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# Psychosis Secondary to Tuberculous Meningitis: A Case Report

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## Abstract

Tuberculous meningitis (TB meningitis) is a subacute meningitis known for its various form of initial manifestations, which often make early diagnosis difficult. Psychosis is a rare manifestation of this disease. We reported a case of 19-year-old woman who presented with worsening psychotic disorder of one year duration. She presented initially with social isolation with subsequent mutism and stupor. Initial brain imaging & Electroencephalography (EEG) was unremarkable. Cerebrospinal fluid (CSF) investigations revealed positive cerebrospinal fluid Mycobacterium tuberculosis polymerase chain reaction (MTB PCR). She was treated with empirical antituberculosis drugs and steroids. Subsequently her psychotic symptoms resolved. As a conclusions, the psychotic disorder was most likely caused by TB meningitis. TB meningitis should be considered in patients with no background history of psychiatric illness presenting with psychotic disorder especially in countries with high TB burden.

**Keywords:** Psychosis; Hallucinations; Catatonia; TB Meningitis

## Introduction

Psychosis refers to an abnormal condition of the mind described as involving a loss of contact of reality. Patients would normally present with one or more of the following: hallucinations, elusions, catatonia or a thought disorder. Impairments in social cognition also occur. It results in impairment that grossly interferes with the capacity to meet ordinary demands in life.

Tuberculous meningitis is not uncommon in central nervous system infection. Its initial manifestation varies widely and may cause difficulty in diagnosis. The rate and extent of recovery have been shown to be strongly related to the rapidity of initiating anti-tuberculous therapy. Thus, it is crucial to diagnose TB meningitis and administer anti-tuberculosis drugs early in the course of the disease. This case report presents a rare initial manifestation of TB meningitis.

## Case Presentation

A 19-year-old female presented to our hospital in January 2015 with chief complain of altered behavior. It was associated with one week history of poor oral intake, low grade fever and dysphagia. Further history from family members revealed that the patient had been having altered behavior for the last one year. The symptoms had worsens two months prior to admission. Initially she complained of constant lethargy which lead her quitting her job as a factory worker. She started to shun from outsiders and locked herself most of the time in her room. At that time, she was still able to care for herself. Two months prior to admission, her behavior worsened. She became quiet, lying most of the time on the bed. She required assistance from her family members for daily self-care. Eventually she refused oral intake and was brought to the hospital by family members for medical attention. She has no known previous medical illness. Her family members denied patient's involvement with high risk behaviors. She has no previous contact with tuberculosis patients.

Upon admission, physical examination revealed a stuporous, emaciated, dehydrated woman. Glasgow Coma Scale was 11/15 (E4V2M5). There was a blank stare, mutism and akinesia. Power was 3/5 on all limbs. Tone were hypertonic. Reflexes were brisk. Plantar reflex were down going bilaterally. Clonus was present. Neck stiffness was present, however Kernig's and Brudzinski's signs were negative. There were no palpable lymph nodes. Other physical examinations were unremarkable.

Initial CT brain scan with contrast, MRI brain, chest X ray and EEG revealed normal findings. Blood investigations on admission showed thrombocytopenia ($145 \times 10^9$/L) with normal white cell count ($9.14 \times 10^9$/L) and hemoglobin level (15.5 g/dL). Renal function test showed hypernatraemia (157 mmol/l). Other electrolytes level were normal. ESR was normal (5 mm/hour). CRP was slightly elevated (14 mg/L). Liver function tests were unremarkable. Hepatitis C and B, HIV and syphilis screening were negative. Connective tissue disease screening was unremarkable.

Lumbar puncture was done on day 4 of admission after obtaining consent from family members. CSF investigations revealed RBC numerous, WBC nil, protein 0.97 g/L, glucose 3.6 mmol/L. Gram stain was negative. C&S showed no growth. However, TB PCR was positive. Patient was started on empirical anti-tuberculosis treatment consisting of isoniazid, rifampicin, ethambutol and pyrazinamide (EHRZ regime) on day 8 of admission. IV dexamethasone was commenced with

