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Deep Vein Thrombosis In Sputum Positive Pulmonary Tuberculosis – A Case Series

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Abstract

India accounts for 1/3rd of global burden of Tuberculosis .Pulmonary TB is a risk factor for DVT. Thromboembolic complications associated with pulmonary TB had been reported in literatures with incidence varying between 1.5 to 3.4%. We are presenting the case series study of 4 cases of smear positive pulmonary TB patients who developed DVT while on treatment for pulmonary TB. Patients were subjected to routine blood investigations, sputum for AFB, CXR and Doppler USG of venous system. All 4 were males and smokers with age ranging between 35 -53 years with low BMI and extensive lesions in chest x-ray and Doppler confirmed DVTof lower limbs. Sputum AFB grading was 2+ in 3 patients and 1+ in a patient. All the patients developed DVT within 4 weeks of diagnosing PTB. All were treated with ATT, heparin and oral acitrom . All responded well to the treatment and none developed pulmonary embolism. Pulmonary TB infection causes elaboration and release of pro-inflammatory cytokines resulting in hypercoagulable state. Rifampicin used in the regimen alters the coagulant and anticoagulant balance resulting in hypercoagulable state. In all 4 cases, factors like cigarette smoking and extensive lung involvement by disease process , poor nutritional of patient and immobility of patient contributed to the development of DVT. In all severely ill pulmonary TB patients, we should be aware of development of DVT and early screening for DVT and encouraging early ambulation in such patients will prevent life threatening pulmonary embolism.

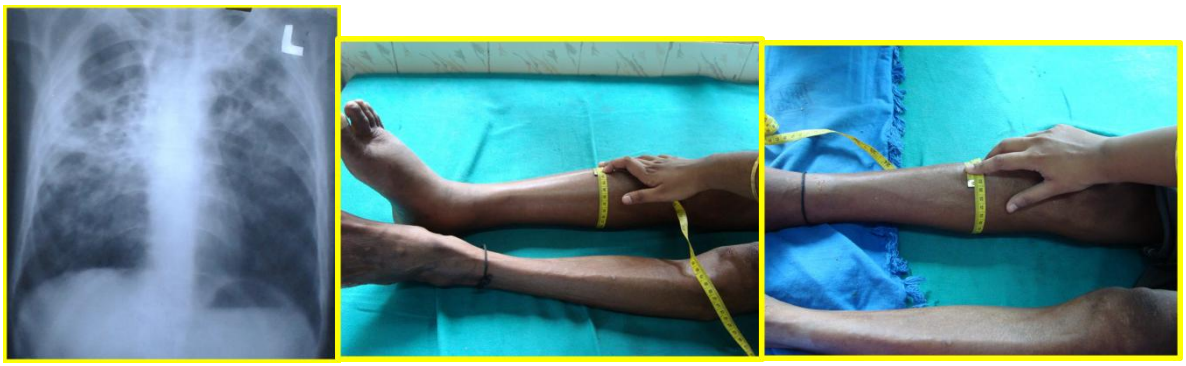
Keywords: Pulmonary tuberculosis, Deep Vein Thrombosis

Introduction

Tuberculosis is one of the most devastating curable infectious diseases in our country and the world. It is caused by *Mycobacterium tuberculosis*, an acid fast bacilli. This disease can affect most organs in the body and lead to various sequel as a result of the organs involved.[1] India accounts for almost 1/3 of the global burden of tuberculosis, one of the most devastating curable diseases. [2] Respiratory infections can increase the risk of VTE Each year 8.8-12.2 million new cases are diagnosed with tuberculosis and 1.5-1.8 million deaths are caused by the same. India contributes a significant burden to these numbers of incidence and mortality and thus tuberculosis remains an important global public health problem with new complications being discovered despite its knowledge and presence since neolithic age.[3] The prevalence of deep vein thrombosis in patients with pulmonary tuberculosis is estimated to be around 3-4%. There is a hypothesized correlation between severe pulmonary or disseminated tuberculosis and risk of developing deep vein thrombosis. That is why it is important to sensitize all clinicians to this complication by reporting a case observed in our institution [4,5]

