Introduction

Deep vein thrombosis is a challenge for physicians of all disciplines. It usually complicates the course of a disease, but it might also be encountered in the absence of precipitating disorders. Thrombosis arises more often in the deep veins of the legs, although it can take place in any section of the venous system.

Genetic or acquired causes are frequently associated [1], which makes it difficult to decide which patients should be tested for hereditary thrombophilia and what diagnostic tests should be performed.

Thrombosis of the IVC has similar etiological factors to lower limb DVT [2]. Hypercoagulability (inherited or acquired thrombophilia), venous stasis secondary to extraluminal pressure (e.g. from tumors or inflammatory processes) and vessel injury (due to trauma) have all been implicated as primary mechanisms in the pathophysiology of DVT.

Case report

We present the case of a 41 year-old-man that 15 years ago was hospitalized for lower back pain (radiating to the inferior limbs and increased in severity during the preceding 72 hours), blushing, heaviness, edema and tumefaction of right inferior limb. Patient reported that these symptoms developed after a recent trauma, caused by a prolonged squatted position, while he was working as a bricklayer. We visited the patient fifteen years after the onset of the first clinical setting showing a severe post thrombotic syndrome, as a consequence of the already diagnosed thrombosis, involving predominantly the right inferior leg. Thrombophilia screening tests showed patient to be a heterozygous carrier of methylenetetrahydrofolate reductase (MTHFR) gene mutation. Computed tomography (CT) scan confirmed the thrombotic obstruction of the infrahepatic IVC, both common iliac veins, right external and internal iliac veins, with multiple collateral pathways. Because of thrombosis extension, inherited prothrombotic condition and the young age of the patient, we decided to continue life-long oral anticoagulant therapy.

Keywords: deep vein thrombosis, inferior vena cava thrombosis, inherited thrombophilia, oral anticoagulant therapy.

In July 2009, patient was referred to our Department for a severe post thrombotic syndrome of the right leg. Ultrasound scan revealed the sequelae of DVT extending from common iliac veins bilaterally and involving right common femoral vein, right superficial femoral vein and right popliteal vein. We repeated an abdominal-pelvic CT scan that excluded congenital malformations of the IVC and confirmed the presence of a complete thrombotic obstruction involving the intrahepatic IVC, both common iliac veins, right external and internal iliac veins, with multiple collateral abdominopelvic (formed by subcutaneous anterior abdominal wall veins; lumbar, azygous, hemi-azygos and spermatic veins; hypogastric, peri-rectal, and peri-prostatic venous plexi. Portosystemic peri-esophageal, peri-gastric and peri-splenic collateral pathways) (see Figures 1–4).

Because of thrombosis extension, inherited prothrombotic condition and the young age of the patient, we decided to continue life-long oral anticoagulant therapy.

Discussion

Pathogenesis of venous thrombosis involves three factors (“Virchow’s triad”): venous stasis, vessel wall damage and hypercoagulability. The first factor (due to immobilization or venous obstruction) inhibits the dilution and clearance of activated coagulation factors; the second prevents endothelium from inhibiting coagulation and initiating local fibrinolysis; the third (inherited or acquired thrombophilia) promotes coagulation.

Thrombosis of the IVC has similar etiological factors to lower limb DVT [2]. Although the lifetime incidence of venous thrombosis is 0.1% (with this rate increasing from 0.01 percent among young adults to 1 percent among those who are at least 60 years old [3]), it still remains a rare condition, especially in subjects below 40 years of age.

Up to 50% of patients with an IVC thrombus presents bilateral lower extremities swelling and dilatation of superficial abdominal veins. Although some patients remain asymptomatic; nephrotic
syndrome, lower back pain, varicocele, chronic venous diseases of the lower limbs, hepatic engorge-ment, cardiac failure and pulmonary embolism have also been described [4].

Idiopathic IVC thrombosis is very rare. Chikaraishi et al. described a case of apparent idio-pathic IVC thrombosis in a 57-year old woman presented with chest pain secondary to pleurisy and a background history of pyelonephritis but no other prothrombotic condition [5].

An endemic variant of IVC thrombosis in Nepalese patients has been also described [6]. This condition is characterized by obstruction or stenosis of the IVC hepatic segment with associated hepatic venous outflow obstruction. Reliable evidences suggest an infective etiology which results in thrombophlebitis, thrombus formation and subsequent fibrinotic stenosis [7]. Organisms thought to be involved are Staphylococcus Aureus and gram-nega-tive enteric organisms, whose bacteremia leads to a transient protein-S deficiency [7].

Congenital malformations of the IVC are unusual with a prevalence of 0.3% to 0.6% in the gen-eral population [8]. IVC is created by the fusion of three sets of paired veins (posterior cardinal, sub-cardinal and supracardinal veins) during week six to eight of embrionic development [9]. The failure of these paired veins to fuse into a unilateral right-sided venous system is the main mechanism which leads to an anomalous IVC [9]. Interruptions or ab-sences of the IVC are often limited to the intra-he-patic segment. Their prevalence increases to 2% in patients with other congenital cardiovascular abnor-malities such as transposition of the great vessels, dextrocardia, and pulmonary artery stenosis [8]. Co-existent visceral anomalies include asplenia, polyplenia, situs inversus and hypoplasia of the kidney [10].

