

Case Report

Rare Clinical Presentation of Tuberculous Meningitis: A Case Report

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Abstract

Introduction: Tuberculosis is the second leading cause of death under the category of infectious diseases, after the human immunodeficiency virus (HIV). Tuberculous meningitis (TBM) constitutes about 5% of all extrapulmonary disease worldwide. This report describes a case of Tuberculous meningitis with rare presentation in a 28-year-old woman, who was treated based on a collection of her social background, clinical findings and Multiplex PCR of tuberculosis.

Case presentation: A 28-year-old Malay woman with no significant medical history presented to HUSM with one month history of on and off fever, two weeks history of generalised limbs weakness and one week history of dysphagia. She was reported to have experienced visual hallucination and significant weight loss. Her laboratory result is significant for leukocytosis, elevated ESR and hyponatremia. Non-enhanced and contrast CT scan of the brain showed severe bilateral frontal cerebral atrophy. Cerebral spinal fluid (CSF) for multiplex PCR for *Mycobacterium tuberculosis* complex was positive. She was promptly started on anti-TB regime combined with dexamethasone. Subsequent follow-up showed significant improvement.

Conclusion: This is a rare clinical manifestation of Tuberculous meningitis that demonstrates the importance of recognising and initiating the treatment early to reduce disabilities and improve clinical outcome.

Keywords: tuberculosis, meningeal, atrophy, multiplex polymerase chain reaction

Introduction

Globally, tuberculosis has a high incidence rate, especially within developing countries. According to the World Health Organisation statistics of 2013, there were 9 million people newly diagnosed with tuberculosis, and 1.5 million of those cases resulted in death. Tuberculosis ranks as the second leading cause of death within the category of infectious diseases, following the human immunodeficiency virus (HIV). In Malaysia, the incidence rate was 78.28 persons per 100,000 people with a mortality rate of 5.37 persons within that same population

during 2013. The number of new cases increased from 15,000 in 2005 to 19,251 in 2011, with the majority of patients ranging from 21 to 60 years of age. In descending order of frequency, the common sites of extrapulmonary tuberculosis are lymph nodes, the pleura, the genitourinary tract, bones and joints, the meninges, and the peritoneum and pericardium. Tuberculous meningitis (TBM) constitutes about 5% of all extrapulmonary diseases worldwide. Atypical and late presentations of TBM often cause a delay in diagnosis, which may severely impact the prognosis of the disease. Furthermore, it is typical for clinical presentations of the acid-

fast bacilli smears and cerebrospinal fluid (CSF) abnormalities to vary between patients with TBM. Delays in recognising and treating tuberculous meningitis may result in severe disabilities and poor outcomes. Hence, it is important to recognise an unusual presentation of the disease, especially in countries in which TBM is highly endemic. Here, we report a case of TBM with uncommon signs and symptoms, in which the patient was hospitalised at Hospital Universiti Sains Malaysia (HUSM); a diagnosis was given based on the woman's symptoms, which suggested involvement of the central nervous system, taking into consideration of her social background, and the use of Polymerase Chain Reaction (PCR) based testing of the CSF for the *Mycobacterium tuberculosis* complex.

Case Presentation

A 28-year-old female patient (ex-factory worker) was admitted to the HUSM medical ward with complaints of on-and-off, prolonged fevers lasting one month, generalised limb weakness for two weeks, and dysphagia (choking while swallowing solid food) for one week. According to her parents' descriptions, she had experienced changes in behavior, become socially withdrawn, and suffered through increasing cognitive decline one month prior to her admission. Moreover, two weeks prior to admission, she started to show a poor appetite and generalised upper and lower limb weakness. She reported one episode of a visual hallucination, and later on became mute, failing to respond to her parents. Eventually, the woman was bed-bound. Persistent lethargy, poor sleep, and the tolerance of only a soft-foods and fluids based diet was exhibited throughout her illness as well.

