When the blood clots unveil the infection: venous thromboembolism associated with tuberculous lymphadenitis

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ABSTRACT

Background: Infections are risk factors for venous thromboembolism (VTE) [1]. The role of chronic infections in VTE pathogenesis, such as tuberculosis (TB), is ill defined although several case reports and small series have suggested an association between TB and VTE [2].

Case presentation: We are presenting a case of a 31-year-old male presented with shortness of breath. Computed tomography showed massive pulmoanry embolism and inferior vena cava thrombus who was therefore thoroughly investigated for an underlying condition. He was found to have significant mediastinal lymph nodes which in turn biopsed. The tissue culture of lymph node grown Mycobacterium Tuberculosis. He was treated successfully with anti tuberculous medications.

Conclusion: Tubeculous lymphadenitis presented with multiple venous thromboembolism in a healthy fit and well young man. His only symptoms was shortness of breath. Improvement shown after starting antituberculous medications.

Keywords: Tuberculous lymphadenitis, pulmonary embolism, multiple venous thromboembolism.

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Background

Infections are risk factors for venous thromboembolism (VTE) [1]. The role of chronic infections in VTE pathogenesis, such as tuberculosis (TB), is ill defined although several case reports and small series have suggested an association between TB and VTE [2]. Deep venous thrombosis (DVT) has been associated with 1.5%-3.4% cases of TB [3]. Early initiation of anti-TB treatment along with anticoagulant therapy decreases the overall morbidity and mortality associated with the disease [3]. TB remains an infectious disease with a high prevalence worldwide and represents a major public health issue. Although VTE is not a common complication of this disease, it may be a potentially life-threatening event and correlates with the disease activity [4,5]. Rarely, VTE can be the only presenting feature of TB [5].

Case Presentation

A fit healthy Asian 31-year-old male presented to our hospital emergency department evening time with 2 days history of pleuritic chest pain and acute onset shortness of breath of few hours' duration. He lived in the UK for 3 years before presentation to the emergency department and used to smoke 10 cigarette per day for 12 years. He has no history of direct contact with TB cases, but he came from an area of high TB prevalence before he settled in the UK [6]. No history of weight loss, decreased appetite, or fever was elicited. There was no cough or hemoptysis. His immunization history included Bacillus Calmette–Guérin vaccine which was given at early childhood. He was afebrile and his observations showed a heart rate of 105 beats per minute, respiratory rate of 18, oxygen saturations of 96% on air and Blood pressure of 110/60 mmhg. His initial assessment included a chest X-ray (CXR), basic bloods tests, and D-dimers. His CXR did not reveal any explanation for his acute shortness of breath. electrocardiography was normal apart from sinus tachycardia. His wells score for PE was calculated as 4, his D-dimer levels were > 24,000 and the rest of his blood tests were unremarkable (Hb 108 gm/dl, normal white blood cells and platelet count, C-reactive protein was 25). A computerized tomography pulmonary angiogram (CTPA) was arranged and showed bilateral pulmonary embolism (PE) with subcarinal lymphadenopathy (Figure 1). The subcarinal lymph nodes which appeared in the first CT was thought to be reactive lymph nodes. Analgesia was given for the chest pain. Apixaban (oral anticoagulant) was started, and the patient was discharged home to follow up with the anticoagulation clinic.

