DOI: 10.7860/JCDR/2022/52973.16852

Case Report

Internal Medicine Section

Disseminated Tuberculosis with Neurotuberculosis Presenting as Status Epilepticus: A Case Report

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ABSTRACT

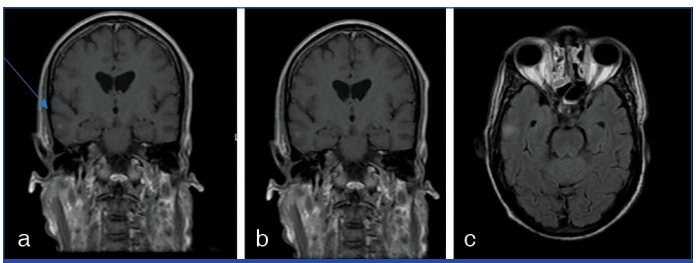
Disseminated Tuberculosis (TB) results when the infection spreads though lymphohaematogenous route involving multiple organ systems. Irrespective of the availability of diagnostic modalities and treatment, it is usually diagnosed late increasing the mortality. Though, it usually occurs in immunocompromised patients, yet, incidence of disseminated TB is rising in immunocompetent subjects. This case report describes a 48-year-old male who presented to the Emergency Department (ED) with status epilepticus. Investigations revealed neurotuberculosis along with generalised tubercular lymphadenopathy involving cervical, axillary, mediastinal and abdominal lymphnodes. Diagnosis was confirmed after Cerebrospinal Fluid (CSF) and lymphnode biopsy. He was started on first line antitubercular drugs and tapering dose of tab. Prednisolone over one month. He was discharged after two weeks of hospitalisation. At 15 days follow-up the patient was asymptomatic.

Keywords: Biopsy, Cerebrospinal fluid, Immunocompetent, Lymph node

CASE REPORT

A 48-year-old male presented to the ED with history of three episodes of generalised tonic clonic seizures since last four hours. He was received in the ED in postictal confusion. Glasgow coma scale was 9 (E-2,M-3,V-4). As per the history provided by the relatives the patient had fever for four weeks, which was intermittent in nature especially with high spikes at night associated with profuse sweating. He visited a local medical practitioner and was given some pills, details of which were not available. There was no history of cough, expectoration, haemoptysis, abdominal pain, diarrhoea, headache, vomiting. There was significant weight loss (approximately 7 kg) in one month.

On examination, axillary temperature was 100 F°. Pallor was present. Jugular venous pressure was normal. SpO_2, while breathing ambient air, was 96%. The CNS examination revealed the following- pupils were normal sized bilateral reacting to light, he was moving all four limbs, deep tendon reflexes were brisk and extensor planter response was present bilaterally. Coordination and sensory examination could not be performed. There was terminal neck stiffness present. An immediate blood sugar value was 180 mg%. Patient was admitted to the Intensive Care Unit (ICU), and given a loading dose of intravenous Phenytoin sodium, i.v. Lorazepam 2 mg. Computed Tomography (CT) scan, and Magnetic Resonance Imaging (MRI) brain revealed tiny peripherally-enhancing lesion in the right temporal lobe with perilesional oedema [Table/Fig-1].

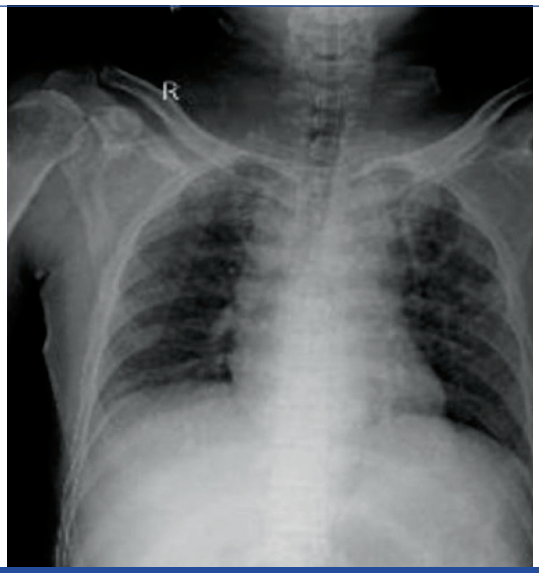


[Table/Fig-1]: MRI Brain Coronal view showing tiny peripherally enhancing lesion in right temporal lobe (blue arrow) appearing hyperdense with central area of hypointensity: a) on T1W1/FLAIR, iso-hypointense on T1W1; b) showing no restriction on D1W1 with no blooming on GRE; c) there is evidence of minimal surrounding perilesional oedema suggestive of tuberculoma.