Upon admission, the patient was disoriented and non-cooperative with a GCS of 10 out of 15 (E3V2M5). She experienced a syncopal episode of 20 minutes without abnormal jerking of the limbs. A physical examination revealed severe dehydration, no palpable lymph nodes, no neck stiffness, muscle wasting with a loss of power on a scale of 3/5 in all limbs, signs of an upper motor neuron lesion with deep tendon reflexes of grade 3+ in all limbs, and the presence of Babinski's

sign bilaterally, but normal muscle tone, and a vertical nystagmus. Her body weighed 36 Kg; her blood pressure was 98/64 mmHg with a body temperature of 36.5 °C and a heart rate of 100 beats/min. Her Modified Rankin Score was 5 during the first presentation. Laboratory results revealed elevated inflammatory parameters with a white blood cell count of $15.5 \times 10^9/L$, an ESR of 38 mm/hr, and hypernatremia (157 mmol/L). CSF examinations showed normal cell, protein, and glucose levels. Non-enhanced and contrast CT scans of the brain showed severe bilateral frontal cerebral atrophy, but an absence of hydrocephalus or tuberculoma formations (Figure 1 and Figure 2). The CSF tested negative for gram stains, acid-fast bacilli, and *Cryptococcus* antigens. The patient was initially treated for meningoencephalitis with ceftriaxone and acyclovir. No significant improvement was seen after 5 days of treatment. HIV testing was done, and it was nonreactive. An electroencephalogram (EEG) was completed and reported as normal. MTB cultures (solid culture media) were made, and also reported negative. Later, however, the CSF tested positive for the *Mycobacterium tuberculosis* complex using a commercial multiplex PCR (Altona).

The patient was promptly started on anti-TB treatment (Isoniazid, rifampicin, ethambutol and pyrazinamide orally) combined with dexamethasone. While on regular treatment, the patient began to show signs of improvement, as she could engage in short conversations and recognise her parents. However, she occasionally demonstrated inappropriate laughter, irrelevant speech, fits of sobbing, and moved all four of her limbs without purpose while still bed-ridden. MRI scans of the brain were taken and found normal with no meningeal enhancements or parenchymal abnormalities. After 3 months of anti-TB treatment, the patient showed significant signs of improvement upon follow-up at the clinic in HUSM. There was a considerable improvement in body weight with a change from her initial 34 kg baseline to 45 kg. Notably, she was able to carry out her daily activities of living independently with no neurological disabilities, no more hallucinations, and displayed an agreeable mood and tolerance for food. Her Modified Rankin Score at the time was 0.

