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CASE REPORT

EXTRA-PULMONARY TUBERCULOSIS IS ASSOCIATED WITH AN UNUSUAL CAUSE OF DVT: A RARE CASE REPORT

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ABSTRACT

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis* complex. The disease most commonly affects the lungs, although other organs are involved in up to one - third of cases. In order of frequency, the extra pulmonary sites most commonly involved in Tuberculosis are the lymph nodes, pleura, genitourinary tract, bones and joints, meanings, peritoneum and pericardium. Despite effective treatment, tuberculosis can lead to significant short-and long-term health consequences. Deep vein thrombosis (1.5%–3.4%) is one the unconventional complication of tuberculosis due to hypercoagulable state secondary to the inflammatory state. We report one case of DVT associated with extra pulmonary tuberculosis.

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INTRODUCTION

India is the second most populated country in the world and it contributes to 23% of the incident cases of tuberculosis (TB) annually out of total 9.6 million incident cases of TB worldwide (White, 1989). India has been engaged in Tuberculosis (TB control activities for more than 50 years). Yet TB continues to be India's severest health crisis. TB kills an estimated 480,000 Indians every year and more than 1,400 every day. Tuberculosis is classified as pulmonary, extra – pulmonary,or both. Depending on several factors linked to different populations and different strains, extra pulmonary TB occurs in 10 – 40% of patients. However, virtually all organ systems may be involved in tuberculosis. As a result of haematogenous dissemination in HIV infected individuals, extra pulmonary TB is seen more commonly today than in the past in the settings of high HIV prevalence. Despite the treatment advances, 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 Complex* have been reported in the literature that occurred in 1.5–3.4% of TB infection. This complication will further add to the morbidity and mortality rates of tuberculosis.

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CASE REPORT

A 49 years old Hindu female from Odisha was admitted in Apollo hospital, Bhubaneswar dated 14/12/2017 with chief complaints pain and swelling in the legs, shortness of breath for 3 days. Lab investigation showed Hb- 9.5gm%, TLC – 13.4, Platelet – 3,58,000, Neutrophils– 86, d-dimer- 4.0. IVC. Pt – 14.4, INR – 1.11. Viral serology was negative. USG left lower limb showed presence of Acute thrombus involving all the deep and superficial veins of left lower limb & upward extension up to left common iliac vein (Fig. 2). CECT thorax and CT pulmonary angiogram showed mild right pulmonary effusion with basal atelectasis. There is no para aortic and inguinal lymph nodes compressing (Fig.1). She was previously admitted in this hospital on 19/10/2017 with complaints of dry cough, weight loss and loss of appetite for 1 month and Lab investigations showed Hb- 12.1, TLC – 8.71, TPC – 5,20,000. X-ray showed pleural effusion (RT lung). CECT thorax showed evidence of moderate to gross pleural effusion. After informed consent, diagnostic and therapeutic pleural tapping was done. Pleural fluid analysis showed Glucose 76mg/ dl, LDH -391u/l, total WBC- 2951 cells/microlit, ADA level was 32.1 u/l and high. Histopathology showed chronic inflammatory cells. TB gamma interferon antigen titre – 3.82 iu/ml which was positive (normal value – 0.35iu/l). She was diagnosed as a case of Extra pulmonary tuberculosis. She was started on ATT on 1/11/2017. After starting ATT, patient improved clinically.