Two hours after stabilisation, repeat clinical examination revealed multiple cervical and axillary lymphadenopathy. The cervical and axillary lymph nodes were discrete to matted, firm in consistency and non tender. Inj. Phenytoin 100 mg i.v. 8 hourly, empirically i.v. ceftriaxone 2 grams 12 hourly was initiated, while the patient was investigated further.

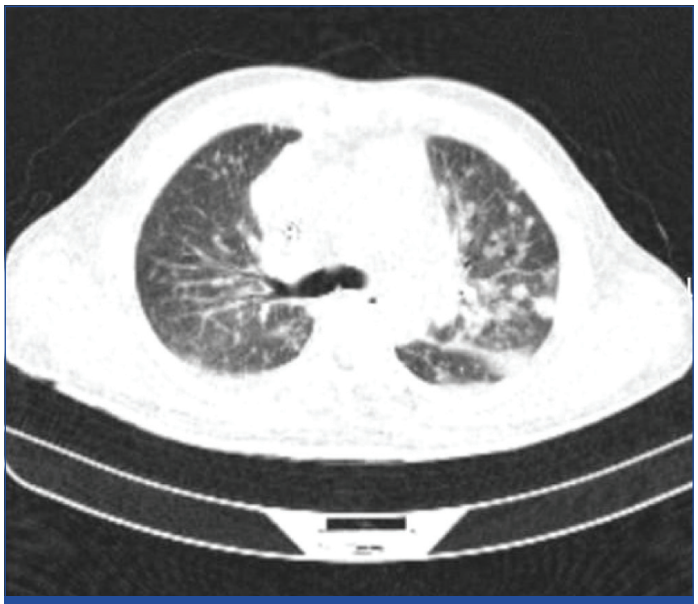
Further investigations revealed: Haemaglobin (Hb)-9 gm%, platelets-2.5 lacs/cumm, Total Leukocyte Count (TLC)- 3800 cells with 45% neutrophils and 50% lymphocytes. Kidney function test showed blood urea-28 mg/dL, serum creatinine-0.9 mg/dL, sodium-141 mEq/L, potassium-4.3 mEq/L. Liver function tests showed serum bilirubin of 2.1 mg% with 1.6 conjugated fraction, AST-98 U/L, ALT-136 U/L, Alkaline phosphatase-312 U/L. The Erythrocyte Sedimentation Rate was 110 mm in 1st hour. A lumbar puncture was performed and examination of CSF showed 18 cells (12 lymphocytes, 4 neutrophils and 2 monocytes), protein of 115 mg/dL and glucose of 44 mg/dL. A Nucleic Acid Amplification Test (NAAT) on CSF was positive for *M. tuberculosis.* Sputum AFB was negative.

Chest radiograph revealed mediastinal widening [Table/Fig-2], High-Resolution Computed Tomography (HRCT) thorax revealed nodular

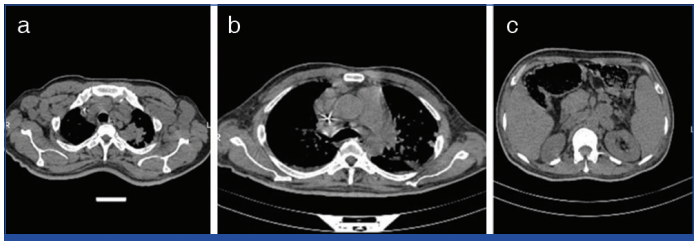


[Table/Fig-2]: Chest radiograph (PA) showing mediastinal widening.

infiltrates, ground glass opacities and patchy consolidation in bilateral lung fields. [Table/Fig-3], CT also revealed multiple enlarged matted lymphnodes in bilateral axilla, paratracheal and abdomen [Table/Fig-4].

