CASE REPORT

Atypical Presentation of Tuberculous Meningitis—Challenges in Diagnosis: A Case Report

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Abstract

Tuberculous meningitis (TBM) is associated with severe mortality and morbidity. Current diagnostic modalities lack sensitivity or specificity, and culture inoculation may take up to 4–6 weeks. Atypical presentations of TBM may lead to delays in diagnosis and treatment and cause complications. We present a case of a 17-year-old male who presented with altered sensorium and was initially diagnosed as bacterial meningitis based on the cerebrospinal fluid (CSF) analysis and was treated for the same. The patient did not improve and later developed third cranial nerve (CN) palsy and obstructive hydrocephalus (HC) requiring ventriculoperitoneal (VP) shunting. Reevaluation revealed TBM and the patient was started on antituberculous therapy (ATT). He improved and had no lasting neurological deficits. A high degree of suspicion of tuberculous involvement should be maintained in all patients with meningitis, especially those who do not respond to standard treatment. Finally, we conclude through our case that early diagnosis and treatment can help prevent complications, and newer diagnostic modalities with better sensitivity are required to facilitate early diagnosis and prevent complications.

Keywords: Atypical presentation, Bacterial meningitis, Case report, Complications, Misdiagnosis, Sensitivity and specificity, Tuberculous meningitis.

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Introduction

Tuberculous meningitis (TBM) involves the meninges of the brain and is associated with significant morbidity and mortality. It is usually caused by hematogenous spread from either primary or secondary pulmonary tuberculosis (TB). In more than half of cases, a chest radiograph demonstrates signs of prior pulmonary lesions or a miliary pattern.[1] TM may lead to hydrocephalus (HC) caused by inflammatory exudates blocking the cerebrospinal fluid (CSF) analysis; granulomatous lesions that develop into tuberculomas, or abscesses which cause focal neurological deficits; and cerebrovascular accidents caused by occlusive vasculitis. As meningeal involvement is more at the base of the brain, cranial nerve (CN) palsies are common. CSF analysis is the cornerstone for the diagnosis of TBM. However, TBM has varied presentations leading to difficulty and delay in diagnosis and treatment.[1]

Case Description

A 17-year-old male, student, with no significant medical history presented with complaints of headache for 4 days and altered sensorium for 1 day. He had two episodes of nonbilious, nonprojectile vomiting prior to developing altered sensorium. There was no history of cough, fever, weight loss, or exposure to patient infected with TB. General examination revealed no abnormalities. Systemic examination revealed neck stiffness with positive meningeal signs (Kernig and Brudzinski). His Glasgow Coma Scale (GCS) on admission was 12 (E4V2M6). Extraocular movements were normal with bilateral pupils equal and reactive to light. Laboratory investigations (Table 1) revealed mild leukocytosis. Electrocardiography showed normal sinus rhythm. Arterial blood gas (ABG) analysis was within normal limits. Chest X-ray (PA view) and CT brain revealed no abnormalities.

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Cerebrospinal fluid (CSF) studies revealed elevated protein levels (324 mg/dL), raised TLC (120/mm^3 65% neutrophils), and low glucose levels (19 mg/dL with random plasma glucose 150 mg/dL), adenosine deaminase (ADA) levels were normal (5 U/L) and CSF for cartridge-based nucleic acid amplification test (CBNAAT) was negative.

A diagnosis of bacterial meningitis was made, and he was started on, injection ceftriaxone 2 gm BD intravenous (IV), injection vancomycin 1 gm TID IV, injection dexamethasone 16 mg IV single dose. Patient's GCS improved to 15/15 by day 3.

Repeat lumbar puncture (LP) on day 3 revealed decreasing protein levels (182 mg/dL) and leukocyte counts (100/mm^3 90% lymphocytes). ADA was normal (3 U/L) and CBNAAT was negative.

On day 5, patient complained of headache and nausea. Fundus examination was normal, but a repeat CSF was done and this

time CBNAAT came back positive. A high-resolution computed tomography (HRCT) thorax was done to look for pulmonary origin of tuberculous infection and it showed multiple centrilobular nodules with tree-in-bud appearance in superior segment and apical segment of right upper lobe which was suggestive of pulmonary TB (Fig. 1). Following the HRCT report, sputum specimens were sent for CBNAAT testing, revealing a positive result. This positive finding substantiates the diagnosis of pulmonary TB.

Patient was started on antituberculous therapy (ATT) [tablet rifampicin (R)—300 mg, isoniazid (H)—600 mg, ethambutol (E)—800 mg, and pyrazinamide (Z)—1500 mg once daily] and IV dexamethasone 8 mg TID.

