

# A Case of Tuberculous Meningitis with Atypical Multiple Lesions

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## ABSTRACT

*This case describes a rare case of tuberculous meningitis. A 50-year old female presented with seven days of numbness on the left side, fatigue and a three-day headache. Magnetic resonance imaging (MRI) showed multiple lesions in the dorsal medulla and upper cervical spine. After admission, she developed a long-term fever, cranial nerves palsy and showed little response to corticosteroid, antibacterial and antiviral therapy. She received a diagnostic anti-tuberculous therapy (ATT); despite that, all examinations for tuberculosis were negative. After ATT lasting 16 days, she recovered and was discharged from hospital with slight asthenia and hypoesthesia.*

**Keywords:** Diagnostic treatment, multiple lesions, tuberculous meningitis

# Un Caso de Meningitis Tuberculosa con Lesiones Atípicas Múltiples

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## RESUMEN

*Este caso describe un caso raro de la meningitis tuberculosa. Una mujer de 50 años de edad se presentó con siete días de adormecimiento en el lado izquierdo, fatiga y dolor de cabeza por tres días. Las imágenes por resonancia magnética (MRI) mostraron múltiples lesiones de la médula dorsal y la espina cervical superior. Después del ingreso, la paciente desarrolló una fiebre de larga duración, parálisis de los nervios craneales, y mostró una reacción pobre frente a la terapia corticosteroidea, antibacteriana, y antiviral. Ella recibió tratamiento antituberculoso (TAT) diagnóstico. A pesar de ello, todos los exámenes para la tuberculosis fueron negativos. Después de 16 días de TAT, se recuperó y fue dada de alta del hospital con leve astenia e hipoestesia.*

**Palabras claves:** Tratamiento diagnóstico, lesiones múltiples, meningitis tuberculosa

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## INTRODUCTION

The features of tuberculous meningitis (TBM) in the early stage are often nonspecific. Detections of tuberculosis infection of the central nervous system (CNS) including acid-fast stain and culture of cerebral spinal fluid (CSF) samples are either low-sensitive or time-consuming. All these features make the initial diagnosis complicated. Here, we present an example of an elderly female admitted with multiple lesions and her illness was finally diagnosed as tuberculous cerebrospinal meningitis.

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## CASE REPORT

A 50-year old woman was admitted to our hospital with 11 days of numbness on her left side, fatigue and three days of headache. She had a history of allergy to penicillin and a history of blood transfusion reaction. On physical examination, her neurological test revealed Glasgow coma scale (GCS) score of 15, uvula deviating to the right, and hypoesthesia of the cheek and left side. Manual muscle testing (MMT) was 4/5 for muscles on the left. Finger-nose test on the left was positive. Magnetic resonance imaging (MRI) showed multiple lesions isointense on T1, hyperintense on T2 in the left dorsal medulla and upper cervical spine (Fig. 1). Enhanced scan showed negative result. She received empiric treatment with edaravone (60 mg·d<sup>-1</sup>), notoginsenoside (400 mg·d<sup>-1</sup>), aspirin (100 mg·d<sup>-1</sup>) and simvastatin (20 mg·d<sup>-1</sup>) in consideration of cerebral infarction. Lumber puncture on day three showed increased

