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### RESEARCH ARTICLE

#### PULMONARY THROMBOEMBOLISM IN A PATIENTS OF PULMONARY TUBERCULOSIS: AN UNCOMMON OCCURRENCE.

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Thromboembolism, Pulmonary tuberculosis, drug or disease.

#### Abstract

Tuberculosis has a high prevalence in India but pulmonary embolism is rarely reported in Mycobacterium tuberculosis infection. We describe a case series of pulmonary embolism associated with severe pulmonary tuberculosis. In our first case pulmonary embolism (PE) occurred within 6 months of pulmonary tuberculosis diagnosis. Patient took ATT for 6 months and after being diagnosed as a case of PE, low-molecular-weight heparin was prescribed for 3 days and after that he was given Tab. warfarin (5mg) OD. Our second case diagnosed as a case of PE after taking 9 months of ATT and he also prescribed Tab. Warfarin and low molecular weight heparin. The association between tuberculosis and pulmonary embolism is rare. Tuberculosis, the disease can itself lead to hypercoagulability, increased venous stasis, and endothelial dysfunction, thus increasing the susceptibility to venous thromboembolism (VTE) particularly in those with severe pulmonary or disseminated tuberculosis. Among the ATT drugs, most commonly associated with thromboembolic events is Rifampicin, an enzyme inducer, and may alter the balance of anticoagulant and coagulant proteins produced by the liver. But it should be in detailed investigation should be done by respiratory physicians to rule out etiology whether it is due to drug or disease itself.

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#### Introduction:-

Tuberculosis is most prevalent infectious diseases worldwide as well as in India. According to WHO TB statistic 2015, globally incidence of TB was 9.6 million and in India it was 2.2 million.<sup>1</sup> Our cases highlights the occurrence of pulmonary embolism in a patient with pulmonary tuberculosis. Tuberculosis, the disease can itself lead to hypercoagulability, increased venous stasis, and endothelial dysfunction, which increasing the susceptibility to venous thromboembolism (VTE).<sup>3</sup> 1.5% to 3.4% of TB cases have been reported with vascular.

Complication along with TB and VTE is considered rare in TB.<sup>2</sup> VTE commonly underdiagnosed condition but has high morbidity and mortality. This could be because many cases may be asymptomatic at first or may present with non-specific symptoms. Occurrence of VTE is rare in patients with pulmonary tuberculosis. The association between pulmonary tuberculosis and VTE has not been documented widely in published literature.

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**Case History:-****Case -1:-**

A 19 years old male patient came to Emergency department with chief complain of leg pain since 15 days, Difficulty in breathing, fever and vomiting since 4 days. Patient was relatively asymptomatic before 4 days and then he developed vomiting which contained food. Patient also developed breathlessness which was more during morning and aggravated by walking. Patient is a known case of pulmonary tuberculosis since 6 months and for that he was taking Anti Tubercular Treatment [H: Isoniazid (300 mg), R: Rifampicin (450 mg), Z: Pyrazinamide (1500 mg), E: Ethambutol (1200 mg)] regularly from government hospital. Patient stopped taking treatment since 4 days because of vomiting. Subsequently he presented to emergency where he diagnosed as a case of pulmonary thromboembolism. On blood investigation, his ESR was elevated (81 mm 1st hr, Westergren). His D-dimer level was also significantly raised (161ng/ml) and in sputum test was also positive for mycobacterium tuberculosis. His radiological reports showed following findings.

1. CXR (Chest) - Blunting of Left CP angle, Opacity in left lower and mid zone, soft tissue opacity in right upper zone (see figure 1 or 2)
2. CT Scan (Thorax) - citatory and bronchiectasis destruction in left lung. ST nodular cavitatory Right middle and lower zone. Right pulmonary Artery s/o Thromboembolism.
3. All other investigations were normal level and patient negative for HIV and HbsAg. Lower limb ultrasound showed no evidence of deep vein thrombosis.

