REVIEW

Association deep veinous thrombosis with pulmonary tuberculosis

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Received 29 May 2013; accepted 9 June 2013
Available online 29 June 2013

KEYWORDS
Tuberculosis; Thrombosis; Anticoagulant; Treatment

Summary  Introduction: Thromboembolic complications associated with infection by Mycobacterium tuberculosis have been reported in the literature that occurred in 1.5–3.4% of TB infection, which is a risk factor for deep vein thrombosis (DVT) related to the hypercoagulable state secondary to the inflammatory state.

Objective: We report in this study the pathophysiological, therapeutic, epidemiological, and clinical aspects, of this association.

Methods: This is a retrospective study done in our department between January 2010 and May 2013. It is about 30 cases of confirmed pulmonary tuberculosis associated with deep vein thrombosis.

Results: It is about 21 men and 9 women. Pulmonary tuberculosis was confirmed by the presence of aciduloalcohol-resistant bacillus on the sputum on a direct examination of 25 cases and bronchial aspiration in 5 cases. All patients had extensive radiological lesions. Phlebitis occurred within a mean of 17 days after the diagnosis of tuberculosis. It was confirmed by venous doppler deep ultrasound of inferior membes. All patients received anti-tuberculosis drugs in association with anticoagulant treatment.

Etiologic investigations showed positive anti-phospholipid antibodies in one case, and decrease in C and S proteins in 2 patients in which phlebitis was complicated by arterial pulmonary embolism. We had difficulties in controlling prothrombin level in 9 cases and we prescribed low molecular weight heparin for 6 months in two cases.

Conclusion: Thromboembolic disease is diagnosed systematically in the TB patients because of the risk of this complication particularly in extensive and severe forms. Prophylactic anticoagulation finds its indications in these forms.

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.
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Introduction

Active pulmonary tuberculosis may be complicated by deep vein thrombosis associated with a hypercoagulable state secondary to the inflammatory state. Vascular complications associated with infection by *Mycobacterium tuberculosis* have been reported in the literature in 1.5–3.4% of TB infection [1,2].

Patients and methods

This is a retrospective study done in our department between January 2010 and May 2013. It is about 30 cases of confirmed pulmonary tuberculosis associated with deep vein thrombosis.

Results

It is about 21 men and 9 women. The mean age was 45 years. Ten patients had a history of pulmonary tuberculosis. In the current episode, pulmonary tuberculosis was confirmed by the presence of acidoalcohol-resistant bacillus on the sputum at direct exam in 25 cases (83.3%) and the fibro-aspiration in five cases (16.7%). It is 25 cases of pulmonary tuberculosis, including 4 cases of complicated pyopneumothorax, and 5 cases of miliary. The chest radiograph showed extensive lung lesions in all patients with bilateral lesions in 12 cases (40%). All patients receiving isoniazid, rifampicin, pyrazinamide and ethambutol Phlebitis occurred within a mean of 17 days after the diagnosis of tuberculosis.

It was revealed by clinical signs and high plasma D-dimer and was confirmed by venous doppler deep ultrasound of inferior members. In 5 cases of phlebitis was complicated by pulmonary embolism. No patient had suggestive of Behcet disease or signs of systemic disease. Etiologic investigations showed the presence of antiphospholipid antibodies in a patient and protein S deficiency and C in 2 patients. The oral anticoagulants (vitamin K antagonists) were associated with low molecular weight heparins (LMWH) hanging five days on average, they are arrested after monitoring prothrombin which is corrected within 15 days on average. We had difficulties for controlling prothrombin level in 9 cases and we must prescribe low molecular weight heparin for 6 months in two cases. In 25 cases, the oral anticoagulation was stopped after 3 months, while in 3 cases, this treatment was extended beyond 3 months. We noted good clinical, bacteriological and radiological progression after 6 months of TB treatment.

Discussion

Our cases show that VTE may complicate severe pulmonary tuberculosis and that these events occur at presentation or later in the course of the disease. Robson et al., found 35 patients with pulmonary TB and DVT. In 33 of them, DVT occurred 7 days after the diagnosis of TB, while only in two, DVT was the presenting feature [3]. Other reports also demonstrate that thrombotic phenomena in patients with pulmonary TB occur in other sites. These may include hepatic veins [4], the vena portae, [5], the inferior vena cava [6], cerebral venous sinuses [7,8], and the central retinal vein [9] which reinforces the link between these conditions. Disseminated TB may induce at the peripheral blood the activation of mononuclear cells, and the interaction of these cells activated with mycobacterial products induces increased synthesis of factor tumor necrosis alpha and interleukin-6 [10–12].

TB has several mechanisms that can induce a hypercoagulable state may lead to thromboembolic complications. Various studies have concluded that the high level of plasma fibrinogen, impaired fibrinolysis associated with a decrease in antithrombin III, protein C and platelet aggregation appear to induce a hypercoagulable state promoting the development of deep vein thrombosis pulmonary tuberculosis [1,3,13].

Some authors have mentioned the high incidence of antiphospholipid antibodies detected in tuberculosis, and the possible relationship between these and protein S. Although studies on the activity of prothrombin in tuberculosis are not numerous, it seems that hypoprophrombinemia that rather hyperactivity of prothrombin exists in appreciable number of cases. Various studies indicate that prothrombin deficiency occurs in approximately one third of TB patients [1,14,15].

Cytokines by their pro-inflammatory character, will activate the vascular intima and make thrombogenic endothelium. They will also lead to a stimulation of hepatic synthesis of coagulation proteins [10,16]. These risks of hypercoagulability are increased by the immobility and bedrest because of the morbidity caused by the disease.

However, thrombosis can also result from venous compression by lymph nodes in ganglionar forms of TB, as ret roperitoneal adenopathies may cause inferior vena cava thrombosis in the absence of any haemostatic abnormalities [17].

These haemostatic changes improve during the first month of TB treatment [15] and for this reason, it should be immediately started in addition to anticoagulant therapy. Frequently, a higher dose of warfarin is necessary to achieve therapeutic INR levels, because of rifampin effects on cytochrome P450 [18]. Additionally, this drug may also contribute to the hypercoagulable state by decreasing production and increasing
clearance of anticoagulant hepatic proteins. Consequently, the initial phase of treatment may result in a higher risk for development of DVT [19,20].

Conclusion

Thromboembolic disease is to search systematically at the TB view of the risk of occurrence of this complication particularly in extensive and severe forms. Prophylactic anticoagulation find its indications in these forms.

Conflicts of interest

The authors declare no conflict of interest.

References