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Case report

An atypical presentation of CNS tuberculosis manifesting with meningoencephalitis and tuberculoma in a New York taxi driver

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ABSTRACT

Mycobacterium Tuberculous (MTb) meningitis is a rare manifestation of extrapulmonary tuberculosis (Tb) but remains the most common form of Central Nervous System (CNS) manifestation of tuberculosis. It is associated with significant morbidity and mortality yet difficult to diagnose given the low sensitivity and specificity of diagnostic testing with cerebral spinal fluid (CSF) analysis which typically shows CSF findings of lymphocytic pleocytosis, elevated protein, and low glucose and is confirmed by acid fast bacillus (AFB) culture. Here, we describe a case of severe meningoencephalopathy in the setting of disseminated tuberculosis with atypical radiological findings of tuberculoma.

Introduction

MTb meningoencephalitis is a form of CNS infection that results from dissemination of Mycobacterium tuberculosis, which is a slow-growing aerobic, non-spore forming acid-fast bacillus with a slow doubling time, into the CSF and meninges. According to the World Health Organization, roughly 10 million new cases of Tuberculosis occur each year with estimates of at least 100,000 individuals who develop MTb meningitis annually [1]. Patients are primarily treated with Rifampin, Isoniazid, Pyrazinamide, and Ethambutol, however despite treatment, mortality and morbidity remain high. In addition, diagnosis of MTb meningitis relies on prompt recognition of characteristic clinical signs and symptoms in combination with neuroimaging and CSF analysis. Acid fast bacilli culture remains widely utilized as a diagnostic and confirmatory tool for MTb meningitis, however it is limited due to its low sensitivity and slow turnaround times.

Case presentation

A 67-year-old Haitian male HIV-negative New York City taxi driver with a past medical history of hypertension, hyperlipidemia, Parkinson's Disease, and Type 2 Diabetes Mellitus and without recent travel history presented with four days of sudden gait ataxia associated with intermittent fevers for same duration and without any respiratory symptoms. He was initially treated at an outside facility with Vancomycin and Ceftriaxone for two days but left against medical advice. While there, the patient had a computerized axial tomography (CT) scan of the head which noted a 1.5 cm hypodense left frontal lobe focus with adjacent multiple subcentimeter hyperdensities and a CT chest which noted bilateral pulmonary tree-in-bud densities and a 1.6 cm enhancing liver lesion. On admission, the patient was tachycardic and hypertensive without leukocytosis. Physical exam was revealing for inability to walk in a straight line, lateral-veering posture, and imbalance. Chest x-ray showed pulmonary vascular congestion and CT head with intravenous contrast (IV) was significant for a 2 cm left parasagittal frontal lobe lesion (Fig. 1) suspicious for an abscess. The patient was empirically started with Vancomycin and Cefepime. Subsequent lumbar puncture (Table 1) showed albuminocytological dissociation with monocytes and lymphocytes on cytology but without malignancy. CSF culture with Gram stain, AFB smear and culture, Herpes Simplex Virus DNA PCR, MRSA nares, serum Toxoplasma gondii DNA PCR, and Treponema antibody were also negative. Additionally, QuantiFERON testing was indeterminate. Further studies with magnetic resonance imaging (MRI) of the brain with and without IV contrast showed subfalcine and supracallosal diffuse enhancements suggestive of leptomeningeal disease (Fig. 2A) with multiple lobulated foci within the arachnoid spaces

Abbreviations: ADA, adenosine deaminase; AFB, acid fast bacillus; BAL, bronchoalveolar lavage; CDC, centers for disease control; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computerized axial tomography; MRI, magnetic resonance imaging; MTb, mycobacterium tuberculosis; NAAT, nucleic acid amplification test; PJP, pneumocystis jerovicii; RIPE, rifampin, isoniazid, pyrazinamide, ethambutol; Tb, tuberculosis.