**Management of patient:-**

Initially patient was treated with Inj.Heparin (5000IU) IV at 5ml/hr. rate for 4 days and then he was switched over to Tab.Warfarin (5mg) OD for pulmonary embolism. Patient recovered and was discharged uneventfully after 10 days. Patient was discharged with ATT and Tab. Warfarin. The case was reported via vigiflow to the National coordinating center for ADR monitoring with reference ID No. is 2017-04625. According to WHO and Naranjo's causality assessment for adverse drug reaction this case falls in to "Possible" causality. This is because that the occurrence of this adverse effect which is VTE could occur because of ATT drugs and can be explained by patient's disease itself.

**Case-2:-**

A 65 years old obese male patient came to Emergency department with chief complain of edema on the both limbs and breathlessness since 30 days. Patient is known case of pulmonary tuberculosis since 12 months and for that he was taking ATT (category -1) from private practitioner. Patient is also known case of Diabetes Mellitus type-2 since 5 years and for that he was taking Tab. Metformin (500mg) BD regularly. Patient had azotemia (S.Creatinine-1.68mg/dl) with hyperkalaemia (S. Potassium – 7.1 mmol/L). His HbA1C was also 9.9 % showing poor control of DM as well.

X-ray (chest AP view) - Irregular opacity seen in bilateral para-hilar region and few nodular opacity in bilateral lower zone.

USG Abdomen – (A+P) mild congestion of IVC seen.

Thorax and pulmonary angiography – Thrombosis of anterolateral segmental/ sub segmental division of left lower lobar pulmonary artery. Partial thrombus in right pulmonary artery, multiple nodular lesions throughout both lungs. Bilateral Para hilar consolidation and scattered fibrotic band, bilaterally mild bronchiectasis.

Right lower limb vein Doppler- Normal

**Management:-**

Patient was given Tab.Warfarin 5mg BD along with Low molecular weight heparin till therapeutic INR level achieved. He required non invasive BiPAP support for first 2-3 days and then patient was stabilized.

**Discussion:-**

Venous thromboembolism is common in hospitalized patient but it also occurs in patient with TB. It is an uncommon occurrence in patient with TB. There are not many studies evaluating the coexistence of TB with venous thromboembolism but there are few case reports suggesting TB as a risk factor for venous thromboembolism.<sup>2</sup> Many possible mechanisms of VTE in patients with TB are as follows. Pathologically it may be because of all the three

parts of Virchow's triad, i.e. hypercoagulability, venous stasis and endothelial dysfunction. Other responsible factors may be higher levels of fibrinogen, fibrin degradation products, tissue plasminogen activator and inhibitor. Decreased anti-thrombin III and reactive thrombocytosis may also cause VTE. Hypercoagulability can also occur by increased clearance or decreased production of anticoagulant proteins.<sup>2,6</sup> Enlarged retroperitoneal lymph nodes and immobility leads to venous stasis which may cause increases risk of VTE.<sup>4</sup> Koch's bacillus reactions may cause endothelial injury. There are certain factors that may increase the risk of venous thromboembolism in patients with TB. That can be increasing age, presence of HIV, obesity, Diabetes Mellitus. As in our second case was elderly, obese, having DM-2 but in case-1 the patient was young 19 years and he was not suffering from any comorbidity. It points to the fact that VT can occur in absence of established risk factors also. There is an emerging concern that VTE could also result from drugs which form a component of ATT. This probable association between rifampicin and DVT stated above does not contraindicate use of this drug. Some measures to prevent DVT should be taken in such patients receiving rifampicin.<sup>5</sup>

The altered haemostatic changes associated with TB improve during the first month of ATT. Hence anticoagulant therapy can be administered in high risk patients. A higher dose of warfarin is may be necessary to achieve therapeutic INR levels, because of rifampin being an enzyme inducer<sup>7</sup>. 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<sup>8,9</sup> Immunoallergic reaction which is induced by rifampicin may activate the coagulation process and initiate the DIC. Rifampicin as an antigen binds to platelets and erythrocytes to form immune complexes. Activated complement may cause platelet and, erythrocyte injury, and vascular endothelium impairment<sup>10</sup>. Because of this mechanism small blood clot formation occur in the vessels which can cause VTE.

