Case Report

Pulmonary Tuberculosis: A Neglected Risk Factor for Deep Venous Thrombosis

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Abstract

A case of deep venous thrombosis (DVT) of the lower limb in the absence of known common risk factors and its link with underlying pulmonary tuberculosis is described in a young female patient. Possible underlying mechanisms and awareness regarding tuberculosis as a risk factor for DVT is also emphasized.

Keywords: Deep vein thrombosis, lower limb, pulmonary tuberculosis

INTRODUCTION

Deep vein thrombosis (DVT) is a common preventable and treatable cause of death worldwide. This is predominantly a disease of the elderly with an incidence that rises markedly with age. There are other several factors also that are associated with increased risk of DVT such as major surgeries, prolonged bed rest, oral contraceptive pills, smoking, malignancy, presence of central venous lines, and inherited hypercoagulable states.

Tuberculosis is largely neglected as a risk factor for DVT. However, several studies have shown an association between infection by Mycobacterium tuberculosis and vascular complications. Therefore, it is essential to identify such tuberculosis patients who are at risk of developing DVT so as to manage them in time and avoid life-threatening consequences.

This report describes a case of DVT in a patient secondary to extensive pulmonary tuberculosis.

CASE REPORT

A 23-year-old female was admitted to our department with complaints of painful swelling of the left lower limb for the last 15 days. She also had dry cough and low-grade fever from the last 2 months. She denied any investigation or specific treatment in the past. She had not undergone any major surgeries in recent past and was not taking any oral contraceptive pills. There was no history of abortions or immobilization also.

General physical examination revealed a poorly built, malnourished female. Her left leg was swollen, shiny, and it was tender to touch with positive Homan’s sign. Her pulse and blood pressure were normal. Cardiovascular and abdominal examination was unremarkable. Respiratory system examination revealed bilateral crepitations and bronchial breath sounds at the right infraclavicular region. Routine investigations revealed anemia (hemoglobin 10.5 g/dl), leukocytosis (white blood cell 13.8 G/L), and a normal platelet count (235,000/mm^3). Biochemical investigations were within normal limits.

Chest X-ray demonstrated bilateral inhomogeneous infiltrates with cavitiation at the right upper zone. Sputum examination showed acid-fast bacilli on routine smear microscopic examination. Due to swelling and tenderness at calf, the possibility of DVT was considered. Ultrasound Doppler study of the left lower limb was performed that revealed DVT at the left pelvic vein, deep femoral vein, external iliac vein, and common iliac vein. Ultrasound abdomen and connective tissue profile did not show any abnormality. Other investigations such as measurement of prothrombin level, antithrombin III, and antiphospholipid

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A diagnosis of microbiologically confirmed new case of Pulmonary tuberculosis with DVT of the left lower limb was made, and a standard antituberculosis treatment regimen (Category I) was initiated according to body weight as per Revised National Tuberculosis Control Program of India. The patient was given enoxaparin subcutaneously (60 mg twice daily) for 7 days and subsequently warfarin (5 mg/day) with close monitoring of prothrombin time and INR. With this treatment, her general condition improved rapidly; swelling and tenderness of the limb also decreased [Figure 1b]. The latter disappeared completely after 3 weeks. As no other significant risk factor for DVT was evident in our case apart from pulmonary tuberculosis and rapid response was observed with antituberculosis treatment along with anticoagulant therapy, DVT was strongly considered as secondary to the underlying pulmonary tuberculosis.

**DISCUSSION**

Active pulmonary tuberculosis can be complicated by DVT, associated with a hypercoagulable state secondary to the underlying inflammation. In about 1.5%–3.4% of tuberculosis infection, there is an association between vascular complications and infection by *M. tuberculosis*.[4,5] DVT is known to complicate severe pulmonary tuberculosis and may occur at the time of presentation of pulmonary disease as seen in our case or may be seen later in the course of disease or even during treatment.[6]

DVT is most commonly seen in postoperative patients and in patients who are ambulatory for a long time. It is rarely suspected due to underlying tuberculosis in day-to-day clinical practice, and very few publications are there in literature, mostly as case reports.[7] Increased awareness along with availability of noninvasive tests such as color Doppler ultrasonography may result in detection of more cases of tuberculosis associated with DVT in future and likely to reduce the so-called unexpected sudden deaths in few of them if managed properly. Peripheral limb edema in patients of tuberculosis is largely attributed to the hypoproteinemia. However, there are certain signs such as pain and increased surface temperature of the affected limb that are helpful for the diagnosis of DVT in such cases. High probability of suspicion with no delay in diagnosis and management of DVT in such patients should be emphasized.

The exact mechanisms responsible for the development of DVT in tuberculosis patients are not clear. All the three components of Virchow’s triad, i.e., hypercoagulability, venous stasis, and endothelial dysfunction, can play a role in the pathogenesis of the DVT associated with tuberculosis. There are several mechanisms in tuberculosis that can produce a hypercoagulable state due to which thromboembolic complications can occur. There are several studies that have shown increased level of plasma fibrinogen, impaired fibrinolysis along with reduction in antithrombin III, protein C, and reactive thrombocytosis resulting in a hypercoagulable state due to which DVT can occur in pulmonary tuberculosis.[4,6,8]

Some reports in literature also mention increase in antiphospholipid antibodies in tuberculosis patients, and there
is some relationship between these and protein S. Although studies on the activity of prothrombin in tuberculosis are not numerous, it seems that hypoprothrombinemia rather than hyperactivity of prothrombin exists in appreciable number of cases. Some studies indicate that there is prothrombin deficiency in approximately one-third of tuberculosis patients.[4,9,10]

Cytokines which are proinflammatory in character can activate the vascular intima and make endothelium thrombogenic. Hepatic synthesis of coagulation proteins can also be stimulated.[11] Increased hypercoagulability state because of the immobility and bed rest due to the morbidity caused by the disease may be potential risk factors in such patient. Thrombosis caused by venous compression from lymph nodes may be another mechanism to cause DVT in such patients.[12]

Literature also states a possible association between the use of rifampicin and DVT with a relative risk of 4.74 in patients treated with rifampicin-containing regimen.[13] It has been suggested that antituberculosis therapy should be immediately started and supplemented with anticoagulant therapy as hemostatic changes improve during the 1st month of treatment.[10] Anticoagulant therapy should be cautiously used in these patients due to the interaction of rifampicin with warfarin analogs, as rifampicin-mediated enzyme induction may reduce the efficacy of warfarin. The newer Xa inhibitors have several advantages over traditional therapy with parenteral anticoagulant, i.e., faster onset of action and lesser bleeding events as compared with the standard therapy.[14]

**Conclusion**

Our case emphasizes on the importance of keeping a high index of suspicion of DVT in patients with pulmonary tuberculosis. Early initiation of antituberculosis treatment along with anticoagulant therapy can prevent the potentially fatal complication of the disease. Low molecular weight heparins are safer and require minimal monitoring. The overall morbidity and mortality may also be decreased if the condition is timely diagnosed and managed properly.

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**Conflicts of interest**

There are no conflicts of interest.

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