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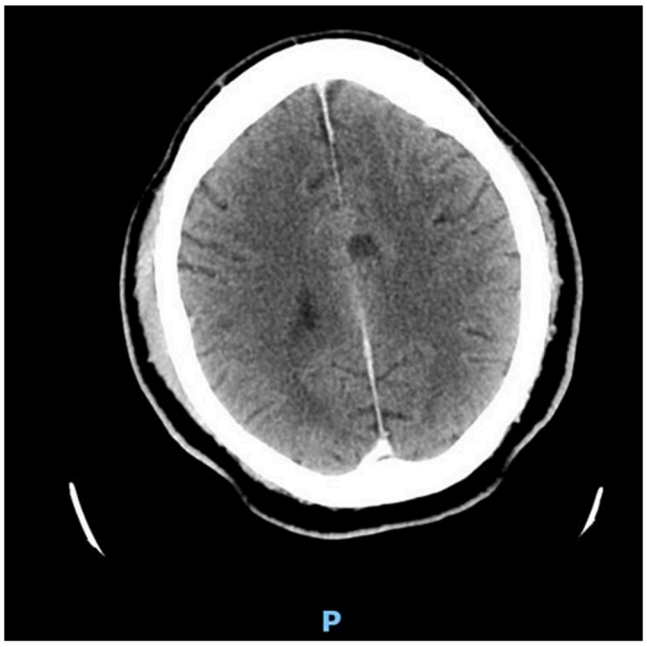

Fig. 1. CT head with IV contrast shows a peripherally enhancing lesion in the left parasagittal frontal lobe measuring 2 × 2×2 cm.

Table 1
CSF Studies Results.

	Day 1	Day 4	Day 14	Day 39
Glucose (mg/dL)	60	57	63	45
Total Protein (mg/dL)	145	156	96	75
Color	Colorless	Colorless	Colorless	Colorless
Appearance	Clear	Clear	Clear	Clear
WBC (cells/μL)	0	105	76	9
RBC (cells/μL)	20	50	0	20
Neutrophils (%)	0	62	33	1
Lymphocytes (%)	0	26	65	15
Monocytes (%)	0	12	2	0
Eosinophils (%)	0	0	0	0
Total Cell Count	0	100	100	16

consistent with an arachnoid space empyema and multiple focal cortical gray matter abscesses (Fig. 2B), while CT chest, abdomen, and pelvis with IV contrast (Fig. 3) showed bilateral pulmonary patchy ground glass opacities, a large hepatic hyperdensity, bilateral renal cortical cysts, and retroperitoneal lymphadenopathy.

The patient had continued clinical deterioration with worsening mental status and intermittent fevers. Antibiotic therapy was broadened to Meropenem. Despite broadening of antibiotics, mental status continued to decline and empirical therapy with Rifampin, Isoniazid, Pyrazinamide, and Ethambutol (RIPE) was initiated along with steroids for high suspicion of disseminated Tb with presumed MTb meningoencephalitis. Additionally, Bactrim was added for concern over Nocardia and Acyclovir for possible underlying HSV. Repeat lumbar puncture on day 4 was significant for elevated protein and WBC count (62% neutrophils, 26% lymphocytes, 12% monocytes) with lymphocytes and neutrophils on cytology but without malignancy (Table 1). Further testing including CSF culture with Gram stain, fungal culture, Cryptococcus antigen, India ink preparation, HSV DNA PCR, BK/JC virus DNA PCR, AFB smear and culture, MTb complex DNA, serum Toxoplasma, HSV, HTLV, P. Jerovicii (PJP), EBV DNA RT-PCR, Parvovirus B19 antibodies, VZV DNA RT-PCR, urine C. trachomatis and N. gonorrhoeae, and histoplasma urine antigen were all unremarkable. Additional QuantiFERON was again indeterminate. However, CSF adenosine deaminase (ADA) levels were elevated.