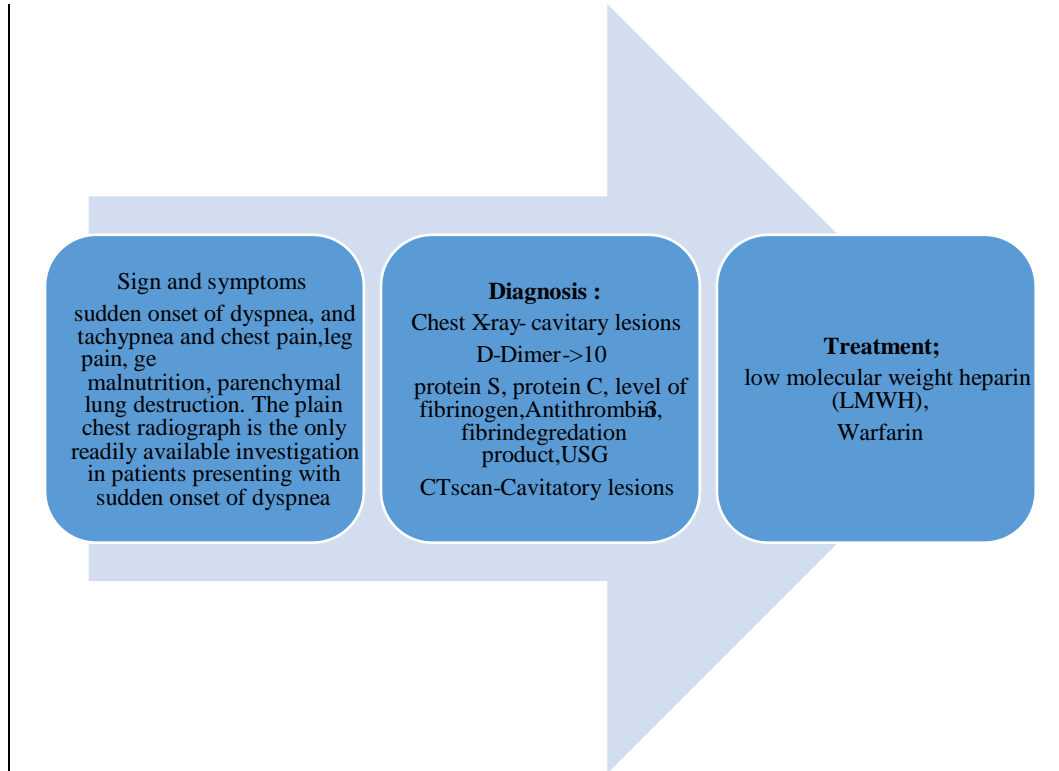
#### Images:-



**Figure 1:-** Chest X-ray PA View  
Suggesting left lower lobe opacity of first case



**Figure 2:-** Chest X-ray PA View suggesting  
Right upper lobe opacity of second case.



**Figure 3:-** Assessment of pulmonary embolism in AKT receiving tuberculosis patients.

### Conclusion:-

This case series highlights that patients with pulmonary tuberculosis are at increased risk of thrombotic events. In our cases it is pulmonary embolism. This is the thing that is not taken into consideration, which might missed in diagnosis and could play a major role in the outcome of the patient. It can be present with mild symptoms in younger age because of drug like Rifampicin. So Physician and pulmonologist should be watchful for this (especially in country like India) life threatening event and patient should be properly followed up for TB and Pulmonary embolism as well (see figure: 3).

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