Case 1

A 46 Years old male patient presented with complaints of painful swelling of right leg for 3 days and fever for 2 days. He took CAT I ATT for 4 months and discontinued for 15 days and then restarted anti-tubercular treatment and was on regular intake of medicine for 1 month before presenting to the hospital.He was not on any other medications except ATT. He was not a known Diabetic/Hypertensive. He was a moderate alcohol consumer but never smoker and he was bed-ridden for 8 days prior to hospital visit. At the time of presentation, he was conscious, oriented, febrile and his weight was 40kg. His right leg was swollen, tender, erythematous and he was having pain while moving the affected limb(fig .2 swollen limb).Blood investigations were normal except Hb-10.4g% and ESR 65mm 1st hour. His sputum status was 2+ grading and chest x-ray (fig 1) showed bilateral cavitary lesions. In view of swelling of lower limbs with pain, Doppler usg was done which confirmed left ilio-femoral thrombosis. He was started on inj heparin in consultation with vascular surgeon then switched to oral anti-coagulant (Acitrom). He was continued with standard cat 1 ATT regimen. Slowly the leg swelling got reduced (fig 3) and became pain free in 10 days. He was discharged on 22 nd day of admission with advice to continue ATT and acitrom and regular follow-up.



Case 2

40 years male with pulmonary tuberculosis who defaulted ATT was admitted with history of cough with expectoration fever and loss of appetite and loss of weight since 1 month and 7 days history of painful swelling of right leg (Fig 4) .He was not a Diabetic/Hypertensive but alcoholic and smoker for past 25 yrs.He was immobile for past 2 weeks. He was malnourished with weight 27 Kg.His left leg was swollen up to knee and it was tender and erythematous. Blood investigations revealed Hb of 10.0 g/dl and ESR 42 mm 1 st hour. His sputum AFB grading was 2 (+) and line probe assay showing M.tb sensitive to INH and RIF and his LFT and RFT were within normal limits, Bleeding time was 2 min, 40 sec and Clotting time was 4 min, 30 species chest x-ray(fig.5) showed bilateral extensive involvement of lung with tuberculosis. Doppler USG of lower limbs revealed acute venous thrombosis in Left external iliac vein, Left common femoral vein, Left common superficial and deep femoral vein, Left popliteal vein, Left anterior & posterior tibial vein. He was started on inj heparin in consultation with vascular surgeon then switched to oral anti-coagulant (Acitrom) so that INR was maintained between 1.5 and 2.5. He was started on cat 2 ATT regimen. Slowly the leg swelling got reduced (fig 3) and became pain free in 10 days. He was discharged on 18 th day of admission with advice to continue ATT and acitrom and regular follow-up.

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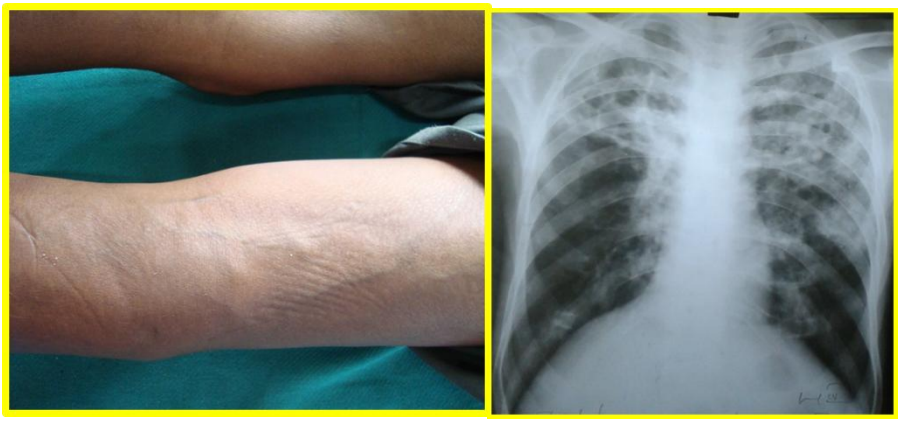
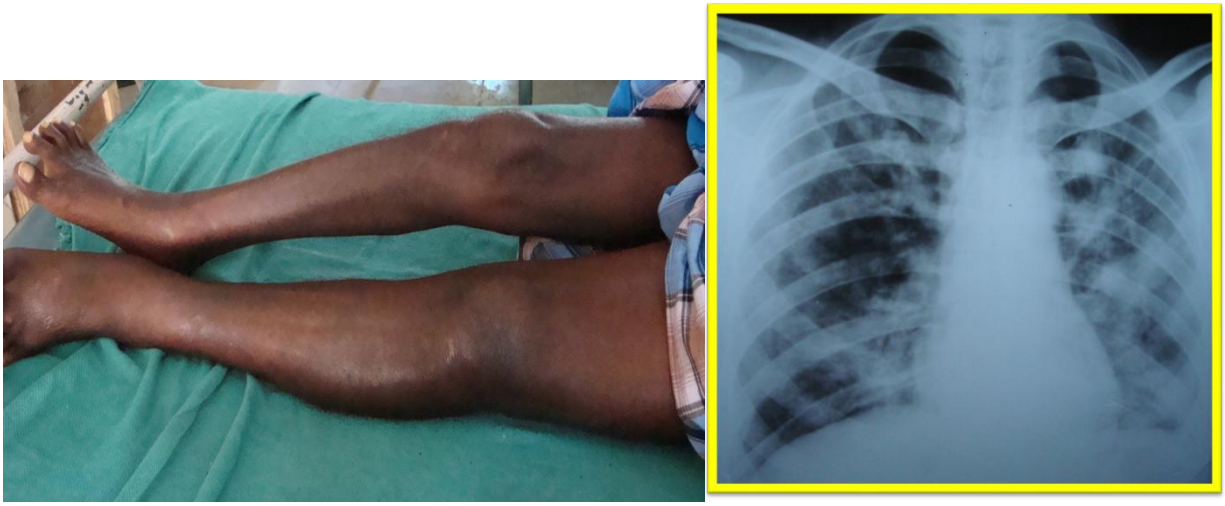