On day 10 of admission, the patient showed improvement in mental status while on RIPE therapy. Subsequent bronchoscopy was performed with grossly unremarkable bronchoalveolar lavage (BAL). Repeat MRI brain showed no changes from prior. Additional lumbar punctures on day 14 and day 39 (Table 1) continued to show elevated protein and WBC count, but downtrending and normalizing from prior studies. On day 42 of admission, MRI brain showed reduction of the enhancing lesions (Fig. 4) following treatment for intracranial Tb and chest x-ray no longer showed any consolidation. The patient was subsequently discharged to acute rehabilitation and outpatient follow up.

Two months after the patient's bronchoscopy was performed, as above, AFB smear from BAL culture (incubated in broth) was positive with pan-sensitive susceptibility. Overall, the patient was treated with RIPE therapy for a total of two months while hospitalized and throughout both admissions. The patient was additionally followed up at his outpatient visits showing improvement in mentation and orientation and after 121 days of RIPE therapy, he was switched to Rifampin and Isoniazid alone, which he remained on for a total of 244 days. He was treated for MTb meningitis for a total of 12 months.

Discussion

This case is an atypical case of disseminated MTb that was complicated by CNS disease manifesting with meningoencephalitis and tuberculoma, which proved challenging to diagnose due to uncharacteristic diagnostic test results. Before pursuing invasive procedures in

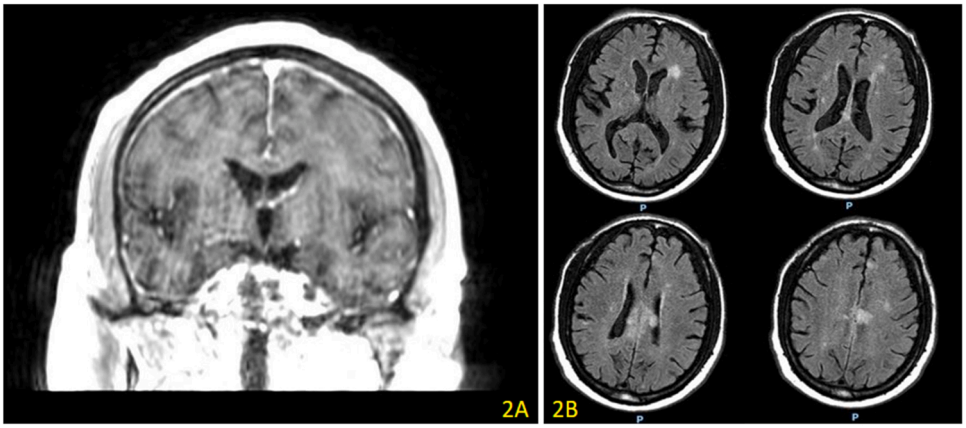

Fig. 2. MRI brain with and without IV contrast shows leptomeningeal disease in the subfalcine and arachnoid spaces extending into the cingulate sulci and supracallosal arachnoid spaces (2A) and multiple lobulated foci within the arachnoid spaces and surrounding cortical tissues consistent with an arachnoid space empyema and multiple focal cortical gray matter abscesses (2B).

