CASE REPORT

The challenge of differentiating tuberculous meningitis from bacterial meningitis

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INTRODUCTION

Tuberculous meningitis (TBM) is a rare disease caused by reactivation of latent tuberculosis infection or primary tuberculosis, such as miliary tuberculosis. Given the moderate burden of tuberculosis in Japan, miliary tuberculosis is an important differential diagnosis for impaired consciousness. Here, we report a case of TBM that was treated as bacterial meningitis but was later revealed to be miliary tuberculosis, and we discuss the challenges of differential diagnosis in this rare case.

CASE REPORT

An 83-year-old woman presented to a local hospital with fever, general malaise and loss of appetite of 20 days’ duration (starting at day −40). On presentation, her Japan Coma Scale (JCS) and Glasgow Coma Scale (GCS) scores were II-10 and E3V4M5, respectively. Investigations revealed an increased cell count and elevated glucose level in cerebrospinal fluid (CSF). She was started on 0.5 g imipenem + cilastatin every 8 h as antimicrobial medication for bacterial meningitis, but her condition did not improve. She was transferred to a second hospital on suspicion for cholecystitis, then to a university hospital when consciousness did not improve and finally to us at a fourth hospital. On day −2, diffuse granulation was seen in both lung fields on chest computed tomography, sputum Mycobacterium test was positive and adenosine deaminase was elevated in spinal fluid. We diagnosed TBM secondary to miliary tuberculosis and started treatment with steroids and anti-tuberculous drugs (day 0). However, her level of consciousness did not improve and she died at a sanatorium on day 178. Delayed treatment of TBM has a prognostic impact and should be kept in mind as a differential diagnosis for impaired consciousness.

KEYWORDS

cognitive impairment, miliary tuberculosis, tuberculous meningitis

Abstract

Tuberculous meningitis (TBM) is a rare but important differential diagnosis in patients with impaired consciousness. Here, we describe a case of TBM in an 83-year-old Japanese woman who presented to a local hospital with fever and decreased consciousness of 20 days’ duration (from day −40). She was started on treatment for bacterial meningitis due to an increased cerebrospinal fluid cell count, but her condition did not improve. She was transferred to a second hospital on suspicion for cholecystitis, then to a university hospital when consciousness did not improve and finally to us at a fourth hospital. On day −2, diffuse granulation was seen in both lung fields on chest computed tomography, sputum Mycobacterium test was positive and adenosine deaminase was elevated in spinal fluid. We diagnosed TBM secondary to miliary tuberculosis and started treatment with steroids and anti-tuberculous drugs (day 0). However, her level of consciousness did not improve and she died at a sanatorium on day 178. Delayed treatment of TBM has a prognostic impact and should be kept in mind as a differential diagnosis for impaired consciousness.
level of adenosine deaminase (ADA) was detected in CSF. Polymerase chain reaction (PCR) test for tuberculosis was positive, so she was transferred to the fourth hospital, the National Hospital Organization Utsunomiya Hospital, to start treatment for tuberculosis (day 0).

On admission, she had a JCS score of III-100 and a GCS score of E1V2M4. Her body mass index was low at 16.6 (height 145.0 cm, weight 34.9 kg). She had a respiratory rate of 16/min and the temperature was 36.5°C. On physical examination, there was no light reflex in her right eye and her right pupil was dilated. There were no other noteworthy findings.

Laboratory investigations revealed elevated hepatobiliary enzymes (aspartate transaminase 24 IU/L, alanine transaminase 27 IU/L, total bilirubin 2.4 mg/dl, lactate dehydrogenase 298 IU/L, gamma-glutamyl transpeptidase 93 IU/L, alkaline phosphatase 300 IU/L), hyponatremia (128 mEq/L), hypokalaemia (2.9 mEq/L) and a mild inflammatory response (white blood cells 7500/μl, C-reactive protein 0.8 mg/dl). There was laboratory evidence of poor nutrition (total protein 5.5 g/dl, albumin 2.8 g/dl). T-SPOT® test (interferon-gamma release assay, Oxford Immunotec, UK) was positive. Mycobacterium culture was positive on day 2. CSF analysis revealed increased cell count, increased protein and elevated ADA level. Mycobacterium culture and tuberculosis-PCR tests of CSF were positive.

In terms of imaging findings, magnetic resonance imaging of the head had been unremarkable at the first hospital. Chest CT had shown a random haematogenous distribution of granular shadows on day 0 at the third hospital (Figure 1) and chest x-ray showed diffuse granular shadowing in the lungs on day 0 (Figure 2).

From day 0, we administered corticosteroids and anti-tuberculosis drugs (rifampicin 450 mg/day, isoniazid 300 mg/day, ethambutol 500 mg/day and pyrazinamide 1.5 g/day). We started corticosteroids at 0.4 g/kg/day with a plan to taper the dosage over time. Mycobacterium sputum smear and culture were negative on day 91, but her consciousness level did not recover and gradually declined to a JCS score of III-300 and GCS score of E1V1M1. She was transferred to a sanatorium on day 113 and died on day 178 after developing repeated opportunistic infections.

**DISCUSSION**

It has been reported that 42.5% of cases of cognitive impairment in the elderly are caused by infection. Tuberculosis meningitis (TBM) is a...
Tuberculosis are accompanied by TBM. If requests for a Mycobacterium smear and culture, PCR and ADA in CSF had been submitted at that time, the diagnosis could have been made.

Obtaining a detailed history and patient background factors are important when submitting laboratory requests for identifying the causative pathogen in meningitis. Unlike the acute clinical course of bacterial meningitis, TBM has a subacute course with symptoms that typically develop over 5 days or longer. TBM must also be considered if there is a history of contact with tuberculosis patients. In our ageing society, it is important to differentiate TBM from fungal meningitis (cryptococcosis, histoplasmosis, blastomycosis and coccidioidomycosis), which is an opportunistic infection with a subacute course. When meningitis is suspected in patients who are immunosuppressed, such as those who are elderly or have acquired immune deficiency syndrome, the causative pathogens considered should include M. tuberculosis and fungi.

The treatment for TBM is multiple anti-tuberculosis drug therapy, the dosage and components of which are based on the possibility of migration of M. tuberculosis to the CSF. Corticosteroids seem to improve overall survival in adults with TBM. Although we provided this patient with standard care for TBM, her impaired consciousness did not improve due to the delay in diagnosis and treatment.

Given the likelihood of poor prognosis if there is a delay in initiating treatment for TBM, all patients with meningitis should be evaluated for tuberculosis in the same way as for those presenting with pneumonia. Both imaging and CSF analysis for tuberculosis are important when making the diagnosis. TBM should be suspected in a patient with impaired consciousness and a subacute course of fever. A systemic search for the cause of the fever using whole-body CT and CSF analysis for mycobacteria is important.

**CONFLICT OF INTEREST**

None declared.

**AUTHOR CONTRIBUTION**

Momoko Kurihara was the treating physician. Tomonori Kuroki, Yushi Nomura, Otohiro Katsube, Takaumi Umetsu and Toshio Numao discussed about the treatment. Taro Shimizu and Kumiya Sugiyama supervised the clinical practice and revised the manuscript.

**DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available upon reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

**ETHICS STATEMENT**

The patient predeceased the author’s attempt to obtain consent for the publication of this case report; attempts to contact their next of kin were unsuccessful. In consultation with the Editor-in-Chief, and with permission of the author's institution ethics committee (The National Organization Utsunomiya Hospital Human Research Ethics Committee...
[HREC] approval number 02-08), the author’s fulfilled the journal’s criteria for a patient consent waiver.

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