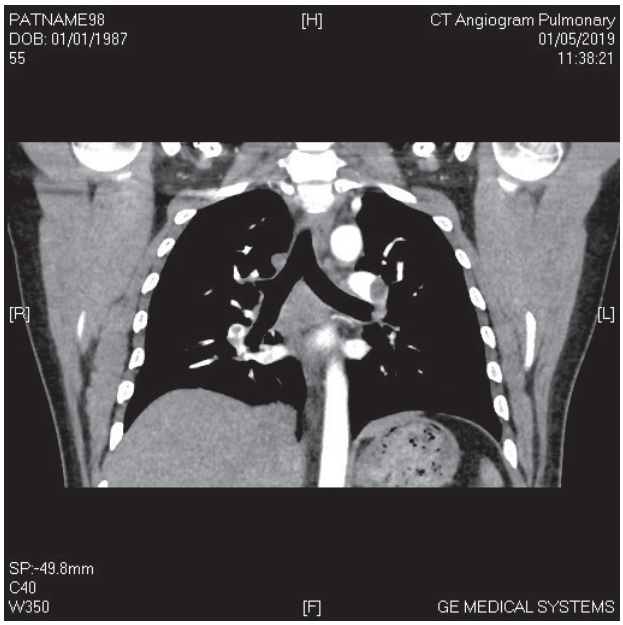

Figure 1. *Bilateral PEs (short arrows) and subcarinal lymphadenopathy (long arrow).*

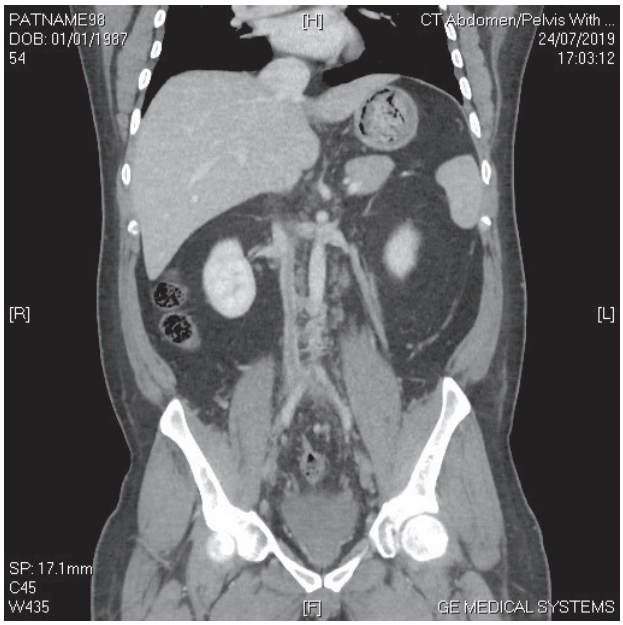

Fig ure 2. *Coronal section showing IVC thrombus, arrowed.*

He attended the anticoagulation clinic 2 months later for follow up, he looked unwell; short of breath, easily fatigued, and generally weak. The patient was subsequently referred to the Ambulatory Care Clinic (AECU) for further evaluation. He was investigated at AECU for a possible cause of VTE in young, actively mobile male. He had another CT scan (this time the CT included chest, abdomen, and pelvis) which showed increasing subcarinal nodal size as compared to the CTPA done earlier with newly enlarged interlobar nodes, numerous new bi-basal lung nodules, inferior vena cava (IVC) non occlusive thrombus and interval volume reduction in bilateral lung emboli (Figure 2).

Further investigations were carried out as below:

- Coagulation profile was within the normal range.
- Negative autoimmune screen.
- Human immune deficiency virus test was negative.
- Low Hb vitamin B12 and vitamin D levels which were done as part of investigations for increasing fatigability.
- Negative tumor markers including lactate dehydrogenase, carcinoembryonic antigen, CA19-9.
- Serum angiotensin converting enzyme was normal.
- Serum calcium was normal.

This case was discussed with the lung multidisciplinary team who agreed to proceed with lymph node biopsy. Elective day case admission done for bronchoscopy and lymph node biopsy:

- Biopsy showed Granulomas seen in (Rapid On-Site Evaluation in Detection of Granulomas).
- GeneXpert TB polymarase chain reaction (PCR) of the lymph node was positive.
- Culture lymph node grew *Mycobacterium* TB.

He responded well to standard quadruple therapy of which the TB was fully sensitive.