| CSF investigations | Results | Normal Values | Common in Tuberculosis [7] |
|---|---|---|---|
| Protein | 0.97 g/L | 0.2-0.4 g/L | 0.5- 3.0 g/L |
| Glucose | 3.6 mmol/L | ½ to ⅔ bloodglucose | <½ blood glucose |
| Appearance | Blood stained | Crystal clear | Turbid/viscous |
| WBC | Nil | Mononuclear cells :< 5/mm$^3$, polymorphs : nil | Mononuclear cells :100- 300/mm$^3$, polymoprhs : 0-200/mm$^3$ |
| Acid-fast bacilli | Negative | Negative | Positive (20-40%) [5] |
| MTB C&S | No growth | No growth | Positive growth (40-80%) [5] |
| TB PCR | Positive | Negative | Positive (overall 56%) [5] |
| C&S | No growth | No growth | - |
| Indian ink for *Cryptococcus neoformans* | Negative | Negative | - |

**Table 1:** Cerebrospinal fluid (CSF) result.

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tapering down dosing every week. Her admission was complicated with hospital acquired infection which resolved with 1 week course of IV piperacillin-tazobactam and cloxacillin. The patient showed gradual improvement in ward with increasing alertness and able to interact with family members and medical staffs. She developed delirium later on, manifested by talking to herself, smiling and laughing inappropriately. Thus, she was started on oral olanzapine by the attending psychiatry team. Subsequently, she was discharged after 1 month stay in ward. On follow up visit one month later, her psychotic symptoms had already resolved. She was able to ambulate and care for herself. She was unable to recall all the symptoms before and during admission. She could not even recall her admission the hospital (Table 1).

## Discussion

TB continues to be an important disease both globally and in Malaysia. In Malaysia, the incidence of TB was 81.4 per 100,000 population in year 2010 [1]. The number of new TB cases in the country increased from 15,000 in 2005 to 19,251 in 2011. While PTB was the commonest form, extrapulmonary TB (EPTB) still posed a threat.

TB meningitis occurs when subependymal or subpial tubercles, also known as "Rich foci" seeded during bacillemia of primary infection or disseminated disease, rupture into the subarachnoid space. Individuals with increased risk for TB meningitis include young children with primary TB and patients with immunodeficiency caused by aging, malnutrition or disorders such as HIV or cancer Eighty percent of TB meningitis patients have foreign travel or other exposure to TB. Many reported cases of TB meningitis are notable for immune-compromise.

In the present case, the presentation was psychosis without any clinical evidence of meningitis. Her presentation was atypical for TB meningitis. She was also immune-competent and had no exposure history. Subsequent unremarkable blood investigations, negative brain imaging and EEG results, normal CXR further complicated the diagnosis. This case serves a good example of the diversity and rarity of the initial manifestations of TB meningitis.

According to an earlier review of 45 cases, Chotmongkol and colleagues found that initial clinical presentations of TB meningitis include headache (95.6%), fever (91.1%), neck stiffness (77.8%), mental impairment (40.0%), motor weakness (11.1%) and cranial nerve palsies (11.1%) [4]. Atypical manifestations include psychosis, internuclear ophthalmoplegia and hemianopia.

A review of 48 cases of TB meningitis admitted to ICU by Renaud Verdon and colleagues showed 46% of the patient was comatose on admission. 65% presented with fever; 15% presented with hypothermia; meningeal stiffness 88%; seizures 17%;neurological signs of localization (52%) [5]. Various degrees of hemiplegia, monoplegia or paraplegia were found in 16 patients. Cranial nerve palsy was found in 15 patients. Three patients presented with cerebellar syndrome.

Another case of TB meningitis presenting with psychosis was reported by Atmesh Kumar and colleagues [2]. In this case, the patient presented with chief complaints of irrelevant talking, irritability, disorganized behavior, poor oral intake and constipation for three days; poor social interaction, withdrawn behavior and disturbed sleep for 2 months; on and off headache for nine years which had become more severe and frequent for 2 months. The patient was treated with EHRZ regime with steroid coverage. The patient's symptoms subsequently resolved after treatment. This patient was treated empirically with anti-tuberculosis drugs based on clinical findings and responded after treatment. No confirmatory laboratory investigation was positive for tuberculosis.

