

CASE REPORT

Recurrent deep venous thrombosis caused by congenital interruption of the inferior vena cava and heterozygous factor V Leiden mutation

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Abstract. Schneider JG, Eynatten MV, Dugi KA, Duex M, Nawroth PP (Ruprecht-Karls-University of Heidelberg, Heidelberg, Germany). Recurrent deep venous thrombosis caused by congenital interruption of the inferior vena cava and heterozygous factor V Leiden mutation (Case report). *J Intern Med* 2002; **252**: 276–280.

A case of a 44-year-old patient with recurrent deep venous thrombosis (DVT) caused by congenital dysgenesis of the inferior vena cava (IVC) in coincidence with heterozygous factor V Leiden mutation is presented. The IVC malformation was a fortuitous finding because the vascular malformation of the

collateral draining thoracic veins were suspected to be a malignant mass in chest X-ray. This vascular abnormality is a rare finding but recent epidemiological research suggests that there may be an association between the congenital absence of the IVC and DVT. In our case, the patient is even at higher risk combining the malformation probably affecting venous blood flow and the hypercoagulable state by heterozygous presence of the factor V Leiden mutation.

Keywords: dysgenesis, factor V Leiden mutation, inferior vena cava, venous thrombosis.

Introduction

Congenital anomaly of the inferior vena cava (IVC) such as atresia or total absence is a rare vascular defect. It becomes usually apparent in childhood if the defect is combined with congenital anomalies of the heart, polysplenia and/or bowel inversion. Patients without associated conditions are typically asymptomatic and the defect is only seen incidentally during abdominal surgery or radiological procedures. The associated azygous or portal continuation provides for sufficient collateral venous return. Thus, the appearance of deep venous thrombosis (DVT) is not typically occurring in those patients. However, the absence of IVC may favour venous stasis and therefore represents at least a risk factor for DVT. We describe a 44-year-old patient with recurrent DVT caused by congenital dysgenesis of the IVC and the right iliacal vein combined with the presence of heterozygous factor V Leiden

mutation. Clinical features of the case as well as diagnostic and therapeutic action taken are discussed.

Case report

A 44-year-old man was presented with suspected DVT of the left thigh. In the last 2 days before hospitalization he complained of increasing pain, swelling and livid colouration of the entire left leg. Interestingly, the patient stopped taking phenprocoumon (Marcumar[®], Roche Pharmaceuticals, Grenzach-Wyhlen, Germany) 4 months before because he suffered from DVT of the left leg involving pelvic region occurring about 1 year before the actual episode. His past medical history was bland apart from occasional alcohol consumption. The physical examination was essentially within normal limits except for an oedematous swelling of the entire left leg that was livid coloured and sensitive to

pressure. The right leg was not involved. The routine laboratory values were normal. Coagulation studies showed a known heterozygous factor V Leiden mutation and elevated D-dimers. Other parameters including antithrombin, protein C, protein S, plasminogen, fibrinogen, homocystein serum concentration (also after methionine load test) and prothrombin gene [G20210A] mutation did not show a defect predisposing to thrombophilia. The patient also had no history of immobilization, trauma, surgery or familial history of thromboembolic episodes. The treatment initiated immediately consisted of immobilization, compression bandage, leg elevation and intravenous heparin. Duplex sonography of the left leg revealed a DVT of the thigh and pelvic region. In addition, phlebography showed extensive thrombotic occlusion of the pelvic and leg veins with fresh parts and portions in different status of organization. It also showed long-standing thrombus formations and enlarged venous collateral veins. A chest X-ray examination then was suspicious for mediastinal lymphoma. Therefore a malignant disease was first assumed to cause the recurrent DVT and further radiological work-up was initiated.

Computerized tomography (CT) scans of the thorax and abdomen surprisingly revealed the diagnosis of agenesis of the IVC including both common iliacal veins. The venous blood from the lower extremities was mainly drained by the periliacal and perisacral venous plexus (Fig. 1f). In the infrarenal part there was a right and left descending IVC (Fig. 1e). Complete agenesis of the IVC was present beginning at the level of the renal veins with the result that the venous blood of the kidneys was drained into retroperitoneal collateral veins (Fig. 1d). The azygous and hemiazygous veins then took over the blood drainage to the heart and at CT imaging, were well visualized with enlarged diameters (Fig. 1b–d). As a result, the lower half of the body was drained by large, dilated azygous and hemiazygous veins (Fig. 1a) into a normal superior vena cava as graphically demonstrated in Fig. 2.

In conclusion, a malformation of the IVC in combination with heterozygous factor V Leiden mutation was diagnosed and the interaction of the defects was suggested to cause the recurrent DVT in this patient. We started the patient again with oral phenprocoumon (Marcumar[®]) therapy and proposed to continue the therapy life-long within a therapeutic

international normalized ratio (INR) of 2–3. In addition, we advised the patient to avoid unusual physical activity and prolonged immobilization.

