A RARE CASE OF PULMONARY TUBERCULOSIS PREDISPOSING TO CEREBRAL VENOUS THROMBOSIS

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HOW TO CITE THIS ARTICLE: Thomas M, Vijay N, Maliekal A. A rare case of pulmonary tuberculosis predisposing to cerebral venous thrombosis. J. Evid. Based Med. Healthc. 2019; 6(25), 1764-1766. DOI: 10.18410/jebmh/2019/359

PRESENTATION OF CASE

A 26-year old female, nurse by profession, with no significant past medical history and family history, was diagnosed with sputum positive pulmonary tuberculosis at an outside hospital following complaints of fever, cough, and night sweats. She was started on anti-tuberculosis treatment (rifampicin, isoniazid, ethambutol and pyrazinamide), and was on treatment for 15 days at the time of presentation. She presented to our hospital with complaints of two days of altered sensorium, headache, nausea and vomiting. There was no history of photophobia, focal sensory or motor deficits. On the day of admission, she had two episodes of generalised-tonic-clonic seizures. On examination, the patient was drowsy and disoriented with a GCS (Glasgow Coma Score) of 12/15, temperature of 99°F, pulse rate of 84/min and blood pressure of 114/84 mmHg. Physical examination showed the presence of BCG vaccination scar on the left shoulder. There were no signs of meningeal irritation, no focal deficits and optic fundus examination was normal. Physical examination was otherwise unremarkable.

Investigations

The patient's haemoglobin was 9 g%, total leucocyte count (TLC) was 5200/mm^{3,} platelet count was 4.2 lakhs/mm^3, random blood sugar was 88 mg/dL, and erythrocyte sedimentation rate (ESR) was 80 mm at the end of 1 hour. Serum electrolytes, liver and renal function tests were within normal limits. Cerebrospinal fluid (CSF) study did not show any evidence of TB meningitis. CT brain revealed features suspicious of venous infarct and hence an MRI plus MR venogram (MRV) was done which confirmed the diagnosis of cerebral venous thrombosis (Figure 1 and 2). In view of the thrombosis, coagulation profile was assessed and it revealed a PT-INR of 1.2 and aPTT of 38 seconds. The patient's thrombophilia panel showed normal anti-thrombin III, protein C, protein S and factor V levels. Antinuclear antibodies (ANA) and homocysteine levels were normal and antiphospholipid antibodies were not detected.

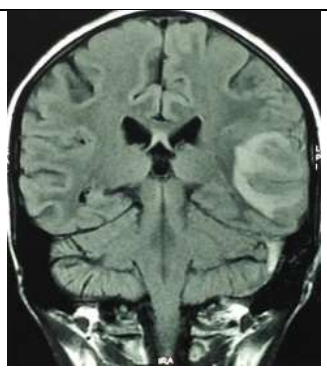

Figure 1. MRI Showing Evidence of Cerebral Infarct

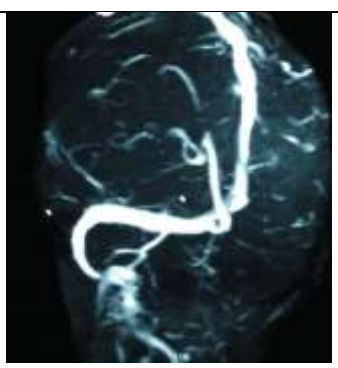

Figure 2. MRV Showing Evidence of Filling Defect Suggestive of CVT

CLINICAL DIAGNOSIS

Pulmonary tuberculosis predisposing to cerebral venous thrombosis.

DIFFERENTIAL DIAGNOSIS

- Tuberculous meningoencephalitis.
- Metabolic encephalopathy.
- Tuberculoma.
- Vasculitis.

DISCUSSION OF MANAGEMENT

The patient was started on anticoagulation with heparin 5000 U intravenously followed by warfarin 5 mg and her PT-INR was maintained at a target range of 2-3. Anti-tuberculosis treatment (ATT) was continued. Antiepileptic therapy was administered with intravenous phenytoin (loading dose of 15 mg/kg followed by 100 mg thrice daily). Intravenous mannitol (2 g/kg) was given to reduce the intracranial tension. Her general condition and sensorium improved over the next one week. There were no more episodes of seizures and her INR was maintained in the

Financial or Other, Competing Interest: None.
Submission 15-05-2019, Peer Review 20-05-2019,
Acceptance 17-06-2019, Published 24-06-2019.
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DOI: 10.18410/jebmh/2019/359

target range. Hence the patient was discharged on ATT, phenytoin and warfarin. Follow up visit at one month showed significant clinical improvement and imaging showed resolution of the infarct (Figure 3). Hence her warfarin was stopped at 3 months and ATT was continued for a total time frame of 6 months.