Our patient presented with one year history of altered behavior with poor social interaction. She had a short history of fever and poor oral intake which brought her to medical attention. The delay in diagnosing TB meningitis was due to the indolent nature of her presentation. The highlight of our case was that her CSF TB PCR sample was positive. This key investigation result has helped us in managing our patient who presented with acute psychosis with vague neurological clinical findings and non-conclusive laboratory and neuroimaging results. Our case presentation showed the importance of CSF TB PCR sample as a part of CSF array of investigations in patients from countries with high TB burden.

Diagnosis of TB meningitis can be difficult and may be based only on clinical and preliminary CSF findings without definitive microbiologic confirmation. Certain clinical characteristics such as longer duration of symptoms (>6 days), moderate CSF pleiocytosis and presence of focal deficits increase the probability of TB meningitis. Characteristic of CSF findings include:

i. Lymphocytic-predominant pleiocytosis. Total white cell counts are usually 100-500 cell/μL. In very early disease, lower counts and neutrophil predominance may be present

ii. Elevated CSF protein level (100-500 mg/dL)

iii. Low glucose (<2.5 mmol/L) or CSF: plasma ratio <0.5.

Tuberculin skin test is positive in only about 50% of patients with TB meningitis.

CSF acid-fast smear should be sent. However single sample has low sensitivity (20-40%). Sensitivity increases with more CSF fluid withdrawn and more spinal taps performed. While CSF MTB culture can take several weeks and also has low sensitivity (40-80%), it has to be performed to determine drug susceptibility. Sensitivity of CSF smear and culture decreases rapidly once treatment initiated [3-5].

CSF adenosine deaminase has high sensitivity and specificity (>90%) in one study. However, it has shown poor specificity in other studies involving certain populations, particularly in HIV-infected adults with concurrent infections or cerebral lymphomas. CSF tuberculous PCR has an overall sensitivity of 56% and a specificity of 98%. The reason for such poor sensitivity is due to the fact that most PCR-based studies use a single target for amplification which can result in false-negative results due to absence of the target gene in some TB-isolates. Thus, most experts conclude that commercial NAA tests can confirm TB meningitis but cannot rule it out. MTB DNA may be detectable in in CSF for up to a month after treatment initiation [5].

Neuroimaging in TB meningitis include classical features such as basal meningeal enhancement and hydrocephalus. Hypodensities due to cerebral infarcts, cerebral edema and nodular enhancing lesion maybe seen. MRI is the imaging of choice in TB meningitis as it is superior to CT for evaluating the brainstem and spine. T2 weighted MRI imaging has been shown to be particularly good at demonstrating brainstem pathology; diffusion weighted imaging is best at detecting acute cerebral infarcts due to TB meningitis. However, CT is adequate for urgent evaluation of TB meningitis associated hydrocephalus for possible surgical intervention [5].

Treatment of TB meningitis follows the model of short course chemotherapy of pulmonary TB; an "intensive phase" of treatment with 4 drugs followed by treatment with 2 drugs during a prolonged "continuation phase" [1]. The first 2 months of treatment should be with isoniazid, rifampicin, pyrazinamide and either streptomycin or

ethambutol. Subsequent continuation phase treatment consists of isoniazid and rifampicin. Total duration of treatment is between 9 to 12 months. Corticosteroids should be used in TB meningitis as it had been shown to improve symptoms and survival in HIV negative patients. Dexamethasone is used with initial IV treatment for 2 weeks followed by oral preparation in tapering dose manner over 4 weeks.

Prognosis of TB meningitis relies upon neurologic status at the time of presentation and time-to-treatment initiation. Various case series indicate mortality rate of 7%-65% in developed countries, and up to 69% in underdeveloped countries [5]. Mortality risk is highest in those with co-morbidities, severe neurologic involvement on admission, rapid progression of disease and advanced or very young age. Neurologic sequelae occur in up to 50% of survivors [5,6,7].

## Conclusion

TB meningitis should be considered in patients with no background of psychiatric illness presenting with psychotic disorder especially in countries with high TB burden. High index of clinical suspicion is needed to diagnose TB meningitis. This report is intended to increase clinician awareness of late and atypical presentation of TB meningitis. Given the fatal consequences of delayed treatment, clinicians are encouraged to initiate empirical therapy in the setting of compatible clinical, epidemiological and laboratory findings.

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