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Splenic Vein Thrombosis as a Rare Complication of Disseminated Tuberculosis – Imaging Diagnosis and Case Report

Authors' Contribution:

- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
- G** Funds Collection

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Summary

Background:

Venous thromboembolism is a known but rare complication associated with *Mycobacterium tuberculosis* infection. The reported incidence of venous thromboembolism is 1.5–3.4% of infected patients, and it occurs due to a hypercoagulable state induced by the associated inflammation.

Case Report:

A young woman with pulmonary tuberculosis was found to have disseminated tuberculosis and a clinically unsuspected partial thrombus in the splenic vein on imaging. Ultrasound demonstrated hepato-splenomegaly with multiple granulomas as well as ascites and a left-sided pleural effusion. An increased calibre of the splenic vein with a hyperechogenicity within it raised the suspicion of a thrombus, which was confirmed on a contrast-enhanced CT examination. CECT of the abdomen also showed a small peripheral splenic infarct, while CECT of the chest revealed bilateral miliary lesions in the lungs along with necrotic mediastinal lymphadenopathy. The final imaging diagnosis was disseminated tuberculosis complicated by splenic vein thrombosis.

A timely institution of anti-coagulant and anti-tubercular treatment led to a complete resolution of the splenic vein thrombosis.

Conclusions:

Contrast-enhanced CT serves as a useful imaging tool for the detection of venous thrombosis and for the estimation of a complete burden of the disease. This condition should be kept in mind by both clinicians and radiologists and looked for in order to prevent life-threatening complications.

MeSH Keywords:

Splenic Vein • Tuberculosis • Venous Thrombosis

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Background

Venous thrombosis is a known but rare complication of pulmonary and extra-pulmonary tuberculosis, occurring in 1.5 to 3.4% of patients [1]. It can involve the cerebral, porto-splenic axis and leg veins or even cause pulmonary thrombo-embolism. Being aware of this entity is important and any clinical suspicion warrants imaging to rule out the presence of thrombosis to prevent life-threatening or serious complications. The role of CECT in imaging venous vessels to diagnose and define the extent of venous thrombosis is highlighted in this case report of a young woman with disseminated tuberculosis associated with splenic vein

thrombosis, which resolved after the institution of anticoagulants and anti-tubercular treatment.

Case Report

A 20-year-old woman presented to the medicine outpatient department with complaints of chronic cough with sputum of a two-month duration and with a history of significant weight loss of 6 kilogram over 6 months. She also had low grade fever of the same duration. Pain in the left hypochondrium was present for 15 days which was also accompanied by abdominal distension. There was a positive family history of pulmonary tuberculosis in the mother

who had been adequately treated 4 years earlier. On physical examination the patient appeared pale and her weight was below the 3rd percentile on the CDC growth chart [2]. A chest examination revealed dullness on percussion and decreased vocal fremitus over the infra-scapular region on both sides and lower lateral chest wall with a diminished air entry on the left side. The abdomen was tender on palpation in the left hypochondrium with mild splenomegaly. The routine blood investigations revealed anaemia, haemoglobin of 8.5 gm/dl (normal range 13–18 gm/dl). The total white blood cell (WBC) counts were within normal limits with a relative lymphocytosis (WBC-5800/mm³ with 52% neutrophils and 48% lymphocytes). The platelet count was 250×10^3 /micro-litre (150×10^3 to 450×10^3 per micro-litre of blood) and ESR was elevated to 86 mm in the first hour (normal range is 0–22 mm/hr for men and 0–29 mm/hr for women). The liver function tests were mildly elevated. The total bilirubin was 2 μ mol/L (normal level 0.2–0.8 μ mol/L) with indirect bilirubin of 1.2 μ mol/L and direct bilirubin of 0.8 μ mol/L. The serum aspartate amino transferase (AST) was 150 units/L and the alanine amino transferase (ALT) level was 84 units/litre (normal range of AST is 10–40 units/L and of ALT is 10–55units/L). Her chest radiograph demonstrated miliary opacities with a left pleural effusion. The sputum examination was positive for acid fast bacilli confirming pulmonary tuberculosis. The patient was started on anti-tubercular (ATT) treatment. The drugs that were given during the intensive phase of 2 months were isoniazid, rifampicin, ethambutol and pyrazinamide in a standard dose regimen, with a possible subsequent continuation of ATT depending on the patient's response.