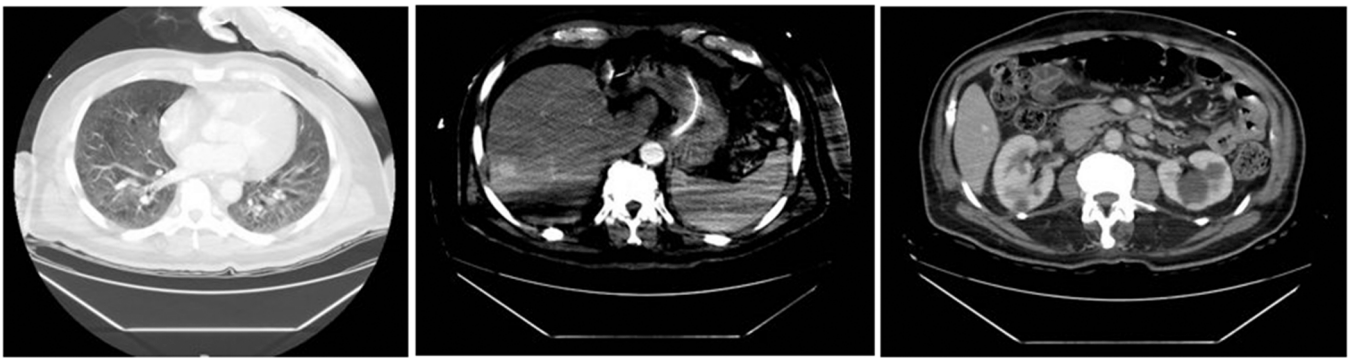

Fig. 3. CT chest, abdomen, and pelvis with IV contrast shows bilateral patchy ground-glass opacities, a large area of ill-defined hyperdensity in the right lobe of the liver, bilateral renal cortical cysts, and retroperitoneal lymphadenopathy.