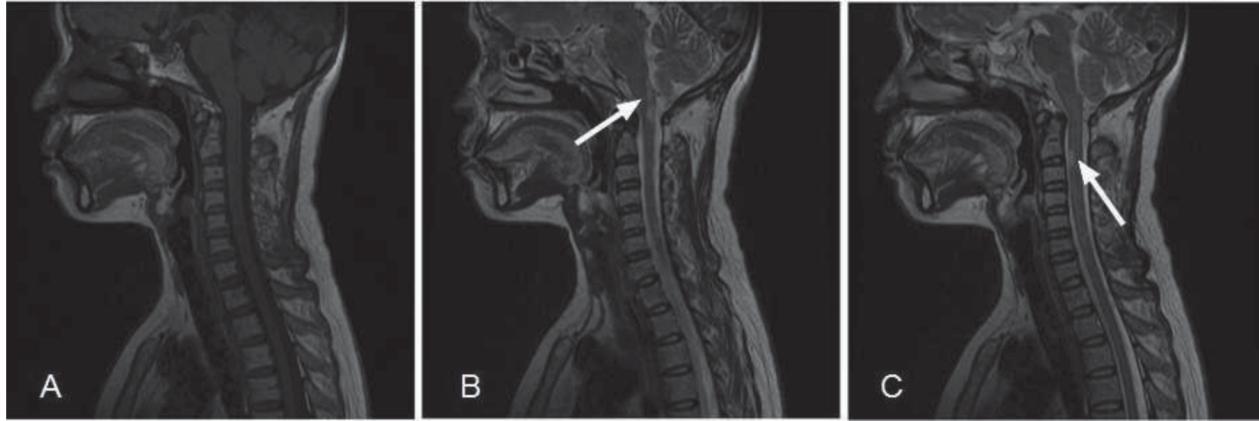


Fig. 1: Sagittal magnetic resonance imaging (MRI) shows multiple lesions isointense on T1 (A) and hyper-intense on T2 (arrows) in the dorsal medulla (B) and C2–3 level of the spinal cord (C).

white blood count (WBC;  $20/\mu\text{L}$ , lymphocyte 80%); biochemical markers were normal. The results of Gram stain, ink capsule stain and acid-fast stain of the CSF sample were negative. On day six, the patient developed hoarseness. Her speech and breathing became laboured. The CSF oligoclonal band detection showed abnormal IgG oligoclonal band. We considered the diagnosis as demyelinating disease, most likely multiple sclerosis, or viral infection in the early stage. Therefore, corticosteroid (pulsed methylprednisolone followed by prednisone) and antiviral (acyclovir  $1500\text{ mg}\cdot\text{d}^{-1}$ ) therapy was started.

Her hoarseness and breathing improved on the 10<sup>th</sup> day; however, she got a fever of  $38.3\text{ }^{\circ}\text{C}$  and became anxious. Computed tomography (CT) of the chest showed inflammation in the right mid-lung (Fig. 2), but her blood test

remained normal (WBC  $6400\text{ mm}^3$ , neutrophil 70%). Repeat lumbar puncture showed only an increase of WBC count ( $42/\mu\text{L}$ , lymphocyte 47%). Infectious screening including virus, parasite and mycobacterium tuberculosis both in the CSF and blood were negative. Bone marrow biopsy eliminated blood disease (*eg* leukaemia or lymphoma). We asked the patient again about her clinical course before admission. She recalled a close contact with a patient with active pulmonary tuberculosis recently. However, the following tuberculosis spot test was negative. She received empiric ciprofloxacin and meropenem on the consideration of nosocomial pneumonia, and steroids were gradually ceased as well as the acyclovir after a 10-day therapy. Over the next 20 days, she was still febrile and gradually developed a diplopia. Visual evoked potential (VEP) showed impairment in the right visual conducting pathway, which meant damage to the right optic nerve. Her condition worsened.

We still suspected TBM due to her close tuberculosis contact and the clinical duration, so anti-tuberculosis therapy was administered as a diagnostic treatment on the 34<sup>th</sup> day, with isoniazid (600 mg), rifampicin (450 mg), pyrazinamide (500 mg), and streptomycin (750 mg) per day.

After initiation of anti-tuberculosis therapy, her body temperature dropped to normal within three days, the headache was relieved gradually, and her mental and neurological status markedly improved. Lumbar puncture findings became negative after 16 days of anti-tuberculosis therapy. The disease was finally diagnosed as tuberculous meningitis. She was discharged on the 54<sup>th</sup> day with slight asthenia and hypoesthesia on her left side. Anti-tuberculosis therapy continued for 18 months.