An abdominal ultrasound (USG) was performed because of the abdominal complaints and it revealed hepato-splenomegaly with multiple small hypoechoic nodules that were scattered throughout the liver and spleen as well as a left-sided pleural effusion. Ascites was noticed in the Morison's pouch, pelvis and the inter-bowel region. The splenic vein had an increased calibre of 1.2cm with a vague hyperechogenicity within it, and demonstrated turbulent flow suggestive of splenic vein thrombosis. The portal vein

was normal in calibre (1.2 cm) and showed a monophasic hepatopetal flow.

CECT of the thorax and the abdomen was performed to assess the burden of the disease in the chest and also to evaluate the splenic vein. Eighty ml of 350 mg% Omnipaque was used to perform the CECT examination after a delay of 35 seconds, from the root of the neck down to the iliac crest. CECT revealed a left pleural effusion with miliary nodules scattered throughout both lungs along with necrotic mediastinal lymph nodes (Figure 1A, 1B)

CT confirmed hepato-splenomegaly with multiple non-enhancing hypodense lesions suggestive of granulomas, as shown in Figure 2. In addition, a 1×1 cm wedge-shaped area was seen with the base abutting the lateral border of the spleen, suggestive of a small infarct, as shown in Figure 3.

A partial linear filling defect was seen in the splenic vein which confirmed the presence of a partial thrombus, as shown in Figure 4A, 4B.



Figure 2. Multiple non-enhancing granulomatous lesions of varying sizes in the spleen, ascites and lesser omental nodes. Also seen are few sub-centimetre granulomatous lesions in the liver.

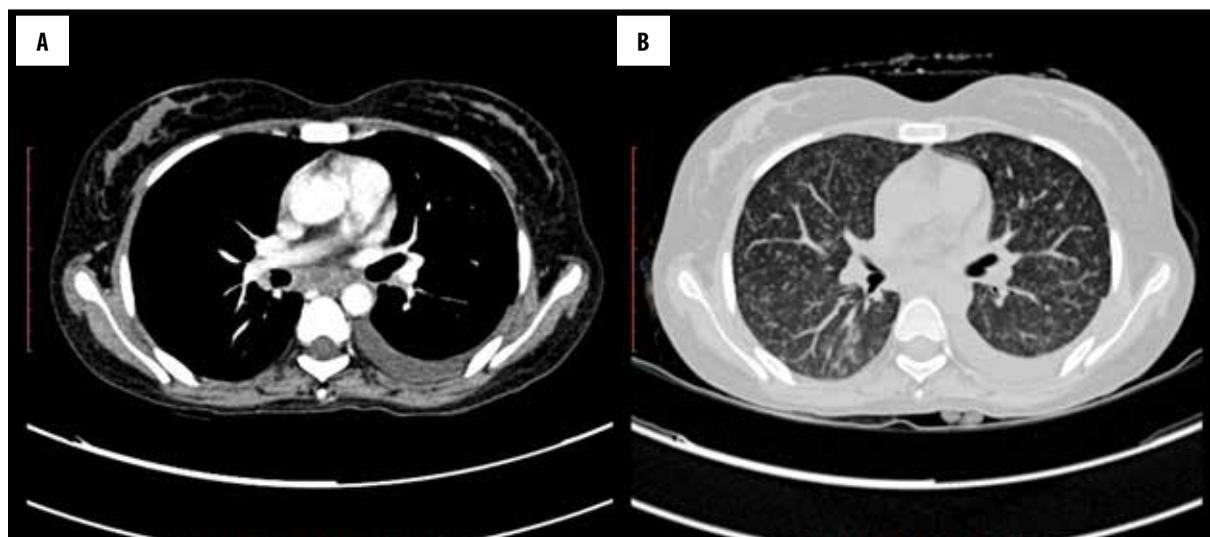


Figure 1. (A) Conglomerate necrotic mediastinal lymph nodes and a left pleural effusion. (B) Corresponding lung windows showing miliary nodules scattered throughout both lungs.