Discussion

Abnormality of the IVC is a rare vascular disease entity caused by disturbances in the development between the sixth and the eighth gestational week. During this period, a complex system of premature veins derives from three pairs of primitive venous channels and forms the mature venous system by replacing one another, building anastomoses and partly disappearing. Failures in the developmental steps result in various malformations, including partial or total absence of the IVC or infrahepatic, prerenal, renal or infrarenal interruption [1, 2]. The causal reasons for the developmental failure are unclear. Hypotheses are either embryonic dysontogenesis that affects separate segments or the entire IVC and intrauterine thrombosis or umbilical vein complication postpartum as causal events. There can be an association between anomalies of the IVC and congenital malformation of abdominal viscera such as polysplenia, asplenia, situs inversus and others [2–4]. Usually those patients are diagnosed early in life. However, if there is a deep venous collateral system that drains the blood from the lower extremities to the heart via azygous and hemiazygous veins, the patients without visceral anomalies remain usually asymptomatic [5–7]. The prevalence of congenital IVC abnormalities has been estimated at 0.5% of the general population [8] but could be underestimated because the vascular defect often is reported as fortuitous finding during abdominal surgery or radiological work-up for other reasons [9–11]. Our patient developed an idiopathic DVT first before diagnosis of the factor V Leiden mutation and a recurrent DVT shortly after discontinuance of oral anticoagulation. The factor V Leiden mutation is a common risk factor that can predispose to DVT [12], however, DVT has a multifactorial aetiology involving both genetic and acquired factors [13] hypothesizing that hypercoagulability by the factor V mutation with a suggested tendency to venous stasis mediated by the IVC malformation must have caused the DVT in our patient. It remains unclear why the DVT did not occur earlier in life time. This could be because of the fact that the incidence of DVT increases with age