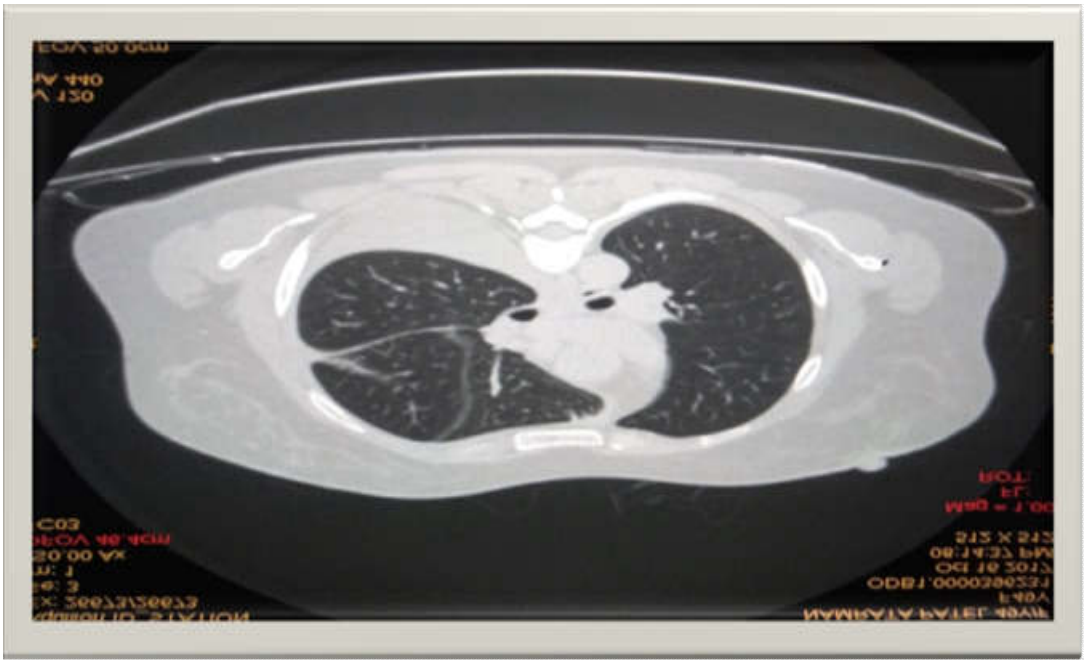

Figure 1. Cect Thorax Image

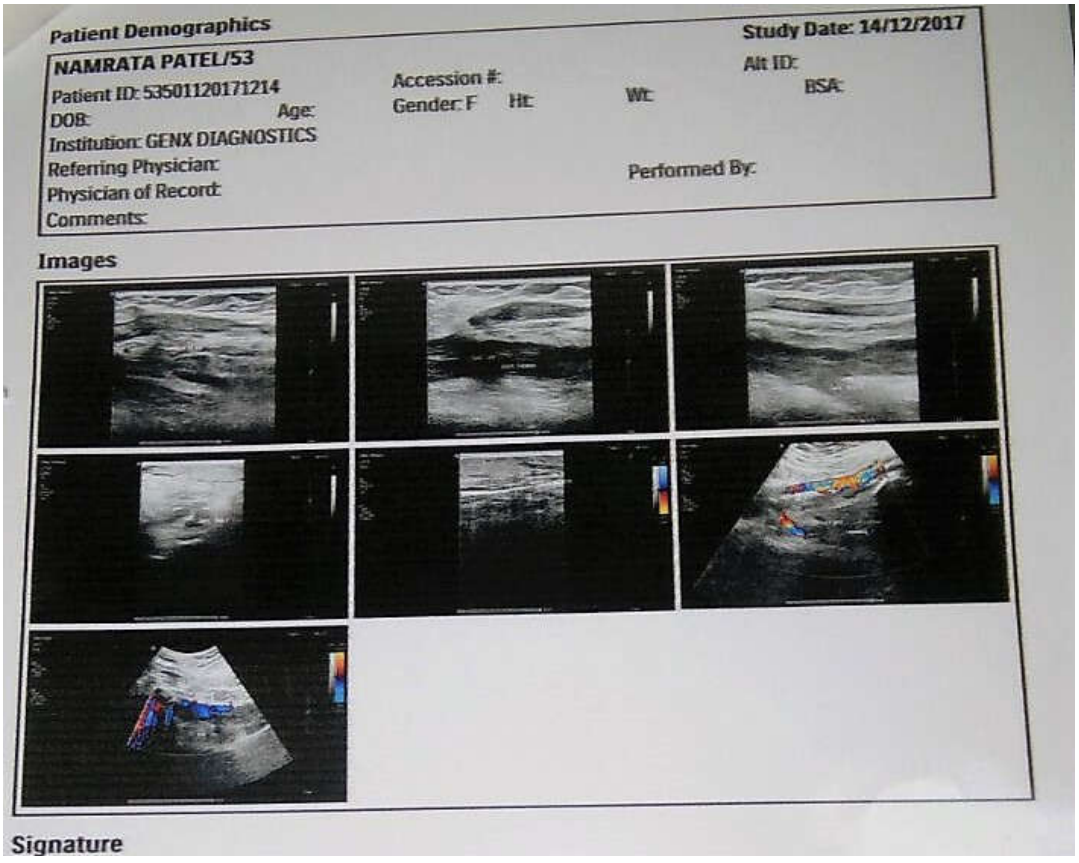

Figure 2. Usg doppler of lower limb

As the patient was on ATT, she was started on high dose of anticoagulants (Enoxaparin & Warfarin) in order to achieve therapeutic PT with INR value due to presence of Rifampicin, a strong enzyme inducer.