Figure 3. Coronal MPR image showing a small peripheral wedge-shaped hypodense lesion in the spleen suggestive of an infarct. Left pleural effusion and free fluid in the perihepatic space are also present.

There was no thrombus in the portal vein or in any of the porto-systemic collaterals. There were sub-centimetre lymph nodes in the omentum, porto-caval region and mesentery. The presence of partial splenic vein thrombosis warranted a work-up for a hypercoagulable state in the patient. The fibrinogen level was elevated to $17.64 \mu\text{mol/L}$ (normal $4.41\text{--}13.23 \mu\text{mol/L}$). Prothrombin time was prolonged to 20 seconds (normal range $11\text{--}13.5$ seconds), the INR was 1.7 (normal range is $0.8\text{--}1.1$ in people who are not on anticoagulant therapy). The levels of protein C, protein S, anti-phospholipid antibodies, anti-thrombin III, factor V Leiden mutation were all normal. Low Molecular Weight Heparin (LMWH) was instituted and the patient was kept under close ultrasound and Doppler follow-up. The thrombus was seen to resolve in 5 weeks.

Discussion

Tuberculosis, an infectious disease caused by mycobacteria, is highly prevalent across the globe, both in the developing and the developed world. A resurgence of the extra-pulmonary form of the disease and atypical manifestations of tuberculosis are encountered with an increased prevalence in HIV patients [3]. Venous thromboembolism can also, albeit rarely, complicate the disease process. It is a potentially life-threatening event and requires immediate medical attention. It is seen both with the localized forms of tuberculosis, such as pulmonary or abdominal tuberculosis, and with the disseminated form of the disease. This case report highlights the importance of imaging with CECT if a suspicion of thrombosis arises on clinical grounds or on preliminary imaging, as was seen on a routine abdominal ultrasound in our patient.

The pathogenesis of vascular complications in tuberculosis is multifactorial. Inflammation leads to haemostatic changes resulting in a hypercoagulable state [4,5]. The activated monocytes and macrophages release interleukins and cytokines which cause endothelial damage and, in turn, incite a thrombogenic response [6,7]. Other factors predisposing to venous thrombosis in TB are an increase in fibrinogen levels causing impaired fibrinolysis as well as a decrease in anti-thrombin III and reactive thrombocytosis [8]. There is evidence supporting an association between this prothrombotic state and the increased levels of antiphospholipid antibodies [9]. The increased fibrinogen levels were the only positive laboratory finding in our case that supported the supposition of a hypercoagulable state.

In some cases, enlarged lymph nodes in patients with tuberculosis may cause venous thrombosis merely by a compressive effect, which was not observed in our case. A ganglionic form of TB presenting with retroperitoneal adenitis can cause compression of the inferior vena cava, predisposing it to thrombosis due to the stasis of blood without any haemostatic abnormalities [10]. A cross-sectional imaging modality is required to monitor cases with large