Unfortunately, on day 8, patient complained of double vision and examination revealed bilateral ptosis with bilateral lateral rectus palsy. Patient's GCS dropped to 10 (E3V2M5) and he was shifted to the intensive care unit (ICU). Magnetic resonance imaging (MRI) brain with contrast was done which showed exudates with leptomeningeal enhancement in the sulcal spaces in the bilateral temporal and right parieto-occipital region and basal cisterns, with dilated lateral ventricle, third, and fourth ventricles suggestive of TBM with communicating HC (Fig. 2). He was taken for emergency ventriculoperitoneal (VP) shunting. Post procedure, noncontrast computed tomography (NCCT) brain (Fig. 3) showed the shunt in the right ventricle. Patient was monitored in the ICU for three more days during which his GCS slowly improved to 15 after which he was shifted to the ward and discharged on ATT. On 15 days of pot discharge, ptosis had partially resolved, and he was continued on ATT with liver function test (LFT) monitoring. Dexamethasone was tapered over 6 weeks and stopped. Patient was on regular follow-up for 1 year, after which ATT was stopped.

Table 1: Laboratory investigations at presentation

Investigation	*Value*
Hemoglobin	11.1 gm%
Total leukocyte count	11,900 (92% neutrophils)
Platelets	330,000/mm^3
Total bilirubin	1.1 mg/dL
Direct bilirubin	0.7 mg/dL
Aspartate transaminase	19 U/L
Alanine transaminase	20 U/L
Alkaline phosphatase	57 U/L
Urea	20 mg/dL
Creatinine	0.9 mg/dL
Serum sodium	140 mEq/L
Serum potassium	3.5 mEq/L
C-reactive protein	5
Serum lactate dehydrogenase	200 U/L
Erythrocyte sedimentation rate	57
ABG on room air	7.43
pH	90
PO_2	38
PCO_2	18.6
HCO_3	20
Urine routine microscopy	Normal
Proteins	Nil
Red blood cells (RBCs), Pus cells	Nil
Dengue profile	Negative

Discussion

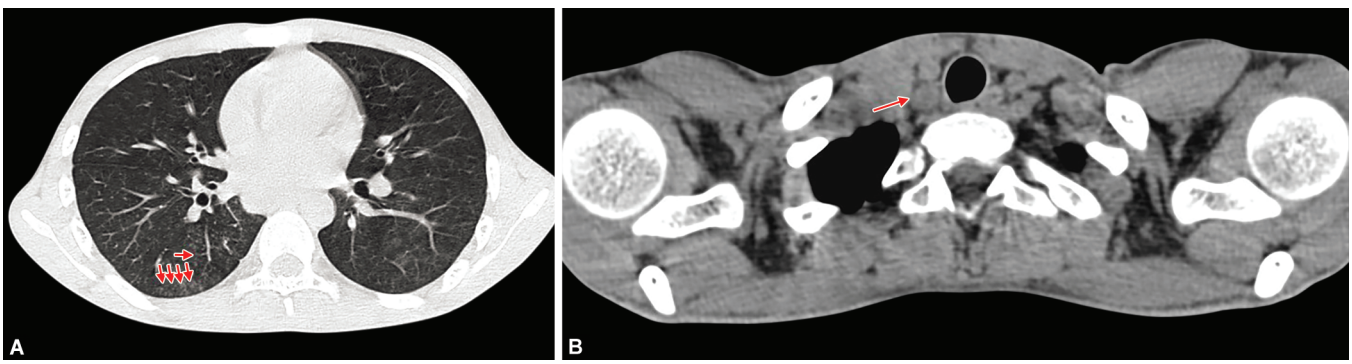
Diagnosis of TBM is challenging due to limitations in current diagnostics.[2] Definitive diagnosis requires identification or culture of acid-fast bacilli (AFB) from CSF.[3] Unfortunately, TBM cannot be confirmed based on clinical and imaging findings as the clinical findings are nonspecific, while laboratory techniques are largely insensitive or slow. For example, the specificity of CSF culture is 100% but the sensitivity is 68%[4] and the inoculation time is quite long (usually 4–6 weeks).