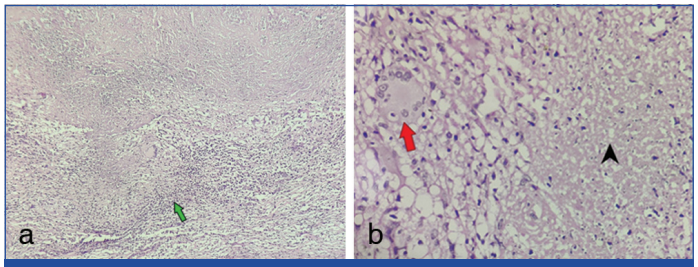


[Table/Fig-3]: HRCT thorax showing mulitiple centrilobtular nodules, ill-defined patchy areas of consolidation and ground glass opacities in bilateral lung fields.



[Table/Fig-4]: CT image showing bilateral axillary (a); thoracic (b) and matted abdominal lymph nodes (c).

A cervical lymph node biopsy confirmed TB lymphadenitis [Table/Fig-5]. A diagnosis of disseminated TB was made because of involvement of central nervous system, lymphatics and liver in view of altered liver enzymes. Patient was started with first line antitubercular therapy, (2EHRZ, 7HRE; E-tab. Ethambutol 800 mg OD, H-tablet Isoniazide 300 mgOD, R-capsule Rifampicin 450 mg OD, P-Pyrazinamide 750 mg BID) as initiation therapy for two months, and; HRE for next seven months as continuation phase along with Tab.prednisolone 40 mg OD for two weeks then tapered in next three weeks, and anti-epileptics (Tablet levetiracetam 500 mg BID). The patient did not have further episodes of seizure. Fever responded in the next four days and he was discharged after a week. At 15 days follow-up, the patient did not have any complaints and was asymptomatic.



[Table/Fig-5]: Section (a-100x magnification) and (b-400x magnification) stained with haematoxylin and eosin showing prominent areas of caseous necrosis, identified as amorphous, eosinophilic, granular debritic material. (black arrowhead in section b).

There are multiple, well organised granulomas formed by the epithelioid cells which are modified macrophages having abundant pale cytoplasm with an elongated slipper-shaped nuclei (green arrow in section [Table/Fig-5] a). These epithelioid cells appear to fuse, to form multinucleated giant cells with nuclei arranged in the cell periphery in a characteristic horse-shoe shaped pattern. (Langhans Giant Cells) (red arrow in section b). Section showing many surrounding lymphoid follicles. Histopathological features are suggestive of tubercular lymphadenitis.

DISCUSSION

Mycobacterium tuberculosis was first identified by a German physicist, Robert Koch in the eighteenth century hence also known as Koch's bacillus [1]. Irrespective of advances in medicine and development of first line and second line antitubercular drugs still TB kills more than estimated 1.7 million people each year. The global incidence of TB, according to a WHO report in 2010, was 8.8 million cases. In 2014, there were estimated 133 cases per 100,000 population that is equivalent to 9.6 million cases of TB globally [2]. It is estimated that less than 2% of all cases of TB in immunocompetent persons account for disseminated TB with military shadows on radiographs [3].

The basic risk factors for TB infection are poverty, overcrowding, malnutrition, chronic alcoholism and immunocompromised states like diabetes, chronic liver and kidney diseases, Human Immunodeficiency Virus (HIV) infection and immunosuppressive chemotherapeutic drugs including prolonged corticosteroid therapy [4]. Although the exact mechanism of dissemination of primary and postprimary TB is vaguely understood, one evident mechanism is once the primary focus present in the lungs breaks the pulmonary alveolocapillary barrier and enters the pulmonary veins the bacilli through the pulmonary veins are drained into the left-side of the heart and disseminate to the systemic circulation involving multiple organ systems. Miliary TB can be a manifestation of dissemination of bacilli through lymphohaematogenous spread via the right side of the heart [5-9].

Tuberculous meningitis is a catastrophic complication of disseminated TB. Clinical presentation may range from headache, vomiting to mental obtundation and seizures. Seizures occurring early in the clinical course of meningitis are usually due to raised intracranial tension and cerebral oedema. Late onset of seizures is due to secondary vasculitic infarction, obstructive hydrocephalus or metabolic cause like hyponatremia because of syndrome of inappropriate secretion of antidiuretic hormone. Tuberculoma of brain can also present as seizures. If not managed properly then recurrent seizures may progress to chronic epilepsy [10].