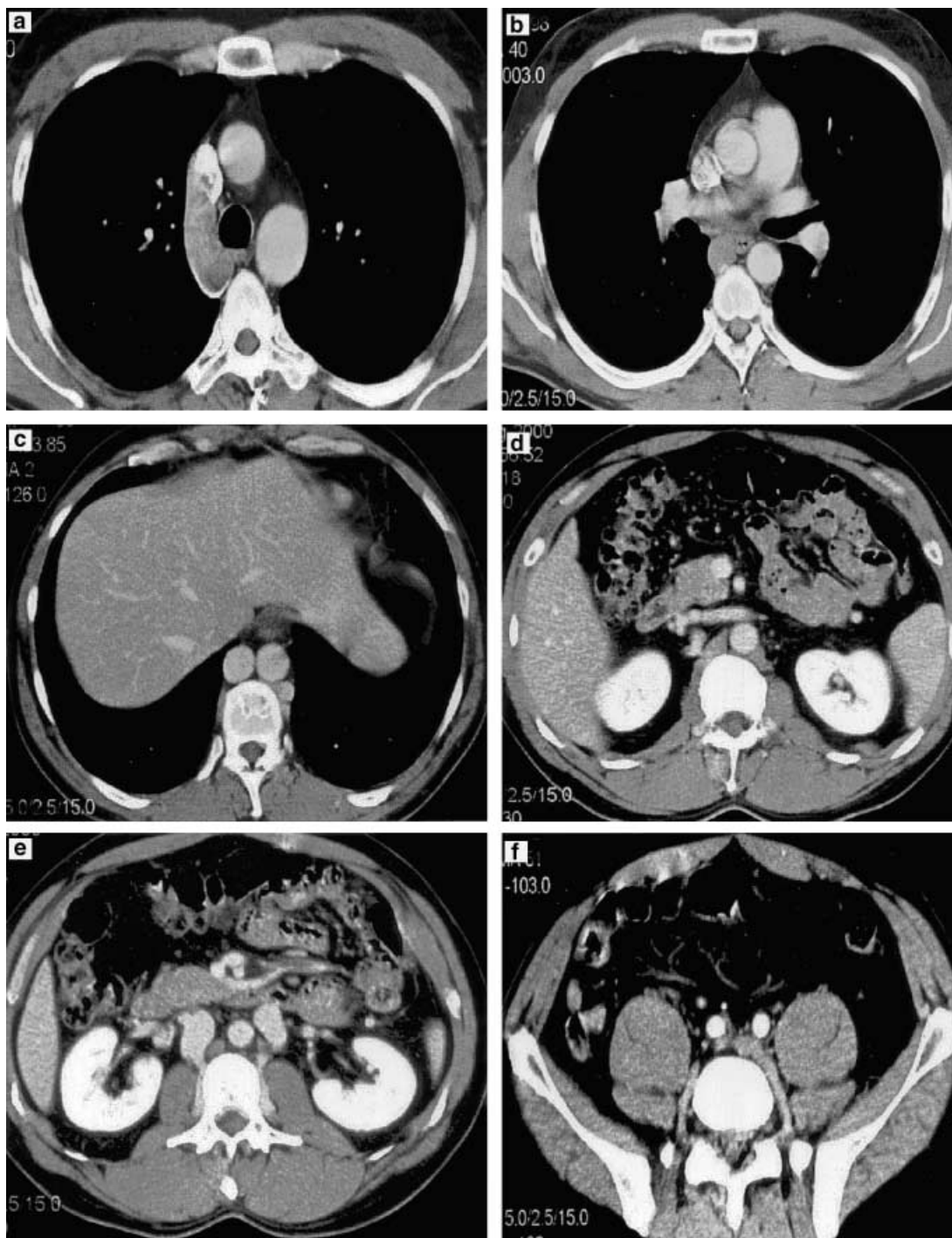


Fig. 1 CT at the level of the upper (a) and middle (b) third of the thorax, the azygos vein is enlarged that at conventional plain film radiography of the thorax had been suspected to be lymphoma. CT at the level of the lower third of the thorax (c), the azygos vein is well enlarged and approximately has the same diameter as the aorta. On the left hand side the hemiazygos vein is enlarged as well. A vena cava inferior is not visible and hepatic veins are draining into the azygos vein (not demonstrated here). CT at the level of the right renal vein draining into retroperitoneal collateral veins (d) because of absence of the vena cava inferior. CT at the level of the hilum of the kidneys; right and left descending vena cava (e) inferior in the infrarenal portion. CT at the level of the pelvis, the common pelvic arteries are well visualized. There is no right or left pelvic vein and the drainage of the venous blood is accomplished by enlarged perilsacral/perisacral veins (f).

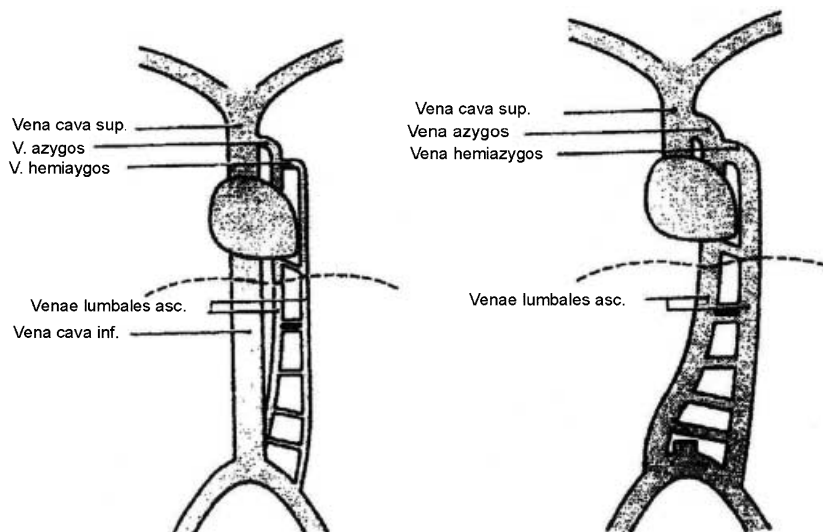


Fig. 2 Sketch demonstrating the difference between normal blood drainage from the lower half of the body (left) and absence of inferior vena cava (right) (modified according to Gaber *et al.* [20]).

and that age can therefore play a role as an independent risk factor [11, 14]. It is noteworthy that the IVC abnormality could not be detected neither by phlebography nor by ultrasonography, which is the procedure of choice in case of suspected DVT [15, 16]. This could be one of the reasons why the IVC malformations may be undiagnosed in patients with DVT. Previous studies report that the abnormality of IVC cannot be detected by ultrasonography [11, 17]. Appropriate screening methods are CT scan or magnetic resonance tomography [18, 19].

The DVT has been described in patients with congenital IVC malformations [5] and there are several reports on the diagnosis of IVC abnormalities in young patients with idiopathic DVT [17]. Thus, IVC malformation may resemble a rare but relevant condition that may favour venous stasis and that results in even higher thrombotic risk in coincidence with other established risk factors for DVT. Our case report and the recent literature suggest a more thorough investigation to be carried out in young patients with idiopathic DVT to exclude IVC abnormality. There is no data about the therapeutic management of DVT associated with IVC malformation. As patients with anomaly of the IVC may be at higher risk for thrombotic recurrence, it is necessary to anticoagulate for at least 6 months without the occurrence of any other risk factor but lifelong oral anticoagulation should be considered, only if the condition is associated with other thromboembolic risk factors or with recurrent DVT.

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