International Journal of Advances in Medicine
Saini R et al. Int J Adv Med. 2019 Apr;6(2):542-546
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20191173

Case Report

Deep vein thrombosis in patient with pulmonary tuberculosis: a rare and interesting causative link?

Rohin Saini*, Arvind Mishra, Kamlesh Kumar Gupta, Monika Kallani

Department of Medicine, King George Medical University, Lucknow, Uttar Pradesh, India

Received: 13 January 2019
Accepted: 01 March 2019

***Correspondence:**
Dr. Rohin Saini,
E-mail: rohinsaini92@gmail.com

ABSTRACT

Pulmonary tuberculosis is a devastating disease affecting millions of people in developing countries such as India. Many complications of this disease are known, however only few of its hematological complications have been reported. Discovery of its unknown thrombogenic potential is one such disturbing new entity. Tuberculosis can induce a hypercoagulable state and can lead to thromboembolic complications and deep vein thrombosis. Here we report an interesting and rare case of 20-year-old male, newly diagnosed case of Pulmonary Tuberculosis presenting with complaints of acute onset right lower limb swelling and pain. He was diagnosed with thrombosis of external iliac vein. All possible causes for a provoked deep vein thrombosis were evaluated for and ruled out. The patient was started with first line anti tubercular treatment-rifampicin, isoniazid, pyrizinamide, ethambutol along with anti-thrombotics injection enoxaparin and warfarin and followed up for 6 months. He made complete recovery of both his pulmonary and limb disease.

Keywords: Deep vein thrombosis, Infectious disease, Pulmonary tuberculosis

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] 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.[2] 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.

CASE REPORT

A 20-year-old non smoker non alcoholic male was admitted to our department for evaluation of low grade fever with evening rise in temperature, cough with copious expectoration and hemoptysis since 1 month along with diffuse non radiating dull aching pain with swelling on right lower limb since 15 days. There was no history of diabetes, stroke or cancer in the family. On physical examination, he had tachypnea and tachycardia with mild pallor. He had diffuse crepitations and rhonchi in his chest (left>right) and used his accessory muscles of respiration and was in a state of respiratory distress. Cardiovascular, and abdominal examinations were within normal limits. Routine investigations and sputum examination was done. His sputum was positive for acid

fast bacilli and cultures of same were sent along with cartridge based nucleic acid amplification test. He underwent subsequent evaluation of his right lower limb complaints which was tense and tender with diffuse swelling from mid thigh to ankle. Homan test and Moses test were positive. Provisional diagnosis of deep vein thrombosis was kept. Color Doppler study of his right lower limb revealed deep vein thrombosis of external iliac vein. Patient was febrile (100 degree fahreinheit) There was no prior history of surgery, trauma or malignancy, prolonged bed rest, smoking, valvular heart disease or stroke. His investigations were sent, and they were as follows (Table 1).

Table 1: Investigations of the patient on admission and on discharge.

Investigation	On admission	On discharge
HB	8.6	10
TLC	18820	8040
DLC	N74L28	N70L28
MCV	98	94
MCH	24	26
PLT	3.8	2.48
RBS	112	
NA+	134	138
K+	3.48	4.2
Urea	78	64
Creatinine	1.11	0.82
Bil.total	1.28	1.16
Bil.direct	0.28	0.24
SGOT	28	26
SGPT	34	32
ALP	588	284
Protein	5.2	6.2
Albumin	2.4	2.8
HBsAG by ELISA	Non Reactive	
HCV by ELISA	Non Reactive	
HIV by ELISA	Non Reactive	
PT	16	32
INR	1.1	3.4
ESR	110	
CRP	92	
Serum fibrinogen	6.66	
D dimer	1750	
FDP	40	
LDH	537	
Protein C	Normal	
Protein S	Normal	
Homocysteine	4 Micromoles/litre	
Anti phospholipid antibody test-lupus anticoagulant, beta 2 microglobulin anti cardiolipin antibodies	Negative	
C3 C4	Normal	
Antithrombin III levels	Negative	
ANCA	Negative	
Cells forCD55 and CD59 markers	Present	
Sputum for AFB	Positive	Positive
Tuberculin TEST/PPD	Positive	

Course and treatment

The overall clinical picture and radiological findings were suggestive of pulmonary tuberculosis. He was registered under DOTS as newly diagnosed sputum positive pulmonary tuberculosis and started on four drug anti tubercular treatment {rifampicin (600mg/d), isoniazid (300mg/d), pyrazinamide (1000mg/d),

ethambutol (800mg/d)}. He was also treated with low-molecular-weight heparin (injection enoxaparin 60mg bid subcutaneous) for 3 days and was started on Tab. warfarin 3mg once a day with a target International Normalized Ratio (INR) of 2.0-3.0. He was initially maintained on nasal prong with 5L/hr oxygen and was slowly weaned off the same.

