliac vein (yellow arrow) suggestive of thrombus.