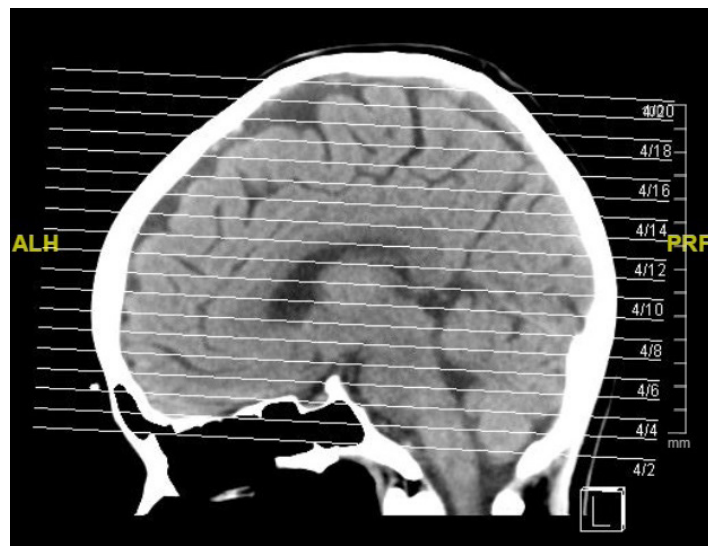


Figure 1. CT scan shows frontal brain atrophy

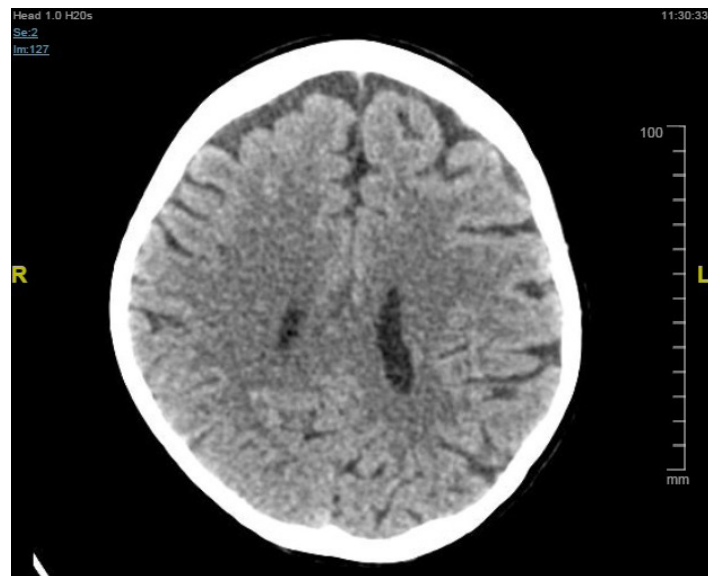


Figure 2. CT scan shows bilateral frontal brain atrophy

Discussion

TBM is a rare form of tuberculosis manifestation in developed countries, but is still considered a significant issue in developing countries (1). The diagnosis of TBM in this patient was solely made based on her clinical manifestations, CSF PCR results, and clinical improvements during the course of anti-TB treatment.

CSF examination is essential for confirmation of TBM. The typical findings of TBM in CSF analysis are lymphocytic-predominant pleocytosis, elevated protein levels, and low amounts of glucose (2). However, the patient's CSF parameters do not match the typical findings of TBM. The goal for an ideal diagnosis is to demonstrate the presence of *Mycobacterium tuberculosis* bacilli in the CSF. However, the smear microscopy of CSF is generally insensitive as it only tests positive in 5%–30% of patients, and culture methods are tedious and lengthy (1). Nowadays, the use of PCR technology for the detection of *Mycobacterium tuberculosis* DNA is widely accepted (3). However, this method exhibits a variable sensitivity and specificity that depends on the types of PCR tests used. A meta-analysis showed that commercial nucleic acid amplification tests have a sensitivity of 56% and specificity of 96% (4). The low sensitivity of this PCR test was attributed to the utilisation of a single target for amplification, resulting in false-negative results (5). Newer PCR tests, called Multiplex PCRs, allow for the amplification of several target genes (IS6110, protein b, and MPB64) simultaneously, and this has helped to increase sensitivity to a level of 85–95% and specificity to 100% (6). The patient's CSF results were positive when employing a Multiplex PCR for tuberculosis. Hence, a diagnosis of TBM was made.

Early diagnosis and prompt treatment for TBM is necessary to ensure successful outcomes and decrease the morbidities and mortality rates of the patients (7). Presentation of TBM is similar to meningoencephalitis, and its diagnosis requires a high index of clinical suspicion, especially in a country with a high burden of TB. The most common neuroradiological findings of TBM are basal meningeal enhancement, hydrocephalus, and infarctions in the supratentorial regions of the brain, parenchyma, and brain stem (8). Bernaerts et

al. (8) reported that local areas of brain atrophy are late radiographical changes in tuberculomas. However, for unknown reasons, this patient did not show the typical signs of neuroradiological or tuberculoma activity for TBM. CT scans of her brain displayed bilateral frontal atrophy. The only possible explanation for the atrophy would be vasculitis as reported by Amin et al. (9).

On the basis of the clinical pictures and laboratory findings, decided decision was made to start her on anti-TB medication. The plan was to put her in intensive therapy for 2 months (Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol) and maintenance therapy for 10 months (Isoniazid and Rifampicin). Administration of glucocorticoids helped provide clinical benefits to the patient, such as facilitating the continuation of the anti-TB medication, and decreasing severe, adverse events related to the medication; it should be given over a course of 6–8 weeks in tapering doses (10). There was marked improvement after two months of initiating the treatment as the patient was no longer bed-bound and showed improvements in independence while carrying out the tasks of daily living.

Authors' Contributions

Drafting of the article: TJL

Critical revision of the article for important intellectual content: TJL

Final approval of the article: SN, AMB

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