Rarely, seizures may be the first manifestation of disseminated TB. Esposito SB et al., described a case of an immunocompetent male who presented with severe headaches, examination revealed signs of meninges irritation. A diagnostic lumbar puncture suggested bacterial meningitis. But the CSF culture and PCR was negative for bacteria and virus. A chest radiograph (CXR) suggested TB. Further the tests confirmed disseminated TB in the brain, spinal cord, meninges, muscle, joint and bone. The patient responded to first line ATT [11].

Mbizvo GK et al., described a case of disseminated TB presenting with epilepsiapartialis continua and haemophagocytic syndrome. MRI brain revealed multiple ring enhancing lesions. The 54-year-old female responded to anti TB therapy and also received etoposide and dexamethasone based chemotherapy for haemophagocytic lymphohistiocytosis [12]. In a case described by Baudel JL et al., a 22-year-old male presented with prolonged seizures and paraplegia. MRI brain revealed tuberculomas in brain stem and spinal cord. Chest radiograph revealed miliary mottling. The CSF Ziehl-Nelson staining revealed *Mycobacterium tuberculosis* [13].

The dilemma in diagnosis of disseminated TB prevails because of lack of precise clinical presentations, localising signs, normal chest X-rays (cryptic TB), choroid tubercules in fundus, and a negative tuberculin skin test [14,15].

Irrespective of the immunologic status disseminated TB should be suspected in any patient who presents with prolonged fever, loss of weight, fatigue, night sweats, abnormal haematologic parameters (anaemia, pancytopenia), variable neurologic signs, hepatosplenomegaly, abnormal liver function tests, renal function tests. The paramount importance is to identify and target the organs involved and obtaining adequate samples for appropriate diagnosis [16]. In addition to the conventional gold standard sputum microscopy and culture, use of NAATs; especially Gene Xpert MTB/RIF assays are mandatory for it has got a sensitivity of 98-100% in patients with sputum positive cases and 57-83% in sputum negative cases [4]. Imaging modalities like CT scan thorax, abdomen, CSF studies, neuroimaging and when signs are present then biopsy specimens can give appropriate diagnosis of disseminated TB [17]. Biomarkers like adenosine deaminase and interferon gamma related assays in pleural fluid, ascites, and CSF has also been used for diagnosis of TB [18].

As far as evidence for management of disseminated TB is concerned, no data exists till date and whatever is available is on the treatment of pulmonary TB [19]. Evidence generated suggests that when antitubercular therapy is started early the outcome remains favourable though the optimum duration is not defined [20]. Apart from the conventional six months regimen, long duration therapy is usually indicated in cases with high disease burden, CNS TB, TB of bone and joints, immunosuppressive states. In susceptible cases of disseminated TB the conventional four drug regimen of rifampicin, isoniazide, ethambutol/streptomycin and pyrazinamide is given daily for two months as initiation therapy and isoniazide and rifampicin are then continued for four more months as continuation therapy. In some cases the continuation therapy may extended to 7 months. Many evidence suggest that the response of first line anti TB therapy is good [3,21].

CONCLUSION(S)

Tuberculous meningitis and tuberculoma are rare presentations of disseminated TB. Clinical features are usually vague in form of low-grade fever, malaise and headache that may persist for days to weeks. Altered mental status, focal neurodeficits, epilepsy are late manifestations. Along with the anti-TB therapy, adjuvant corticosteroids are given to reduce mortality. Data suggest that addition of steroids reduce the mortality by approximately 30%. The mortality rate of disseminated TB with tuberculous meningitis remains as high as 65% and nearly 50% of survivors residual neurodeficit remains.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Oct 26, 2021
- Manual Googling: Jan 20, 2022
- iThenticate Software: Sep 11, 2022 (6%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Oct 22, 2021**
Date of Peer Review: **Dec 11, 2021**
Date of Acceptance: **Jan 29, 2022**
Date of Publishing: **Oct 01, 2022**