Cerebrospinal fluid (CSF) microscopy for AFB has sensitivity rates of about 10–20% in extrapulmonary TB especially TBM.[5] Meticulous microscopy of large CSF volumes improves sensitivity, but it rarely exceeds 60%.[5,6]

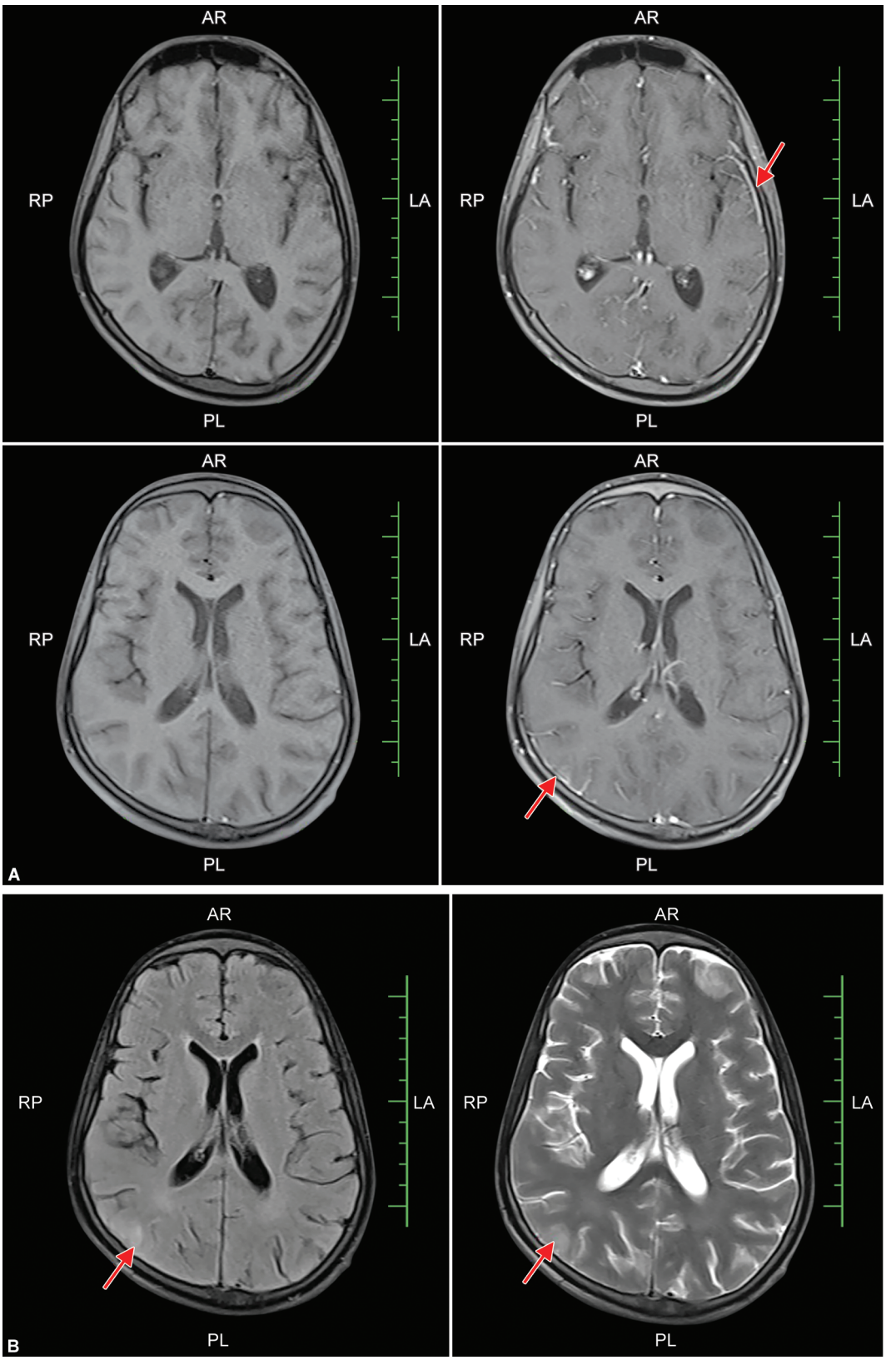
Kennedy and Fallon determined that the first LP sample had only 37% sensitivity for microscopy and 52% sensitivity for culture which increased to 83 and 87%, respectively, when up to four LP were performed.[3] ADA in CSF has a sensitivity of 84–91%[7] but is inconclusive by itself.[5]

The sensitivity and specificity of commercial CBNAAT were 56 and 98%, respectively, according to a comprehensive review and meta-analysis.[3,5,6] In our patient, it was the third CSF-CBNAAT that came back positive. Interferon-gamma release tests on CSF have a specificity of 70–90% but low sensitivity (50–70%) and unclear results were frequently obtained unless CSF volumes of 5–10 mL were used.[6]