Case 3

A 53 years male with pulmonary tuberculosis on CAT I ATT since 1 month reported to hospital with pain and swelling of left leg(fig 6) since 1 week. Not a known Diabetic/Hypertensive.He was an alcoholic and smoker for past 10 yrs.,he was a poorly built, malnourished man weighing 27 Kg. His left leg was swollen up to knee and tender.he was tachypneic with RR OF 28/min and SpO2 - 85% room air, JVP-not elevated.his echo was normal with no findings suggestive of pulmonary hypertension. Blood Investigations reveale presence of anaemia with Hb - 8.8 g/dl and raised ESR (30 mm 1 st hour).LFT and RFT were within normal limits. His Sputum AFB grading was 1 (+),Bleeding time-2 min, 40 sec and Clotting time -4 min, 40 sec.he had bilateral extensive lung inviolvement(fig 7) Doppler USG of left lower limb revealed Thrombosis extending from the internal iliac vein involving the common femoral and deep femoral vein and also extending into the popliteal vein. Anticoagulant was started ,initially heparin and then acitrom with INR maintained within 1.5 to 2.5.Patient improved and discharged on 25th day of admission with advice to continue ATT and acitrom and regular follow up.



Case 4

A 35 years old male who was taking irregularly the CAT II ATT for sputum positive PTB, got admitted with history of Cough with expectoration and fever for 2 months and loss of appetite and weight since 10 days. He also had history of Painful swelling of right leg- 15 days .he was Not a Diabetic/Hypertensive,.he was a Smoker and alcoholic since 10 yrs., weight was 40Kg at the time of admission. His right leg was swollen and tender. his Hb level was 8.6 g/dl. Sputum AFB severity grading was 3 (+).other blood investigations were within normal limits. Bleeding time-2 min, 40 sec and Clotting time- 5 min, 10 sec. his sputum line probe assay confirmed INH and RIF sensitivity and hence started on cat 2 ATT.his chest xray(fig 8) had cavity and consolidation in left upper and mid zone and consolidation in right upper and

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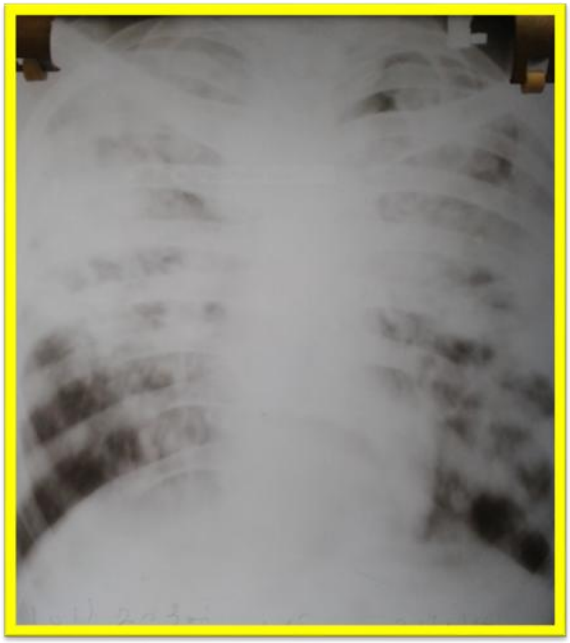
mid zones and left lower zone DOPPLer USG confirmed Thrombus in the common femoral vein extending into the superficial femoral vein up to the lower 1/3 of the thigh. He was initiated on Inj Heparin and overlapped with oral anticoagulant and maintained INR between 1.5 – 2.5. Patient improved ,discharged at request on 15th day.



