

Tuberculosis and Acute Deep Vein Thrombosis in a Paediatric Case

JAYESH SANGANI¹, SATARUPA MUKHERJEE², SOUMYADEEP BISWAS³, TARUN CHAUDHURI⁴, GAUTAM GHOSH⁵

ABSTRACT

Deep vein thrombosis (DVT) may be associated with tuberculosis infection. DVT in tuberculosis (TB) is implicated to the release of inflammatory cytokines, decrease synthesis of anti-coagulant proteins and increased fibrinogen levels. Drugs may also predispose to the hyper-coagulability. DVT may correlate with the severity of mycobacterium infection. We report a case of DVT in an 11-year-old child with sputum positive pulmonary tuberculosis. The patient was put on low molecular weight heparin after Doppler documentation of thrombosis of left femoral vein. She was then put on oral warfarin with complete resolution of the thrombosis. A clinician should be aware of this rare but dangerous association of tuberculosis and must not delay in early diagnosis and intervention.

Keywords: Hyper-coagulability, Pulmonary tuberculosis

CASE REPORT

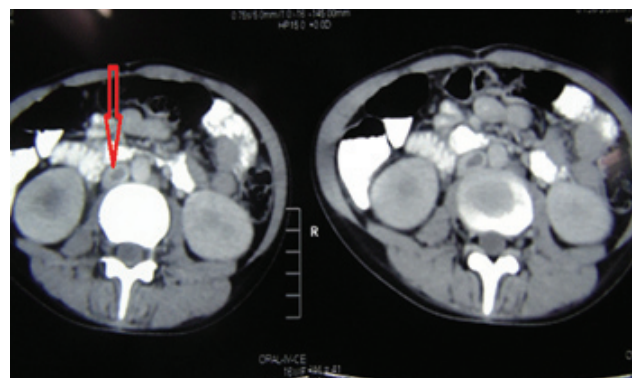
An 11-year-old girl got admitted at BR Singh Hospital, Kolkata with swelling of the left leg for last seven days and difficulty in walking with restricted flexion at the hip, knee for last three days [Table/Fig-1]. The swelling was insidious in onset over five days, starting from the foot rising up to involve the entire left leg up to the groin. It was painful without any colour changes of the overlying skin. On examination there was tenderness throughout the left leg with restriction of flexion at hip and knee joints. The oedema was pitting in nature. There was no history of any trauma, prolong immobilization. She was recently diagnosed as case of sputum positive pulmonary tuberculosis and was started on anti-tubercular drugs since last 10 days [Table/Fig-2]. The drugs were isoniazid, rifampicin, ethambutol and pyrazinamide. There was no significant past history nor any similar illness in the past. Her weight was below the third percentile of WHO growth chart. X-ray left leg and hip did not show any abnormality. USG with Doppler showed thrombosis of the left femoral vein with extension to the infra-renal



[Table/Fig-1]: Showing swollen left leg in comparison to the right leg due to deep vein thrombosis



[Table/Fig-2]: X-ray chest showing diffuse right lung infiltrates due to pulmonary tuberculosis



[Table/Fig-3]: Scan of the abdomen showed filling defect in IVC (arrow head) from infra renal part extending to left common iliac, external iliac & left femoral vein, all suggestive of acute thrombosis

part of the IVC. CT scan of the abdomen [Table/Fig-3] also showed the presence deep vein thrombosis (DVT) and significant retro-peritoneal lymph nodes. Routine of blood tests showed normocytic, normochromic anemia with raised ESR (60 mm in 1st hr). D-dimer assay was positive (10 µg/ml; ref <0.5 µg/ml). Fibrinogen level was elevated (677). Levels of protein C, protein S, anti-phospholipid antibody, anti-thrombin III, Factor V Leiden mutation all came out to be normal. Patient was started on low-molecular weight heparin (LMWH) subcutaneous injections. After 5 days of treatment the swelling gradually started decreasing with decreasing pain and tenderness. A repeat USG Doppler showed fragments of thrombus with established distal blood flow. Low molecular weight heparin continued along with ATD. After one month warfarin was started at 0.2mg/kg/day orally with a short period of overlap with LMWH till the INR was maintained between 2 to 3. Warfarin doses required further escalation till the desired INR could be maintained due to the effect of rifampicin on its metabolism. Patient was followed up at the OPD. The ATD continued for six months. Fibrinogen, protein C, protein S, anti-thrombin levels were repeated at the end of six months which showed normal results. Warfarin was stopped at six months and at present the patient is under regular follow-up for the last one year.

DISCUSSION

Vascular complications in TB, as DVT have been reported several times in literature. Our case presented with thrombosis of inferior vena cava (IVC) and femoral vein. Kouismi H et al., reported 30 cases of pulmonary TB with DVT after a retrospective study from 2010 to 2013 [1]. Venous thromboses not only of extremity veins

but involving other veins have also been reported. Gogna et al., reported a case of hepatic vein thrombosis in TB [2]. Ozseker B et al., reported a case of abdominal TB and portal vein thrombosis in a 43-year-old male [3]. Sundaram et al., reported superior sagittal vein thrombosis following calvarial tuberculosis [4]. Central retinal vein obstruction may also be a presenting feature in pulmonary tuberculosis [5]. Vascular complications may even progress to the extent of pulmonary thromboembolism [6], though we did not have it in our case. Ekuwe NC et al., reported a case of bilateral proximal pulmonary artery emboli and tubercular cavitation in the lung of a 52-year-old man presenting with dyspnea [7]. Thromboembolism may be a cause behind sudden cardiac death in patients with Pulmonary TB. Robson et al., found 35 patients with pulmonary TB and DVT. In 33 of them, DVT occurred seven days after the diagnosis of TB, while only in two, DVT was the presenting feature [8]. The mean duration between TB diagnosis and DVT was around 10 days in our case. Vascular complications often correlate with the severity of tuberculosis [9]. Our patient had diffuse right lung infiltrates with cavitations signifying a severe tubercular infection.

