CASE REPORT

Deep vein thrombosis and tuberculosis: a causative link?

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SUMMARY

Pulmonary tuberculosis is very devastating in developing countries and its thrombogenic potential is a disturbing new entity. We report an 18-year-old woman who presented with a first episode of deep vein thrombosis. Pulmonary, hepatic and splenic tuberculosis was diagnosed while looking for secondary causes. The patient was treated with rifampicin, isoniazid, pyrazinamide and ethambutol along with low-molecular-weight heparin and antivitamin K. Tuberculosis has several mechanisms that induce a hypercoagulable state and can lead to thromboembolic complications.

BACKGROUND

Tuberculosis (TB) is one of the most devastating curable infectious diseases in our country and in the world. Seven to eight million new cases of TB are diagnosed every year worldwide.¹ Therefore, despite recent progress, TB remains an important global public health problem.²

In the literature, a prevalence of 3–4% deep vein thrombosis in patients with pulmonary tuberculosis has been reported.³ Also reported is a correlation between severe pulmonary or disseminated tuberculosis and the risk of developing deep vein thrombosis (DVT).⁴ That is why it is important to sensitise all clinicians to this complication of tuberculosis by reporting a case observed in our institution.

CASE PRESENTATION

An 18-year-old Caucasian woman was admitted to our department for exploration of DVT in the left external iliac vein documented by ultrasound examination. She had a 2-month history of prolonged fever and productive cough without haemoptysis. She also reported of night sweats, anorexia and weight loss within the past 6 months. There was no prior history of other diseases, surgery or drug intake.

Clinical examination revealed an ill appearing woman weighing 56 kg. She was febrile (rectal temperature 40°C). Cardiovascular, pulmonary and abdominal examinations were normal. Her left leg was swollen and tender to the touch.

INVESTIGATIONS

Laboratory findings on admission revealed a normal white cell count (6070/mm³), normocytic anaemia (haemoglobin 8.6 g/dL) and normal platelet count (340 000/mm³). The erythrocyte sedimentation rate was elevated (109 mm). The C reactive protein was high (92 mg/L) and also the

level of plasma fibrinogen (6.66 g/L). Biochemical analysis revealed lactate dehydrogenase 537 U/L and glutamyl transpeptidase (GT) 115 U/L. Other biochemical findings were within normal limits.

Aetiological investigations of thrombosis including protein S, protein C, level antithrombin, resistance to activated protein, α -amino nitrogen (AAN), antiphospholipid antibodies, antineutrophil cytoplasmic antibody (ANCA) and tumour markers were negative.

Chest X-ray showed bilateral reticulomicronodular opacities suggestive of miliary tuberculosis (figure 1). Arterial blood gas analysis showed: pH 7.47, pO₂ 84.9 mm Hg, pCO₂ 34.6 mm Hg, HCO₃ 25.7 mmol/L and oxygen saturation 97.1%.

Acidoalcohol-resistant bacillus on the sputum was negative at direct examination. Tuberculin skin testing was positive (15 mm). Serological testing for HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) were negative.

Chest CT showed necrotic mediastinal adenopathies without compression of vessels or other organs. There were diffuse centrilobular nodules in both lung fields (figure 2). Abdominal CT revealed homogeneous hepatomegaly with multiple hypodense micronodular lesions. The spleen was heterogeneous with multiple hypodense and diffuse micronodular lesions. There were no intra-abdominal adenopathies.

TREATMENT

Since tuberculosis is a common infection in Tunisia and given the overall clinical picture and radiological images, these findings were felt to be most consistent with miliary tuberculosis. That's why standard antituberculosis treatment (ATT) was initiated adjusted to weight: isoniazid (300 mg/J),

Figure 1 Chest X-ray showing bilateral reticulomicronodular opacities.

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Figure 2 Chest CT showing miliary tuberculosis.

rifampicin (600 mg/J), pyrazinamide (1000 mg/J) and ethambutol (800 mg/J). The patient was treated with low-molecular-weight heparin and 3 days later, warfarin was started with a target International Normalised Ratio (INR) of 2.0–3.0.

OUTCOME AND FOLLOW-UP

On ATT and after 2 weeks in hospital the patient presented a favourable response with improvement in constitutional symptoms. The fever had disappeared and she responded well to anticoagulation therapy. The level of γ GT was an improved 50 U/L. *Mycobacterium tuberculosis* (MT) infection involving the lung, liver and spleen complicated by DVT was diagnosed. Her treatment continued for 9 months with a good clinical response. No adverse effects were seen. After stopping of anticoagulation, the levels of protein S and C were normal.

DISCUSSION

Our case shows that venous thromboembolism may complicate severe pulmonary tuberculosis. This event can occur at presentation or later in the course of the disease.⁵ The pathophysiological process that can explain the relation between tuberculosis and DVT include: increase in plasma fibrinogen and factor VIII, reactive thrombocytosis, local compression of veins by the enlarged reactive lymph nodes, injury to endothelium and alteration in the normal blood flow.^{3–7} All these factors described in tuberculosis induce a hypercoagulable state and can lead to thromboembolic events. Furthermore, there are other mechanisms that could explain this hypercoagulable state including direct endothelial injury caused by Koch's bacillus, or the use of rifampin.⁵ In our case, compression of the vein from enlarged lymph nodes was not found.

Classically, thrombosis in the lower limbs are more common in patients with pulmonary TB. However, other unusual sites have been reported in the literature in patients with pulmonary TB, namely cerebral venous sinuses or hepatic vein.^{8,9}

In this case, the diagnosis of disseminated tuberculosis was difficult because the sputum for acid-fast stain was negative. Tuberculosis was considered because of fever, worsening general status and bilateral miliary lung nodules in an endemic zone patient. Successful treatment by a trial of antituberculous therapy consolidates this diagnosis. No other predisposing cause of DVT was found.

Once diagnosis of TB and thromboembolic events is made, anticoagulation and antituberculosis therapy should be introduced as soon as possible to improve haemostatic disorders.

Learning points

- ▶ These clinical reports emphasise that patients with severe pulmonary tuberculosis are at risk of developing thromboembolic events.
- ▶ Therefore these complications should be investigated especially in those who do not improve on antituberculosis treatment (ATT), who have other predisposing factors or are hospitalized for long periods.

Competing interests None.

Patient consent Obtained.

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