Discussion

Mycobacterium tuberculosis is an acid fast bacilli responsible for causing tuberculosis.1 Mortality is higher in cases diagnosed late due to increase incidence of complications and advanced stage of the disease itself. Complications of tuberculosis can be local pertaining to the organ infected such as bronchiectais, end stage lung disease, pleural effusion, constrictive pericarditis or systemic as seen in military tuberculosis which can lead to Addisonian crisis, shock on one end and disseminated intravascular coagulation at the other end.3,4 Hematological complications of tuberculosis are known but rarely seen.[6] These include bronchial arteritis, Rasmussen aneurysm etc.5 Rarely can pulmonary tuberculosis also present with deep vein thrombosis. There have been reports of deficiency of protein S and concurrent antiphospholipid antibody syndrome in patients of tuberculosis and therefore tuberculosis can be complicated by venous thromboembolism also.[7] Deep vein thrombosis is can either be caused by inherited/hereditary factors or acquired factors. It is caused by disturbance in endothelial function or venous stasis or a hypercoagulable state.[8] It is more commonly seen in post surgical cases or in patients on prolonged bed rest. Though medical conditions such as thrombophilias such as factor V leiden mutation and activated protein C resistance and prothrombin gene mutations have been commonly implicated for unprovoked deep vein thrombosis, these are rarely seen and most patients with medical cause of deep vein thrombosis end up with the diagnosis of malignancy induced thrombophilia.[9] Our case did not have any recurrent venous thrombosis, any valvular heart disease nor was involved in any trauma, surgery or had any episode of prolonged bed rest. He was tested for protein C and protein S deficiency along with APLA profile, however all were normal. [10] Unprovoked thrombosis in this case in absence of hereditary factors shows that severe pulmonary tuberculosis may be complicated by venous thromboembolism. This event can occur at the time of presentation or later in the course of the disease. This is not absolute for all cases of tuberculosis. Provisional hypothesis for this occurrence can be:9-12 .Tuberculosis induces an acute phase response by activation of mononuclear cells.[11] The interaction between these activated mononuclear cells causes increase synthesis of TNF-alpha, Interleukins and proinflammatory cytokines, which can activate

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vascular intima and render the endothelial surface more thrombogenic and the blood more hypercoagulable thereby increasing the risk of deep vein thrombosis. Tuberculosis causes anemia, reactive thrombocytosis, increase in plasma fibrinogen and factor VIII and decrease levels of antithrombin III, and protein C levels. Local compression of veins by the enlarged lymph nodes. [13]Direct endothelial injury caused by Koch's bacillus. Immobility imposed by hospitalization. These factors can lead to a hypercoagulable state that can lead to thromboembolic events. 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 veins.[14] In this case, the diagnosis of pulmonary tuberculosis was considered because of fever, worsening general status and cough with expectoration and sputum was positive for AFB. Good response to antitubercular therapy and culture reports consolidates this diagnosis. No other predisposing cause of DVT could be found. Anticoagulation and antitubercular therapy were started as soon as possible to improve outcome of lung as well as vascular pathology[15]

Conclusions

These clinical reports emphasize 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 ATT, who have other predisposing factors or are hospitalized for long periods . Prophylactic anticoagulant therapy should also be considered and the use of central venous catheters avoided in order to prevent venous thrombosis and its complications . Noteworthy, the absence of cavitary lesions from TB in our patient's chest x-ray and other TB symptoms such as night sweats, anorexia and weight loss caused attention was paid to the most likely diagnosis for a DVT patient with haemoptysis, that is, pulmonary embolism, although some diagnostic changes, sign or symptoms may appear in severe or more advanced stages of the disease. It is not exactly clear whether DVT in our case is associated with TB or not but what matter is paying attention to this differential diagnosis along with other possibilities in confronting with a DVT patient with hemoptysis, especially, in patients with similar symptoms who live in endemic TB areas.

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