There was resolution of cough along with edema of the limbs and was discharged on same medications. He was followed up for 6 months. His sputum was negative for acid fast bacilli after 1 month and CBNAAT was negative. Cultures showed growth of *M. tuberculosis* sensitive to rifampicin and isoniazid. The patient made complete recovery of both his pulmonary and limb disease.

Chest X-ray showed bilateral ill-defined patchy shadowing right upper middle zone and non homogenous opacity at left middle lower zone with fibrosis (Figure 1). Arterial blood gas analysis showed: pH 7.47, pO2 84.9mmHg, pCO2 34.6mmHg, HCO3 25.7mmol/L and oxygen saturation 97.1.

Contrast Enhanced Chest Computerized Tomography showed multiple nodular infiltrates in bilateral lung fields with tree in bud appearance. Patchy consolidation is noted in whole of left lung with cavitatory changes and cystic bronchiectasis in left upper lobe and apical segment of left lower lobe along with consolidation of right middle lobe (Figure 2).

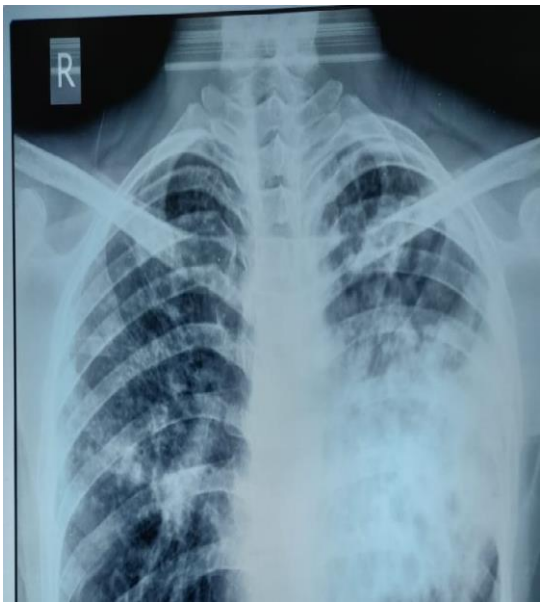

Figure 1: Chest x-ray of the patient with left middle and lower zone consolidation.