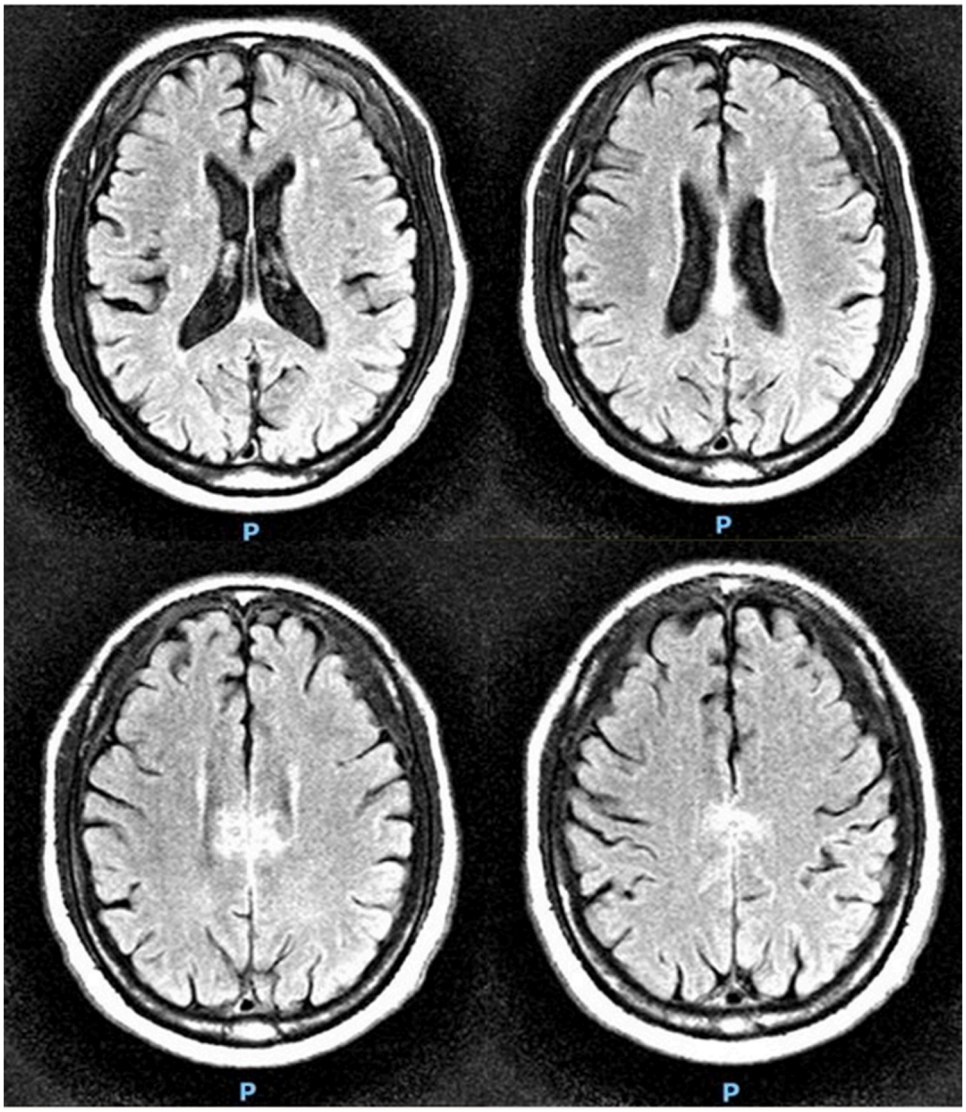

Fig. 4. MRI brain with and without IV contrast shows interval changes with improvement of the enhancing abnormalities.

patients suspected with MTb meningitis, imaging should first be utilized. Abnormalities on chest radiograph typically include focal cavitary lesions (10%), parenchymal infiltration (48%), miliary patterns (34%), and centrilobular nodules (8%) as noted in one study with 73 cases [2]. In our patient, however, chest imaging showed pulmonary congestion and ground glass opacities. On neuroimaging, classic findings of basilar meningeal enhancements especially with the presence of hydrocephalus is suggestive of MTb meningitis. Other findings include basal meningitis, ischemia or infarct, and tuberculoma [2,3]. Although our patient did not present with hydrocephalus, marked enhancement was noted in the frontal lobe. This prompted us to perform a lumbar puncture for CSF analysis. In patients suspected with MTb meningitis, definitive diagnosis

is typically made with CSF analysis involving positive smear for AFB, positive culture for M. tuberculosis, or positive on nucleic acid amplification test (NAAT). However, diagnosis is still difficult as AFB smears are only 20–40% sensitive with one study showing 37% sensitivity in a population of 52 patients [4,5]. In addition, patients with confirmed postmortem M. tuberculosis diagnoses have been found with negative smear for AFB on CSF analysis. Along with low sensitivity, these tests can take some time to result. In our patient, given poor response to empiric broad spectrum antibiotics and continued worsening mental status, treatment with RIPE therapy was initiated with relevant clinical and presumed epidemiological information given the estimated incidence of Tb (168 in 100,000 individuals) from the patient's country of origin [6]. It should be noted that M. tuberculosis culture has suboptimal sensitivity at $< 50\%$. On the other hand, NAAT has a higher sensitivity and specificity at 82% and 99%, respectively, but should ideally be used with a combination of both smear and culture, not as a substitute given variable prevalence throughout endemic regions [3,5]. Typically, CSF findings of MTb cases include WBC around 100–500 cells/μL with lymphocytic pleocytosis, elevated protein typically 100–500 mg/dL, and reduced glucose concentration often < 45 mg/dL. In addition, earlier in the course of disease, a neutrophilic predominance may instead be observed. Our patient displayed lymphocytes, as well as neutrophils on initial CSF analysis and during the early course of his disease. ADA levels can also be measured but should only be used as an adjunctive test for diagnosis of MTb meningitis as elevations in CSF ADA can be seen in the setting of meningitis from bacterial infections or neurobrucellosis. One study showed CSF ADA with a sensitivity of 75–94% and a specificity of 86–97% [7]. This can be a very useful test especially in endemic regions. However, the test results become non-specific for diagnosis of MTb meningitis in patients with concurrent HIV infection [7]. Furthermore, some studies even showed no distinction between MTb meningitis and bacterial meningitis by ADA alone [4]. Thus, when suspecting MTb meningitis, it is important to not only use a combination of biochemical analyses but also varying imaging modalities to rule in or out MTb meningitis. At the same time, one must rule out other infectious etiologies including HIV, toxoplasmosis, hepatitis, PCP, or other bacterial, viral or fungal infections.