## DISCUSSION

Tuberculous meningitis is the most severe form of extrapulmonary tuberculosis. Despite modern anti-tuberculosis therapy, the fatality and disability rate still remains high (1), especially in developing countries, and 9.8%–33.3% of the TBM patients will die, with the rest (15.4%–60.6%)

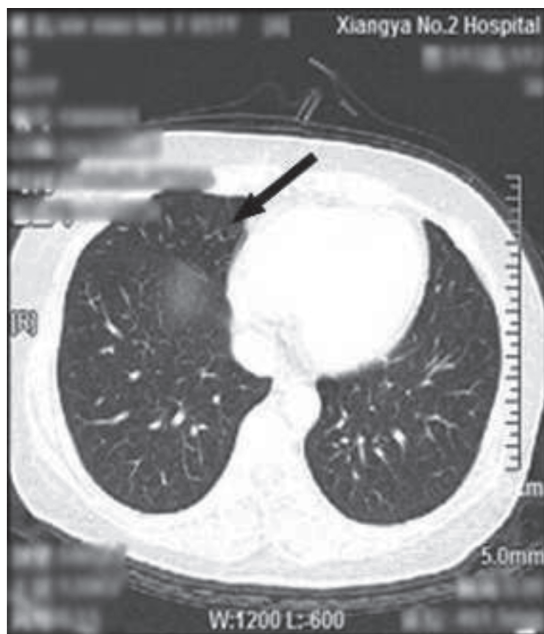


Fig. 2: Chest computed tomography (CT) shows string-like and patchy shadow (arrow) in the medial region of the middle lobe of the right lung.

developing significant neurological deficits (2). China ranks second among the 22 high-burden countries which account for 80% of the tuberculosis cases (3).

The gold standard for diagnosis of TBM is the isolation of *Mycobacterium tuberculosis* in CSF, either by direct microscopy or culture (4, 5). However, the sensitivity of acid-fast smear varies between 10% and 60%; culture of CSF is positive between 25 and 75% of cases, and takes two to six weeks (1). According to the Thwaites criteria, patients can be defined as “possible” and “probably” TBM cases based by the symptom duration, biochemical marker changes of CSF and evidence of tuberculosis at other sites (4, 5). Some Chinese scholars suggested changes on CT or MRI, and abnormal findings on fundoscopic examination as additional features for diagnosis in Chinese cases.

Our case was probably TBM according to the Thwaites criteria (5). Distinguishing features worthy of suspicion of TBM are as follows: (i) close contact with an active pulmonary TB case; (ii) long-lasting fever; (iii) changes in mentation; (iv) focal neurologic deficits (diplopia, hoarseness, distaxia, fatigue and numbness on the left side) and (v) predominance of lymphocytes in the cerebrospinal fluid. Though there was no direct evidence for tuberculosis infection and cranial MRI showed multiple lesions in the atypical “tuberculous zone” (6) without enhancement around the side, we still suspected TBM by the clinical features, and the diagnostic treatment with anti-tuberculosis therapy gave a curative effect.

Laboratory and imaging findings can be nonspecific in atypical TBM cases. As for the CSF changes, neutrophils can reach a high proportion since a neutrophilic response is predominant in the early stage of infection (1); glucose and chlorine can be normal (7) and protein reflects the TBM grade and may be low in the first stage (1). Sensitivity and specificity of tuberculosis-specific antibody in CSF are 52%–93% and 58%–99%, respectively (2). For MRI scanning, decreased immune responses to the mycobacterium may lead to absence of the typical imaging features (8). According to Katrak *et al*, patients with HIV infection are more likely to develop cerebral atrophy, infarcts and granuloma compared to the HIV negative patients (9). Besides, the presence of CSF oligoclonal IgG bands is not specific for multiple sclerosis; it is found in 85% of patients who have defined multiple sclerosis, but can also be seen in cranial infectious disease (10). This proved a fact that it is not always a straightforward approach for the diagnosis of TBM.

There must be a high index of suspicion for TBM when patients complain of headache and long-standing fever, together with cranial nerve palsy, focal neurologic deficits and changes in mentation. They tend to have subacute courses. General antibiotic and antibacterial therapy would not relieve the fever. Imaging changes, both in the cranial MRI and chest CT, can be slight especially as it relates to an elder or HIV-positive patient. At the first suspicion of tuberculous meningitis, effective anti-tuberculosis therapy should be initiated and this might be an approach to diagnosis. The CSF parameters usually return to normal two to three weeks after initiation of anti-tuberculosis therapy. Thus, TBM is confirmed.

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