Deep vein thrombosis

The classical presentation of deep vein thrombosis (DVT) is sudden onset of pain, redness, and swelling of one leg spreading from the calf to the thigh with marked swelling of the dorsum of the foot and tenderness along the deep venous system. The more severe condition of iliofemoral thrombophlebitis can result in marked swelling and femoral arterial occlusion (plegmasia dolora albus). Fortunately, this condition is rare, but must be recognised early as emergency thrombectomy can save the limb. Marked venous thrombosis can cause swelling/haemorrhage in compartments of the lower limbs resulting in the absence of an arterial pulse and requiring urgent surgical decompression. Equally, DVT can be completely silent, with the first manifestation being a massive pulmonary embolism causing sudden death. Submassive pulmonary embolism presents with chest pain and severe dyspnoea, while branch arterial emboli may present with pneumonic changes or pleural effusion. Repeated minor embolisms from silent thrombi in the legs or pelvis present with progressive pulmonary hypertension and decreased exercise tolerance. The differential diagnoses of swelling in one leg are many, and include cellulitis, lymphangitis, gout, arthritis, and ruptured Baker’s cyst in the knee. In fact, DVT is clinically misdiagnosed in approximately half of all patients with pain and swelling in one leg. Modern imaging techniques have, however, increased the sensitivity and specificity to more than 90%.

Compression ultrasound venography with Doppler studies (Duplex ultrasound) is reliable and is rapidly replacing contrast venography for the demonstration of venous thrombosis of the lower limbs up to the femoral region. This technique has been found to be more sensitive and cheaper than computed tomography (CT) venogram, although the latter can demonstrate thrombi in the iliac and pelvic veins or extension into the vena cava. For pulmonary embolism, perfusion scans and pulmonary angiograms have been replaced by helical CT pulmonary angiogram (HCTPA) which is non-invasive, rapid, and can demonstrate emboli up to the third generation branches. The sensitivity and specificity of HCTPA were reported to be 74.1% and 89.5%, respectively. For thrombosis in the smaller sub-segmental branches, which occurs in patients with thromboembolic pulmonary hypertension, angiogram, ventilation-perfusion lung scan, or lung biopsies may be required to differentiate pulmonary embolism from primary pulmonary hypertension. Recent studies have shown that HCTPA followed by CT venogram as a single-step investigation has a sensitivity and specificity of 97% and 100%, respectively, for femoro-popliteal DVT. Becattini and Agnelli cite that the factors resulting in venous thrombosis have been described by Virchow in his classical triad of defects in the blood vessels, blood flow, or blood components. Indeed, presence of varicose veins, prolonged bed rest, and hyperviscosity of the blood predispose a person to thrombosis and recent interest has centred on thrombophilia due to defective blood components and thrombosis associated with malignancy.

Inherited thrombophilia is characterised by recurrent spontaneous DVT before the age of 45 years, pulmonary embolism, family history of venous thromboembolism, frequent spontaneous abortion, or unusual sites of unprovoked thrombosis (cerebral, organ, or axillary). There may be triggers such as the use of oral contraceptives, long flights with the resulting inactivity, obesity, prolonged bed rest, pregnancy, major surgery, or cancer. Antithrombin III, protein C, and protein S deficiency affect all races, but there are racial differences. For example, these conditions are only noted in 10% of Caucasians with venous thrombosis while these defects were reported to account for 30% to 40% of cases in Chinese people. This discrepancy can be ascribed to the rarity of thrombophilia in the Chinese compared with Caucasians in whom the majority of cases of thrombophilia are due to factor V Leiden, prothrombin G20210A mutation or factor VIII excess (>150%) which account for approximately 50% of cases. In both races, however, the defects for many patients with thrombophilia remain undefined. Moderate homocystinaemia has been associated with venous as well as arterial thromboembolism and ongoing trials of vitamin (folic acid) supplements on thrombotic risk are of interest. Venous thromboembolism also occurs in patients with lupus anticoagulants, an acquired defect that can be demonstrated by the prolongation of activated partial thromboplastin time (aPTT) and the presence of antiphospholipid antibodies. Hyperviscosity due to thrombocytopenia, marked leukocytosis, or paraprotein also predisposes to venous thrombosis. Malignancy is a potent cause of venous thrombosis and 4% to 10% of idiopathic spontaneous DVTs are due to internal malignancies.

The mainstay of treatment of DVT is unfractionated heparin followed by the oral anticoagulant, warfarin. Unfractionated heparin also has anticoagulant activity that potentiates the effect of antithrombin-III and anti-Xa, anti-serotonin, and anti-inflammatory action. Unfractionated heparin is an ideal treatment for pulmonary embolism, which may cause severe vasoconstriction as well as DVT associated with marked inflammation. Meticulous control is required to maintain the aPTT at 2.5 to 3.5 times the normal time to prevent excessive bleeding. The availability of low-molecular-weight heparins has revolutionised the treatment and prevention of DVT, especially for pregnant women. The indications for the use of fibrinolytic agents, urokinase, streptokinase, or tissue plasminogen-activator are controversial, but these treatments should be considered for young patients with submassive pulmonary embolism and DVT in the iliofemoral region to avoid post-phlebitic...
syndrome. Direct infusion of fibrinolytic agents to the thrombosed area via a direct intravenous route is feasible, but needs to be further studied and compared with systemic infusion. Inferior vena cava filters (Greenfield filters) are effective to prevent further emboli moving to the lung from pelvic and lower limb thrombi and can be introduced via the venous system, but the indications for this treatment remain controversial and further studies are required.12

The incidence of venous thromboembolism is lower in Chinese people than in Caucasians.12 Systematic studies using 131I-fibrinogen scan showed that subclinical DVT occurs in 2.6% to 10.5% of Chinese patients undergoing gynaecological operations13 and 17% of patients with stroke,14 which is only 10% to 30% that of Caucasians in similar situations. Studies of orthopaedic operations using contrast venogram15 and a recent study using duplex ultrasound during surgery for cancer of the colon16 showed incidences of subclinical DVT of 53.1% and 41.7%, respectively, in Hong Kong Chinese people, which is comparable to that of Caucasians. No clinical thrombosis or pulmonary embolism was observed in these two studies however, suggesting that these subclinical thrombi often did not progress. Chan et al17 reported clinical venous thromboembolism in 5.1/1000 gynaecological operations performed between 1998 and 2000. Most of the DVTs were limited to the calf veins and there were only two pulmonary embolisms among 6077 patients. Liu et al18 reported 376 patients with venous thromboembolism admitted to a regional hospital in Hong Kong in a 4-year period. Most patients had DVTs and 40 had pulmonary embolisms. The calculated annual incidence of 0.167 per 1000 population is only 5% to 10% of that reported in similar studies of Caucasians. Although DVT and pulmonary embolism occur less frequently in Chinese patients, doctors should be alert to venous thromboembolism in patients at high risk, for example, those with thrombophilia, who are obese, require prolonged bed rest or orthopaedic care, have cancer, or are undergoing a major operation.

Although antithrombin III, protein C, and protein S deficiencies have been reported,13 the most common defects of factor V Leiden and prothrombin G26201A mutation have not been found in Chinese people.19-21 This could partly account for the rarity of DVT, both spontaneous and those triggered by risk factors, in this population. Previous studies of the presence of subclinical thrombosis with no clinical manifestation and/or pulmonary embolism could be due to a more effective fibrinolytic mechanism in Chinese people, which has been demonstrated among women using oral contraceptives.22 However, the contributions of different lifestyles, diet, and other environmental factors may be important and changes in these parameters may have resulted in more clinical thrombosis reported during the past decade.

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References