Identification of TB in pulmonary and other extrapulmonary sites in patients with TBM is crucial as it may aid to initiate treatment but is also often challenging. Miliary shadows on chest radiograph are seen in patients with miliary TB, which frequently coexists with TBM. However, chest radiographs have a sensitivity of only 60–70% for the detection of miliary nodules, and miliary shadows in the lungs



Figs 1A and B: High-resolution computed tomography (HRCT) thorax; (A) Marked arrows showing centrilobular nodules with tree-in-bud appearance in right upper lobe; (B) Marked arrow showing enlarged lymph node



Figs 2A and B: Magnetic resonance imaging (MRI) brain with contrast (A) pre-contrast T1 sequence and post-contrast T1 sequence—marked arrows shows leptomeningeal (inner meningeal layers) enhancement in post-contrast scans; MRI brain with contrast (B) fluid-attenuated inversion recovery (FLAIR) and T2 sequence—marked arrows shows hyperintensity in same regions

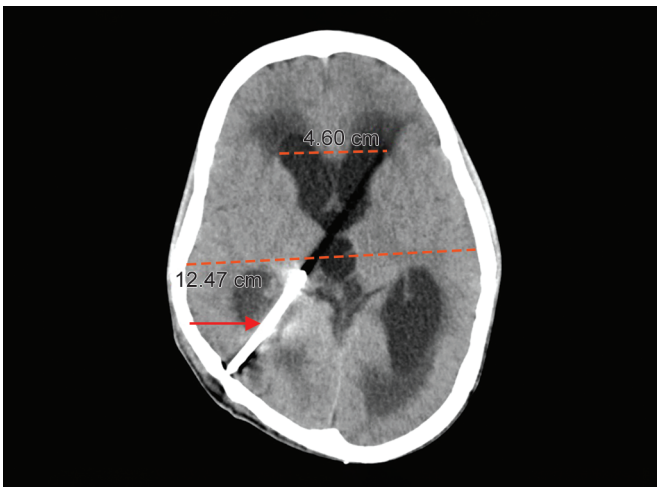


Fig. 3: Computed tomography (CT) brain plain—arrow showing right sided VP shunt

are seen in only 30–93% of cases of miliary TB.[7] The "tree-in-bud" appearance is a nonspecific CT finding seen in a range of diseases, with studies indicating that HRCT has a sensitivity of 88.57% and a specificity of 84.62% in diagnosing TB.[8] Lipoarabinomannan assay, GeneXpert Ultra, TRCReady 80, volatile organic compounds, assays for diagnosis of latent tuberculosis Infection, automated microscopy platforms, surface plasmon resonance sensing, nanoparticles, lab-on-a-chip, and future next-generation sequencing platforms are a few of the future projects for diagnosis.[8]

Prompt administration of dexamethasone and ATT decreases morbidity and mortality in patients with TBM, irrespective of the severity of the disease.[9] Delay in treatment may lead to complications like HC, cerebrovascular accident, vasculitis, CN palsies, seizures, and hyponatremia.[10]

Our patient initially improved likely due to dexamethasone injection although his condition later declined because of delay in initiating ATT. He developed oculomotor nerve palsy and HC which ultimately had to be managed by a VP shunt insertion. Early diagnosis and treatment can help prevent such complications. TBM should be ruled out in all patients who present with meningitis, especially in those with atypical presentations not responding to standard treatment.

Conclusion

In conclusion, patients diagnosed with pulmonary tuberculosis, as well as tuberculosis affecting other parts of the body may not consistently exhibit the classical symptoms associated with pulmonary TB. Given the variability in clinical presentations, it is important for healthcare professionals to consider the possibility of pulmonary tuberculosis in every patient with disseminated tuberculosis. A comprehensive diagnostic approach, including appropriate testing and a high index of suspicion, is crucial to ensure timely identification and management of pulmonary tuberculosis in these individuals, thereby contributing to improved patient outcomes and preventing potential diagnostic oversights.

Tuberculous meningitis (TBM) can have varied presentations, sometimes mimicking bacterial or fungal meningitis and this can lead to delays in diagnosis and treatment. A high degree of suspicion should be maintained in all patients with meningitis, especially in those who fail to respond to standard treatment. Early diagnosis and treatment can help prevent complications. Newer diagnostic modalities are necessary to facilitate early diagnosis.

Clinical Significance

The importance of this case report is to create awareness among healthcare professionals about the atypical presentation of TBM, challenges faced in diagnosis, and prevention of complications by early treatment.

Informed consent was obtained from the patient for the purpose of publication.

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