Conclusions

MTb meningitis is typically diagnosed on CSF analysis with characteristic findings of lymphocytic pleocytosis, elevated protein, and decreased glucose. However, current diagnostic laboratory testing has suboptimal sensitivity and a lag-time to finalize results. Additionally, chest radiograph abnormalities may be seen in approximately half of those with CNS tuberculosis and typically range from focal consolidations to reactive upper lobe infiltrations to a disseminated-type miliary pattern. Similarly, CT chest findings of pulmonary Tb may reveal characteristic homogeneously dense centrilobular nodules or micronodular miliary lesions. If suspecting MTb meningitis, MRI brain may be warranted whereby classic findings include hydrocephalus, basilar meningeal enhancement, periventricular infarction, and less commonly tuberculomas or radiculomyelopathy. Typical findings of tuberculomas on imaging represent discrete single or multiple, ring-enhancing lesions with surrounding vasogenic edema. At times, however, as in our case, chest radiographs may show nonspecific findings that are less indicative of tuberculosis. It is recommended to start treatment with RIPE therapy while results are pending given the length in turnaround time if there is a high index of suspicion for MTb meningitis with clinical presentation despite atypical findings on cell count, cytology, and imaging.

Ethics approval

The study was approved by the Bioethics Committee at NewYork-Presbyterian Brooklyn Methodist Hospital. The study was conducted according to the principles of the World Medical Association Declaration of Helsinki, Good Clinical Practice Guidelines, and local laws and regulations.

Declaration of generative AI in scientific writing

The authors declare that no AI or AI-assisted technologies were utilized in the writing process.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report.

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CRediT authorship contribution statement

Aaron Yee: Conceptualization, Investigation, Writing – original draft preparation, Writing – review & editing, Visualization. **Ting Ting Wong**: Validation, Writing – review & editing, Supervision. All authors revised the manuscript critically for important intellectual content of the manuscript. All authors read and approved the final manuscript.

Declaration of Competing Interest

The authors declare that they have no conflict of interest associated with this manuscript.

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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References

[1] Seddon JA, Tugume L, Solomons R, Prasad K, Bahr NC, Tuberculous Meningitis International Research Consortium. The current global situation for tuberculous meningitis: epidemiology, diagnostics, treatment and outcomes. Wellcome Open Res 2019;4:167. https://doi.org/10.12688/wellcomeopenres.15535.1.

[2] Pehlivanoglu F, Yasar KK, Sengoz G. Tuberculous meningitis in adults: a review of 160 cases. ScientificWorldJournal 2012;2012:169028. https://doi.org/10.1100/2012/169028. Epub 2012 Apr 24.

[3] Rock RB, Olin M, Baker CA, Molitor TW, Peterson PK. Central nervous system tuberculosis: pathogenesis and clinical aspects. Clin Microbiol Rev 2008;21(2):243–61. https://doi.org/10.1128/CMR.00042-07.

[4] Marx GE, Chan ED. Tuberculous meningitis: diagnosis and treatment overview. Tube Res Treat 2011;2011:798764. https://doi.org/10.1155/2011/798764. Epub 2011 Dec 21.

[5] Thwaites G., Chau T.T., Mai N.T., Drobniewski F., McAdam K., Farrar J. , 2000. Tuberculous meningitis. J Neurol Neurosurg Psychiatry. 2000 Mar;68(3):289–99. doi: 10.1136/jnnp.68.3.289. Erratum in: J Neurol Neurosurg Psychiatry 2000 Jun;68(6):802.

[6] ⟨https://www.cdc.gov/globalhivtb/where-we-work/haiti/haiti.html⟩.

[7] Ghosh GC, Sharma B, Gupta BB. CSF ADA determination in early diagnosis of tuberculous meningitis in HIV-Infected patients. Scientifica (Cairo). 2016;2016:5820823. https://doi.org/10.1155/2016/5820823. Epub 2016 Apr 6.