CASE REPORT

Psychosis secondary to tuberculosis meningitis

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SUMMARY

We report a case of a 19-year-old immunocompetent Malay woman who presented with a worsening psychotic disorder of 1-year duration. She initially presented with social isolation with subsequent mutism and stupor. Physical examination revealed a stuporous, emaciated, dehydrated woman with Glasgow Coma Scale of 11/15 (E4V2M5). She had a blank stare, mutism and akinesia. Motor examination revealed upper motor neuron findings. Neck stiffness was present, however, Kernig's and Brudzinski's signs were negative. There were no other findings on other systems. Brain imaging and EEG were normal. Cerebrospinal fluid investigations revealed positive cerebrospinal fluid *Mycobacterium tuberculosis* PCR (MTB PCR). The patient was treated with empirical antituberculosis drugs and steroids. On follow-up visit 1 month later, her psychotic symptoms had fully resolved. She was able to ambulate and care for herself; she was unable to recall the symptoms she had experienced before and during admission.

BACKGROUND

Tuberculous meningitis (TB meningitis) is a subacute meningitis known for its various forms of initial manifestations—this often makes early diagnosis difficult. It is the most severe form of TB, and has higher mortality and morbidity than other forms of TB. Early diagnosis is difficult as TB meningitis shows non-specific clinical symptoms. It is crucial to recognise TB meningitis at an early stage as this disease can result in mortality. The rate and extent of recovery have been shown to be strongly related to the rapidity of initiating antituberculous therapy.

Our patient presented with psychosis, which is a common manifestation of TB meningitis. She was, however, immunocompetent. The indolent nature of this patient's initial presentation delayed the diagnosis of TB meningitis. This case highlights the importance of having a high index of suspicion to empirically treat the condition, especially in countries with a high TB burden.

CASE PRESENTATION

A 19-year-old Malay woman presented to Hospital Universiti Sains Malaysia, Kelantan, in January 2015, displaying a non-specific behaviour disorder. This was associated with a 1-week history of poor oral intake, low grade fever and dysphagia. Further history from family members revealed that the patient had been exhibiting altered behaviour for the past 1 year. The symptoms had worsened 2 months prior to admission. Initially, she had reported of constant lethargy, which led to her quitting her job as a factory worker. She had

started to shun outsiders and locked herself in her room most of the time. At that time, she was still able to care for herself. Two months prior to admission, her behaviour worsened. She became quiet, lying in bed most of the time. She had lost interest and motivation in her daily routine. She even 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 had no history of hallucinations and no seizures prior to admission. She had no known previous medical illness. Her family members denied the patient's involvement in high-risk behaviour. She had no previous contact with patients with tuberculosis.

On admission, physical examination revealed a stuporous, emaciated, dehydrated woman. Glasgow Coma Scale was 11/15 (E4V2M5). She had a blank stare, mutism and akinesia. Power was 3/5 in all limbs. Tone was hypertonic and reflexes were brisk. Plantar reflexes were down-going bilaterally. Clonus and neck stiffness were present, however, Kernig's and Brudzinski's signs were negative. There were no palpable lymph nodes. The rest of the physical examination was unremarkable.

INVESTIGATIONS

Chest X-ray is crucial in TB meningitis, as 40% of TB meningitis will have disease in the chest or in other organs. However, this case revealed a normal chest X-ray. Initial CT brain scan with contrast, MRI of the brain and EEG were also normal. It is possible to have a normal brain MRI but this is not the situation in the majority of TB meningitis cases. Blood investigations on admission showed thrombocytopenia ($145 \times 10^9/L$) with normal white cell count ($9.14 \times 10^9/L$) and haemoglobin level (15.5 g/dL). Renal function test showed hypernatraemia (157 mmol/L). Hypernatraemia in this case was due to dehydration. Other electrolyte levels were normal. Erythrocyte sedimentation rate was normal (5 mm/h). C reactive protein was slightly elevated (14 mg/L). Liver function tests were unremarkable. Hepatitis C and B tests, HIV and syphilis screening were negative. Antinuclear antibodies, double stranded DNA, extractable nuclear antigen and anti-neutrophil cytoplasmic antibody results were all unremarkable. Complements were also normal.

Lumbar puncture was performed on day 4 of admission after obtaining consent from family members. Table 1 shows the cerebrospinal fluid (CSF) results of our patient.

DIFFERENTIAL DIAGNOSIS

The first challenge on presentation was to differentiate other infectious diseases that may have been

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Table 1 Cerebrospinal fluid results

CSF investigations	Results	Normal values	Common in tuberculosis ¹
Protein	0.97 g/L	0.2–0.4 g/L	0.5–3.0 g/L
Glucose	3.6 mmol/L (ratio 0.6)	½ to ⅔ blood glucose	<½ blood glucose
Appearance	Blood stained	Crystal clear	Turbid/viscous
White cell count	Nil	Mononuclear cells: <5/mm ³ , polymorphs: nil	Mononuclear cells: 100–300/mm ³ , polymorphs: 0–200/mm ³
Acid-fast bacilli	Negative	Negative	Positive (20–40%) ⁵
MTB culture and sensitivity	No growth	No growth	Positive growth (40–80%) ⁵
MTB PCR	Positive	Negative	Positive (sensitivity 56%, specificity 98%) ⁵
Culture and sensitivity	No growth	No growth	–
India ink for <i>Cryptococcus neoformans</i>	Negative	Negative	–

*Blood glucose 6 mmol/L.