Investigations

Differential Diagnosis

Diagnosis of TB. was challenging as the patient's initial presentation mimicked a picture of malignancy (multiple VTE, disseminated lymphadenopathy). His main presentation was shortness of breath because of the bilateral pulmonary. He had no typical features of TB such as fever, cough, weight loss nor haemoptysis. Further tests revealed multiple lymphadenopathies and TB was confirmed by biopsy and culture. It is important to consider TB in any patient presenting with multiple lymph nodes enlargements and a history of living in high prevalence area.

Outcome and Follow-Up

Although there was interval volume reduction of the PEs with Apixaban the patient remained short of breath. His symptoms dramatically improved after commencing anti-TB drugs. CT chest repeated 12 weeks later showed significant reduction in the right hilar and subcarinal lymph nodes size.

Discussion

VTE is a rare complication of TB infection. The association between inflammation, hemostatic changes, and hypercoagulable state has been established in TB. Another mechanism of VTE is retroperitoneal adenopathy's in patients with TB causing compression of the IVC in the absence of any hemostatic abnormalities [7].

Hypercoagulability in TB is attributed to decreased antithrombin lll and protein C, elevated plasma fibrinogen level, increased platelet aggregation and reactive thrombocytosis. Apart from high frequency of antiphospholipid antibody levels in a patient with TB, deficiency of protein S has been mentioned [4].

Turken et al. [8] in a case control study demonstrated hemostatic disturbances in 45 patients with active pulmonary TB.

Robson et al. [9] found 35 patients with pulmonary TB with DVT but only two of them had DVT as the presenting feature similar to our case. Some reports indicate that thrombotic phenomena in patients with pulmonary TB can occur in other sites as well [9].

Our patient had no risk of thromboembolism apart from TB infection, we believe our patient had TB before he developed his VTE as he had an enlarged sub carinal lymph node on his CTPA when he was first diagnosed with his PE and DVT.

Conclusion

Infections can increase the risk of developing VTE. Here, we present a case of a young gentleman with PE, IVC thrombosis and right leg DVT associated with TB lymphadenitis. Although multiple case reports showed a link between active pulmonary TB and VTE, only a handful of cases reported the association of VTE with TB lymphadenitis. Investigations to look for a cause of his thromboembolism revealed his TB lymphadenitis.

What is new?

Infections can increase the risk of developing VTE. Here, we present a case of a young gentleman with PE, IVC thrombosis and right leg DVT associated with TB lymphadenitis. Although multiple case reports showed a link between active pulmonary TB and VTE, only a handful of cases reported the association of VTE with TB lymphadenitis. Investigations to look for a cause of his thrombo-embolism revealed his TB lymphadenitis.

Learning Points/Take Home Messages 3-5 Bullet Points

- It is important to consider TB in any patient presenting with multiple L.Ns enlargements and a high risk ethnic background.
- This case highlights the unusual presentation of TB in the form of multiple VTE in an actively mobile young man.
- This case confirms the importance of PCR-based techniques and tissue culture in TB diagnosis especially when the presentation is not straight forward.

List of Abbreviations

ACE	Angiotensin converting enzyme
AECU	Ambulatory Emergency Care Unit
AMU	Acute medical unit
CA 19-9	Cancer Antigen 19-9
CEA	Carcinoembryonic antigen
CRP	C-reactive protein
ECG	Electrocardiography
LDH	Lactate dehydrogenase
PCR	Polymarase chain reaction
PE	Pulmonary embolism
WBC	White blood cells

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this case report.

Funding

None.

Ethical approval

Ethical approval is not required at our institution for publishing an anonymous case report.

Consent for publication

Written informed consent was taken from the patient.

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Summary of the case

1	**Patient (gender, age)**	31-year-old male
2	**Final diagnosis**	TB lymphadenitis
3	**Symptoms**	PE, right leg DVT and IVC thrombosis
4	**Medications**	Quadrable anti-TB first line medications
5	**Clinical procedure**	Bronchoscopic subcarinal lymphnode biopsy
6	**Specialty**	Infectious disease and respiratory medicine