The pathogenesis of vascular complications in tuberculosis is multifactorial. Activation of monocytes, macrophages there by release of interleukins and cytokines causing endothelial injury have been implicated. Increase in fibrinogen, impaired fibrinolysis, decrease in antithrombin III and reactive thrombocytosis can predispose to venous thrombosis in TB [8].

Venous thrombosis can also occur due to venous compression by enlarged lymph nodes in tuberculosis [10]. Here, thrombosis can occur without any haemostatic abnormalities. There may also be a relationship between tuberculosis and antiphospholipid antibodies and protein S deficiency behind the aetiopathogenesis of DVT [9]. Studies also demonstrated a possible association between DVT and the use of rifampicin with a relative risk of 4.74 in patients treated with rifampicin containing regimens [11]. This did not contraindicate the use of this drug in patients at risk, but such patients should be supervised. Our patient demonstrated a raised fibrinogen level which might have been the cause behind the hypercoagulable state.

DVT in tuberculosis in children have been rarely reported. Casanova et al., reported a case in a child due to transient protein S deficiency and elevated anti-phospholipid antibodies [12].

CONCLUSION

DVT is thus not a rare association with pulmonary tuberculosis. Even children can have this complication, often correlating with the severity of the infection. Clinicians should remain aware of this rare condition and should have a high index of suspicion when a patient presents with an acute, painful, swollen limb.

REFERENCES

- [1] Kouismi H, Laine M, Bourkadi JE, Iraqi G. Association of deep vein thrombosis with pulmonary tuberculosis. *Egyptian Journal of chest Diseases and Tuberculosis*. 2013;62(3):541-43.
- [2] Gogna A, Grover S, Arun A, Saluja S. Isolated hepatic inferior vena cava thrombosis in a case of tuberculosis. *JACM*. 2004;5(3):266-68.
- [3] Ozseker B, Ozseker HS, Kav T, Shorbagi A, Karakoc D, Bayraktar Y. Abdominal tuberculosis leading to portal vein thrombosis, mimicking peritoneal carcinomatosis and liver cirrhosis. *Acta Clin Belg*. 2012;67(2):137-79.
- [4] Sundaram PK, Sayed F. Superior sagittal sinus thrombosis caused by calvarial tuberculosis. *Neurosurgery*. 2007;60(4): E776, discussion E776.
- [5] Fullerton DG, Shrivastava A, Munavvar M, Jain S, Howells J, MacDowall P. Pulmonary tuberculosis presenting with central retinal vein occlusion. *The British Journal of Ophthalmology*. 2007;91(12):1714-15.
- [6] Goncalves IM, Alves DC, Carvalho A, do Ceu Brito M, Calvario F, Duarte R. Tuberculosis and Venous Thromboembolism: a case series. *Cases Journal*. 2009;2:9333.
- [7] Ekuwe NC, Bain LE, Jingi AM, Sylvia K, Minton P, Menanga A. Bilateral pulmonary embolism in a patient with pulmonary tuberculosis: a rare association in Yaoundé, Cameroon. *The Pan African Medical Journal*. 2014;17:262.
- [8] Robson SC, White NW, Aronson I, Woolgar R, Goodman H, Jacobs P. Acute-phase response and the hypercoagulable state in pulmonary tuberculosis. *Br J Haematol*. 1996; 93:943-49.
- [9] Ortega S, Vizcaino A, Aguirre IB, Sanchez PM, Saade MEA, Galan EA, et al. Tuberculosis as risk factor for venous thrombosis. *An Med Interna*. 1993;10(8):398-400.
- [10] Gogna A, Pradhan GR, Sinha RS, Gupta B. Tuberculosis presenting as deep venous thrombosis. *Postgrad Med J*. 1999;75:104-05.
- [11] White NW. Venous thrombosis and rifampicin. *Lancet*. 1989;2:1397.
- [12] Casanova-Roman M, Rios J, Sanchez-Porto A, Casanova-Bellido M. Deep venous thrombosis associated with pulmonary tuberculosis and transient protein S deficiency. *Scand J Infect Dis*. 2002;34(5):393-94.

PARTICULARS OF CONTRIBUTORS:

1. Junior Resident, Department of Pediatrics, B.R.Singh Hospital & Centre for Medical Education and Research, Kolkata, India.
2. Senior Resident, Department of Pediatrics, B.R.Singh Hospital & Centre for Medical Education and Research, Kolkata, India.
3. Senior Resident, Department of Pediatrics, B.R.Singh Hospital & Centre for Medical Education and Research, Kolkata, India.
4. Chief Specialist II, Department of Pediatrics, B.R.Singh Hospital & Centre for Medical Education and Research, Kolkata, India.
5. Consultant Pediatrician, Department of Pediatrics, B.R.Singh Hospital & Centre for Medical Education and Research, Kolkata, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Satarupa Mukherjee,
Senior Resident, Department of Pediatrics, B.R.Singh Hospital & Centre for Medical Education and Research, Kolkata-700014, India.
Email: satarupamukherjee2003@gmail.com

Date of Submission: **Oct 26, 2014**

Date of Peer Review: **Jan 30, 2015**

Date of Acceptance: **Apr 28, 2015**

Date of Publishing: **Jun 01, 2015**

FINANCIAL OR OTHER COMPETING INTERESTS: None.