MTB, *Mycobacterium tuberculosis*.

causing the chronic meningitis, namely, bacteria (neurosyphilis), parasites, fungus (*Cryptococcus*, toxoplasmosis) and HIV. Other important differentials that need to be ruled out in a young woman with chronic meningitis are non-infectious causes such as autoimmune diseases, those being, neuropsychiatric lupus or vasculitis, medications and neoplasms. Common neoplasms that can cause meningitis are small-cell lung cancer and melanoma. In up to one-third of patients with chronic meningitis, no cause is found.

In this case, autoimmune markers and HIV screening were both negative.

TREATMENT

Empirical treatment was started on day 8 of admission after confirming the diagnosis of TB based on clinical findings, CSF with increased protein and PCR detection of *Mycobacterium tuberculosis*. Antituberculosis treatment consists of isoniazid, rifampicin, ethambutol and pyrazinamide (EHRZ) regimen. Intravenous dexamethasone was started, tapering down dosing every week. The patient's admission was complicated by a hospital-acquired infection during the second week of admission, which resolved with a 1-week course of intravenous piperacillin-tazobactam and cloxacillin.

OUTCOME AND FOLLOW-UP

The patient showed gradual improvement in the ward, with increasing alertness, and was able to interact with family members and medical staff. She developed delirium after the third week in hospital, manifested by talking to herself, smiling and laughing inappropriately. She claimed there was a demon inside her. Sometimes she would scream when examined by medical staff. Initially, she was started on oral risperidone by the attending psychiatry team. After 4 days, the risperidone was changed to oral olanzapine due to no response. The patient was discharged after a 6-week stay in the ward. Her symptoms continued to improve until the day of discharge. Her family members refused a repeat lumbar puncture prior to discharge. It was noted that she was not on any antipsychotic medication after discharge from the ward.

On follow-up visit 1 month later, her psychotic symptoms had resolved. She was able to ambulate and care for herself. She was unable to recall the symptoms she had experienced before and during admission. She could not even recall her admission to the hospital.

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 2010.¹ Among all TB cases in Malaysia, 13.9% were among foreigners.¹ According to recent data reported by the WHO, the number of new TB cases in this country has increased to 103 per 100 000 population in 2014.² While pulmonary TB was the commonest form, extrapulmonary TB still posed a threat.

TB meningitis occurs when subependymal or subpial tubercles, also known as 'Rich foci', seeded during bacillaemia of primary infection or disseminated disease, rupture into the sub-arachnoid space. Individuals with increased risk for TB meningitis include young children with primary TB and patients with immunodeficiency caused by ageing, malnutrition, or disorders such as HIV or cancer.³ In the present case, the presentation was psychosis without any clinical evidence of meningitis. Although her initial presentation had more negative symptoms, the patient had recorded positive symptoms in the ward, which persisted despite treatment with antipsychotics. Her psychotic symptoms resolved despite her defaulting antipsychotic treatment shortly after discharged. It is important to note that the total duration of her antipsychotic treatment was only 3 weeks.

Prior to her presentation, the duration of her psychotic symptoms had persisted for nearly 1 year. She was also immunocompetent and had no exposure history. Many reported cases of TB meningitis are notable for immunocompromise.⁴ Subsequent unremarkable blood investigations, negative brain imaging and EEG results, and normal chest X-ray, further complicated the diagnosis.

Conventional CSF investigations (cell count, protein and glucose concentration) are not sensitive by themselves in diagnosing TB meningitis.⁵ Overall, the sensitivity of culture to detect *M. tuberculosis* in CSF is low and ranges from 40% to 60% as culture is less sensitive in paucibacillary conditions.⁶ In regard to MRI findings, there are reported cases of TB meningitis with normal brain MRI.⁷ As stated in a review by Grace *et al*, CSF tuberculous PCR has an overall sensitivity of 56% and a specificity of 98%. PCR tests are more sensitive and specific in detection of specific DNA sequences. In this case, the pretest probability of TB was only 56.86%. However, with a background prevalence of high disease burden in Malaysia, a false-positive PCR result is highly unlikely.

Given the overall improvement in symptoms after initiating antituberculosis treatment and high specificity of the CSF tuberculous PCR result, the likelihood of TB meningitis was high.

This case serves as a good example of the diversity and rarity of the initial manifestations of TB meningitis. Another case of TB meningitis presenting with psychosis was reported by Kumar *et al*.⁸ In their case, the patient presented with chief symptoms of irrelevant talking, irritability, disorganised behaviour, poor oral intake and constipation for 3 days; poor social interaction, withdrawn behaviour and disturbed sleep for 2 months; and on and off headache for 9 years, which had become more severe and frequent over the 2 months prior to presentation. The patient was treated with an EHRZ regimen with steroid coverage, and the symptoms subsequently resolved after treatment. Our patient presented with a 1-year history of altered behaviour with poor

social interaction. She had a short history of fever and poor oral intake, which had brought her to medical attention. She had no fulminant symptoms. The delay in diagnosing her TB meningitis was due to the indolent nature of her presentation.

TB meningitis should be considered in patients with no background of psychiatric illness presenting with psychotic disorder,

especially in countries with a high TB burden. A high index of clinical suspicion is needed to diagnose TB meningitis. This report is intended to increase clinician awareness of late 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.

Learning points

- ▶ Tuberculous meningitis (TB meningitis) is not uncommon in the central nervous system.
- ▶ Initial manifestation varies widely and may cause difficulty in diagnosis.
- ▶ TB meningitis should be considered in all patients with altered behaviour, mainly with duration of more than 1–2 weeks, with or without fever, and with or without meningeal signs, especially in countries with a high TB burden.
- ▶ Cerebrospinal fluid analysis is crucial for suspicion: lymphocytic pleocytosis and increased protein are very common and suggestive findings.
- ▶ Imaging is very important in the decision-making for empirical treatment in real life, if available.

Competing interests None declared.

Patient consent Obtained.

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