DISCUSSION

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.

One-third of patients with symptomatic VTE manifest pulmonary embolism (PE), whereas two-thirds manifest DVT alone. VTE recurs frequently in the first few months after the initial event, with a recurrence rate of 7% at 6 months. Overall, 25%–50% of patient with first-time Venous Thromboembolism have an idiopathic condition, without a readily identifiable risk factor. Death occurs in 6% of DVT cases and 12% of PE cases within 1 month of diagnosis (Prandoni, 1996 and Heit, 2002). Our case showed that VTE may complicate tuberculosis and such events can occur

anytime during the disease. Ambrosetti *et al*. (2006) reported an incidence of 0.6% (5 cases of DVT and two cases of pulmonary embolism) among 1237 TB patients from Italy. A study done by Bikdeli (Bikdeli, 2010) in 2010 mentioned the use of color Doppler, D-dimer, and computed tomography as the diagnostic modality for diagnosis of VTE. We have used USG Doppler for the diagnosis of DVT. Various mechanisms may be responsible for the development of venous thromboembolism in patients with TB. It may act through all the three parts of Virchow's triad, i.e. hypercoagulability, venous stasis and endothelial dysfunction. The haemostatic and inflammatory changes in TB can result in hypercoagulable state. Hypercoagulability in tuberculosis is attributed to decreased antithrombin lll and protein C, elevated plasma fibrinogen level, increased platelet aggregation and reactive thrombocytosis (Robson, 1996). Thrombosis occurs in patients with pulmonary TB occur in various sites. These sites include hepatic veins (Gogna *et al*., 2004), the portal vein (Ozşeker *et al*., 2012), the inferior vena cava (Raj, 2006), cerebral venous sinuses (Júnior, 2005; Sundaram, 2007), and the central retinal vein (Fullerton *et al*., 2007). 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 (Monero, 1989). Thrombosis can also result from venous compression by lymph nodes, as retroperitoneal adenopathies may cause inferior vena cava thrombosis in the absence of any haemostatic abnormalities (Gogna, 2004). Studies have mentioned the high incidence of antiphospholipid antibodies detected in tuberculosis, and the possible relationship between these and protein S. Various studieshave indicated that prothrombin deficiency occurs in approximately one third of TB patients (World Health Organization, 2014; Mark *et al*., 2009; Monero, 1989). Cytokines activate the vascular intima and make thrombogenic endothelium. They will also lead to a stimulation of hepatic synthesis of coagulation proteins (Andus, 1991). These risks of hypercoagulability is directly proportional to the immobility and prolonged bedrest because of the morbidity caused by the disease. Turken *et al*. (2002) also made similar observations regarding these hemostatic disturbances in 45 patients of active TB. It has stated that haemostatic disturbances improved within 4 weeks of commencing ATT.

White *et al*. (1989) reported that there is a possible association between DVT and the use of rifampicin with a relative risk of 4.74 in patients treated with rifampicin-containing regimens. Patients of pulmonary TB having extensive disease are not ambulatory for a long duration, which is one of the risk factors of developing VTE. Studies have shown that the risk of developing deep venous thrombosis is proportional to the severity of tubercular disease as there is a close correlation between the hematological abnormalities and the severity of clinical findings of pulmonary TB. The studies have revealed that hematological abnormalities are relatively more common in severe pulmonary TB (Suárez Ortega, 1993; Bozóky, 1997). These hemostatic changes improve during the first month of TB treatment 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 rifampcin effects on cytochrome P450 (Self, 1975). The newer Xa inhibitors offer several advantages over traditional therapy with parenteral anticoagulant such as faster onset of action, the lack of need for a heparin lead-in phase, and lesser bleeding events compared with standard therapy. Concomitant use with rifampicin leads to decrease in the plasma concentration of these drugs by 50%–54% (Cabral, 2015).

Conclusion

The relationship between inflammation induced by tuberculosis and a hypercoagulable state has been established. It is important to suspect venous thromboembolism to make an early diagnosis and initiate prompt treatment. It is difficult to achieve therapeutic INR level due to ATT drug interaction. Therefore, the patients should be closely followed up to prevent complications and mortality from pulmonary embolism.

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Consent: The authors declare that they have provided written informed consent from the described patient for the case report to be published.

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Abbreviations: DVT-Deep vein thrombosis, ADA-Adenosine deaminase, ATT-Antitubercular treatment.

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