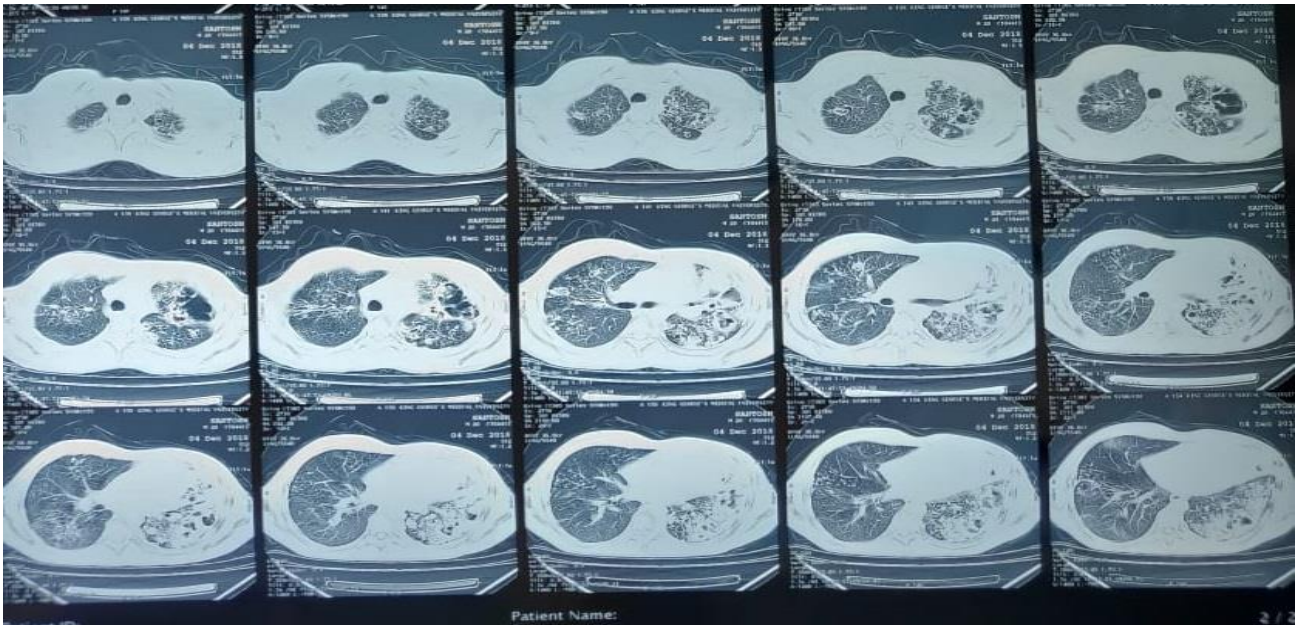

Figure 2: CECT thorax of the patient showing left sided patchy consolidation and bronchiectatic changes secondary to tuberculosis.

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. 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.[6]

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.[7] 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.[8] 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. 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.[7] The interaction between these activated mononuclear cells causes increase synthesis of TNF-alpha, Interleukins and proinflammatory cytokines, which can activate 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.
- 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.[13] 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.

CONCLUSION

This clinical report emphasize that patients with severe pulmonary tuberculosis are at risk of developing thromboembolic events and deep vein thrombosis maybe one of the many atypical manifestations of pulmonary tuberculosis and the possibility of tuberculosis should be considered in those who present with unprovoked deep vein thrombosis of lower limbs.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Brennan PJ. Structure, function, and biogenesis of the cell wall of Mycobacterium tuberculosis. Tuberculosis. 2003 Feb 1;83(1-3):91-7.
2. Zumla A, George A, Sharma V, Herbert RH, Oxley A, Oliver M. The WHO 2014 global tuberculosis report-further to go. The Lancet Global Health. 2015 Jan 1;3(1):e10-2.
3. Kim HY, Song KS, Goo JM, Lee JS, Lee KS, Lim TH. Thoracic sequelae and complications of tuberculosis. Radiographics. 2001 Jul;21(4):839-58.
4. Wang JY, Hsueh PR, Lee LN, Liaw YS, Shau WY, Yang PC, et al. Mycobacterium tuberculosis inducing disseminated intravascular coagulation. Thrombosis and haemostasis. 2005 Apr;93(04):729-34.
5. Keeling AN, Costello R, Lee MJ. Rasmussen's aneurysm: a forgotten entity?. Cardiovas Inter Radiol. 2008 Jan 1;31(1):196-200.
6. Cervera R, Asherson RA, Acevedo ML, Gómez-Puerta JA, Espinosa G, De La Red G, et al. Antiphospholipid syndrome associated with infections: clinical and microbiological characteristics of 100 patients. Annals Rheumatic Dis. 2004 Oct 1;63(10):1312-7.
7. Brotman DJ, Deitcher SR, Lip GY, Matzdorff AC. Virchow's triad revisited. Southern Medical J. 2004 Feb 1;97(2):213-5.
8. Horowitz N, Brenner B. Thrombophilia and cancer. Pathophysiology of haemostasis and thrombosis. 2007;36(3-4):131-6.
9. Turken O, Kunter E, Sezer M, Solmazgul E, Cerrahoglu K, Bozkanat E, et al. Hemostatic

changes in active pulmonary tuberculosis. Int J Tuber Lung Dis. 2002 Oct 1;6(10):927-32.
10. Lang IM, Mackman N, Kriett JM, Moser KM, Schleef RR. Prothrombotic activation of pulmonary arterial endothelial cells in a patient with tuberculosis. Human Pathol. 1996 Apr 1;27(4):423-7.
11. Robson SC, White NW, Aronson I, Woollgar R, Goodman H, Jacobs P. Acute-phase response and the hypercoagulable state in pulmonary tuberculosis. British J Haematol. 1996 Jun;93(4):943-9.
12. Suárez SO, Artiles JV, Balda IA, Melado PS, Arkuch MS, Ayala EG, Betancor PL. Tuberculosis as risk factor for venous thrombosis. InAnales de medicina interna (Madrid, Spain: 1984). 1993;10(8):398-400.
13. Naithani R, Agrawal N, Choudhary VP. Deep venous thrombosis associated with tuberculosis. Blood coagulation and fibrinolysis. 2007;18(4):377-80.

Cite this article as: Saini R, Mishra A, Gupta KK, Kallani M. Deep vein thrombosis in patient with pulmonary tuberculosis: a rare and interesting causative link?. Int J Adv Med 2019;6:542-6.