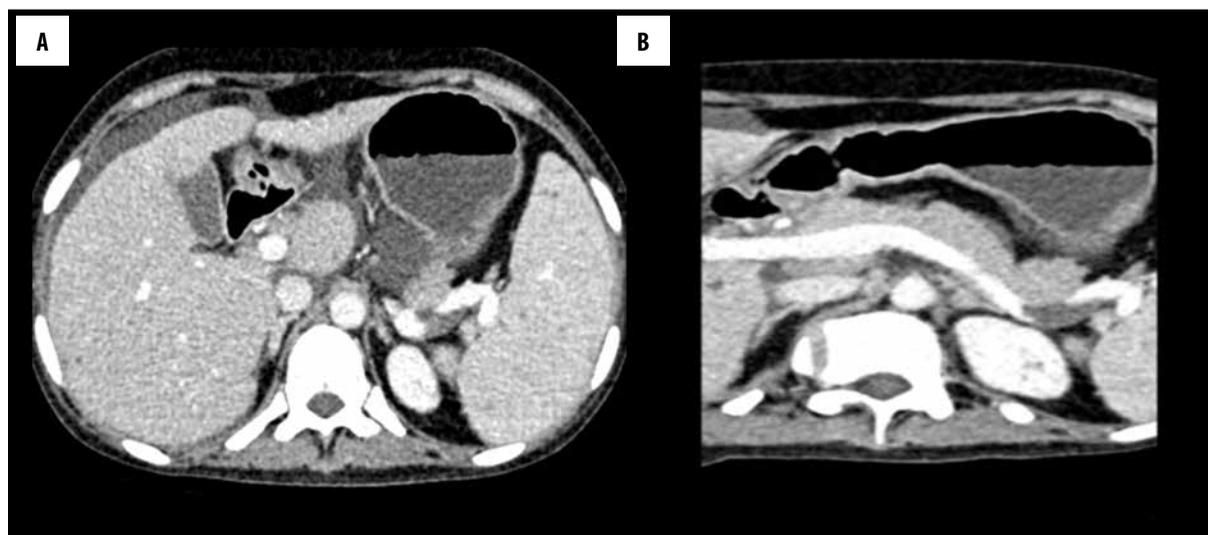


Figure 4. (A) MPR images showing a partial thrombus. Ascites and sub-centimetre granulomas in the spleen are seen as well. (B) Curved MPR images showing a linear hypodense filling defect in the location of the splenic vein thrombus.

lymphatic nodal masses found in close proximity of a major venous channel.

In our case, splenic vein thrombosis was diagnosed 10 days after starting ATT. after an abdominal ultrasound was performed because of abdominal symptoms. Venous thrombosis complicating systemic tuberculosis may be detected at the time of presentation or at a later stage. A study conducted by Robson et al., reports the largest number of patients with pulmonary tuberculosis complicated by venous thrombosis (n=35). Of those patients, two presented with deep venous thrombosis (DVT) initially, while in the majority of patients (33 patients) DVT occurred a week later after the diagnosis of tuberculosis [8].

It is advisable to begin treatment with ATT in addition to anticoagulant therapy, as the haemostatic changes are usually found to improve within the first month of ATT [11].

Splenic vein thrombosis, being a rare entity in tuberculosis, has not been studied in controlled therapeutic trials assessing the role of anti-coagulants. Thus, the therapeutic value of anticoagulants remains unknown in this condition [12]. There is no recommendation with respect to using anticoagulation in asymptomatic patients, unless there is a risk of mesenteric ischemia with an extension of the thrombus into the mesenteric vein [13]. An additional possible

benefit of anticoagulants is the reduction of the risk that the thrombus extends into the portal venous system, which can prevent the formation of porto-systemic collaterals.

In cases of splanchnic vein thrombosis, the anticoagulant drugs used are warfarin or LMWH as well as ATT for the associated tuberculosis. The enzyme-inducing effects of rifampicin on cytochrome P450 result in a higher dose requirement for warfarin to attain its therapeutic effect [14]. Rifampicin also has undesired effects on the anticoagulant hepatic proteins, which may result in a pro-coagulant milieu increasing the risk for development of DVT. Thus, during the initial phase of anti-tubercular treatment, the patient should be closely monitored clinically and/or by sonography and Doppler if a clinical suspicion arises. When necessary, CECT should also be performed to detect the presence of thrombus in the venous circulation.

Conclusions

In our patient, CECT served as a useful tool in detecting an early and life-threatening complication of splenic vein thrombosis that was suspected on abdominal ultrasound. Ultrasound and Doppler were crucial in the treatment phase and were used to monitor the thrombus until it showed complete resolution following LMWH and ATT administration.

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