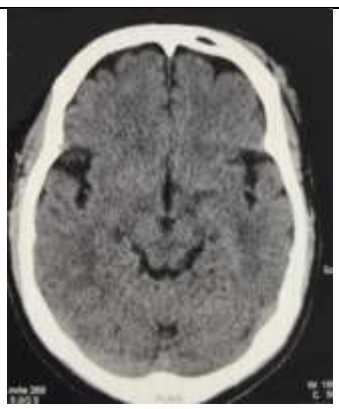

Figure 3. Follow-Up Imaging Showing Evidence of Resolution

PATHOLOGICAL DISCUSSION

Cerebral venous thrombosis (CVT) is a rare disease characterized by its clinical polymorphism and multiplicity of risk factors. The most important risk factors for CVT are prothrombotic conditions, oral contraceptives, pregnancy, puerperium, malignancy and infections.[1-3] Infections represent less than 10% of the etiologies and are usually caused by bacterial, fungal or parasitic infections.[4,5] There are reported cases of tuberculous meningitis and pulmonary TB predisposing to CVT and systemic thrombosis like DVT (deep venous thrombosis) respectively,[6] but a review of literature showed only few cases of CVT predisposed by pulmonary tuberculosis.

Tuberculosis infects about one third of the world's population per year and is a major cause of morbidity and mortality worldwide. As per the Global TB report 2017, the estimated incidence of TB in India was approximately 28,00,000 accounting for about a quarter of the world's TB cases.[7] Despite this high prevalence of TB in India, its association with CVT has been scarcely reported.[8]

It should be kept in mind that CVT can also present with altered sensorium and other neurological manifestations. The other important causes for altered mental status in TB are tuberculous meningoencephalitis, tuberculoma, hydrocephalus and metabolic encephalopathies like hyponatremia. The pathophysiological process involved in TB predisposing to thrombosis are (a) endothelial damage from inflammatory response, (b) increased platelet aggregation and release of procoagulant factors, and (c) altered venous blood flow.[4] Microglial cells infected with Mycobacterium tuberculosis release several inflammatory mediators, cytokines and chemokines like TNF-α, IL-6 and IL-1β[9] which leads to endothelial damage. TNF-α and IL-1β have an additive effect on pro-coagulation and play an important role in thrombosis.[10] The intracranial sinuses are low pressure system without valves which predisposes to venous stasis. TB also results in a hypercoagulable state from increased platelet aggregation.[6]

MRI plus MR venogram (MRV) is the investigation of choice to diagnose CVT.[1] An abnormal signal in a sinus along with a corresponding absence of flow or filling defect on MRV supports the diagnosis of CVT.[11] The signal intensity of the clot shows evolving changes due to the paramagnetic properties of haemoglobin and its secondary products. Acute thrombus (first 5 days) may be isointense on T1 weighted image (T1W1) and hypointense on T2-weighted image (T2W1), as it is rich in deoxyhaemoglobin. The clot may appear hyperintense on T1W1 and T2W1 images due to its high content of methaemoglobin between days 6 and 15 (subacute stage). After 15 days, thrombus becomes isointense on T1W1 and hyperintense in T2W1 images.[11-13] According to the EFNS guidelines, the recommended treatment of CVT is anticoagulation with low molecular weight heparin followed by oral warfarin for 3 months,[14] since TB is a transient reversible risk factor. Low molecular weight heparin is superior to unfractionated heparin in CVT, in terms of efficacy and safety.[15] Similar treatment protocol was followed in our patient and resolution of thrombosis was demonstrated in the follow-up imaging (Figure 3).

FINAL DIAGNOSIS AND CONCLUSION

Pulmonary tuberculosis induced cerebral venous thrombosis.

The presence of altered sensorium or other neurological signs in cases of tuberculosis (pulmonary/extrapulmonary) is not always due to encephalitis, hydrocephalus, metabolic encephalopathy, tuberculoma or ischemic stroke; the possibility of cerebral venous sinus thrombosis should also be kept in mind. This is important since, though pulmonary tuberculosis is a very rare cause of CVT, the prognosis is good if diagnosed and managed early.[2] Hence, a high index of suspicion is needed for early diagnosis and timely intervention.

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