Inherited thrombophilic disorders strongly in-crease the risk of IVC thrombosis. These include: factor V Leiden, mutation of factor II (prothrombin) gene, homozygous C677T mutation in the methylentetrahydrofolate reductase gene, antithrombin de-fi ciency, protein C and S deficiency, dysfibrinogen-enemia, homozygous homocystinuria and increased levels of factors VIII, IX, XI and fibrinogen [11].

The interaction between acquired and genetic causes makes it difficult to decide which patients should be tested for inherited thrombophilia, what tests to perform and when.

The gold standard for the diagnosis of deep vein thrombosis remains contrast venography. However, it is an invasive procedure associated with a 2-10% rate of postprocedural DVT [2]. Ultrasound scan ning is now the first-line investigative modality, al-though it is operator dependant and can be limited by body habitus and occasionally fails to identify any IVC abnormality [11]. CT is a non-invasive method which can accurately diagnose and assess the extent of thrombus as well as delineate any as-sociated IVC anomaly [2]. MRI is now replacing CT as the optimal diagnostic tool, giving more ac-curate delineation of thrombus as well as any IVC anomaly and avoiding ionizing radiations.

Chronic thrombosis of the IVC is usually treat-ed with anticoagulation. There are no studies in sci-entific literature describing the ideal duration of anticoagulation therapy in this condition; however, clinical evidence shows a trend toward treatment for a minimum of one year. The coexistence of inherited coagulative disorders makes often necessary to continue oral anticoagulation indefinitely. Further-more, a caval anomaly is a permanent risk factor for venous stasis and thrombosis and anticoagulation therapy should be lifelong [12].

Other options for treatment of IVC thrombosis without anatomical variance include mechanical thrombectomy, angioplasty and stent placement, systemic thrombolysis, transcatheter regional thrombolysis, pulse-spray pharmacomechanical thrombolysis [2, 13]. Surgical reconstruction of the IVC is sometimes feasible for the most severe cases and is associated with considerable morbidity and mortality risk [14]. Interventional techniques are limited by anatomical factors such as the extent of thrombus, the involvement of the IVC branches (particularly renal and hepatic veins), the presence of extensive collateral compensatory venous circu-lation and the presence of congenital caval abber-cancy and abnormalities.

This case we described represents an example of how inherited and acquired conditions interact in causing IVC thrombosis. Patient was carrier of a heterozygous mutation of the MTHFR gene that, per se, unlikely causes the formation of an IVC throm-bus; furthermore he was subject, as resulted from his clinical history, to a trauma due to a prolonged squatted position as a consequence of his work. We hypothesized, in fact, that this event provoked a silent and transient retroperitoneal hematoma to the iliopsoas muscle which led, via mass effect, to compres-sion of the IVC, hence the formation of an in-tra luminal thrombus.

**Conclusion**

The diagnosis of this condition requests a high index of suspicion in young patients with lower limbs and back pain, dilatation of superficial ab-dominal veins, varicocele and a persistent increase of inflammatory markers. Although ultrasound scanning is the first line diagnostic technique, CT and/or MRI are mandatory for the exact definition of IVC thrombus and presence of IVC congenital ab-nomalities. Although percutaneous and surgical therapeutic modalities exist, long-term or often life-long oral anticoagulation is required. Warfarin is cumbersome to use, because of its multiple interac-tions with food and drugs, and it requires frequent laboratory monitoring. Therefore, it is often not used and rates of discontinuation are high [15]. Many pa-tients receiving warfarin still present inadequate anticoagulation [16]. The use of new safe, effective and convenient to use anticoagulant drugs is a hope for patients with IVC thrombosis and any type of DVT. We think that efforts must be made to promote clinical trials comparing classical anticoagulant agents (vitamin K antagonists such as warfarin) with new agents, such as dabigatran etexilate, a direct thrombin inhibitors, which has recently demonstrat-ed to be effective and convenient to use in patients with atrial fibrillation [17].
Riassunto

L’incidenza di trombosi venosa profonda (TVP) nella popolazione generale è approssimativamente pari allo 0.1% e risulta ancora più bassa al di sotto dei 40 anni di età. La trombosi della vena cava inferiore (VCI) è una condizione clinica eccezionalmente rara, con fattori eziologici analoghi a quelli della trombosi del sistema venoso profondo degli arti inferiori. In questo lavoro viene presentato un caso di ostruzione cronica post-traumatica della VCI in un giovane adulto, verosimilmente conseguente ad un prolungato accovacciamento. Il paziente si è presentato alla nostra attenzione, quindici anni dopo l’insorgenza del quadro clinico, per una grave sindrome post-trombotica, coinvolgente in particolar modo l’arto inferiore destro. Lo screening della trombofilia ereditaria ha documentato una mutazione eterozigote del gene codificante per la metilentetraidrofolatreduktasi (MTHFR). La TAC ha confermato l’occlusione trombotica della VCI infraepatica, di entrambe le vene iliache comuni, delle iliache interna ed esterna destra, con multipli circoli collaterali. A causa della estensione della trombosi, della presenza di fattori protrombotici ereditari e della relativamente giovane età del paziente, abbiamo optato per la terapia anticoagulante orale a tempo indefinito.

Parole chiave: trombosi venosa profonda, trombosi vena cava inferiore, trombofilia congenita, terapia anticoagulante orale.

ACRONYMS

IVC: inferior vena cava
DVT: deep venous thrombosis
CT: computed tomography
MRI: Magnetic Resonance Imaging
MTHFR: methylenetetrahydrofolate reductase

References