


Case Report

Tuberculous meningitis with good outcome following appropriate timing of ventriculoperitoneal shunting for hydrocephalus

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Background: Tuberculous meningitis is often associated with hydrocephalus. However, the appropriate timing for shunt placement to treat hydrocephalus remains controversial.

Case Presentation: A 43-year-old man presented with high fever and disturbance of consciousness. Cerebrospinal fluid (CSF) findings showed pleocytosis, increased protein levels, and hypoglycemia with an elevated pressure of 30 cm H₂O. Brain magnetic resonance imaging revealed cerebral infarctions and hydrocephalus resulting in suspicion of tuberculous meningitis. A few days after admission, external ventricular drainage was carried out for acute hydrocephalus. Four antitubercular drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol) as well as dexamethasone sodium phosphate were given. The CSF polymerase chain reaction test for tuberculosis was found to be positive 2 weeks later. Once CSF protein levels improved, a ventriculoperitoneal shunting operation was undertaken.

Conclusions: When tuberculous meningitis is suspected, treatment with antitubercular drugs should be initiated prior to definitive diagnosis, and a shunt surgery should be carried out in a timely manner.

Key words: Cerebrospinal fluid, hydrocephalus, Thwaites' diagnostic criteria, tuberculous meningitis, ventriculoperitoneal shunt

INTRODUCTION

The rate of tuberculous meningitis in extrapulmonary tuberculosis is reported to be approximately 1%–5%.¹ Hydrocephalus is a complication occurring in approximately 80% of cases of tuberculous meningitis; however, there is still controversy regarding the appropriate timing of shunt placement to treat hydrocephalus.²

We report a case of tuberculous meningitis in which ventriculoperitoneal (VP) shunting was carried out at an appropriate time to treat associated hydrocephalus.

CASE REPORT

A 43-year-old man consulted his primary care doctor with a complaint of a headache. Computed tomography (CT) scan of the brain showed no abnormal findings. The patient

became febrile on day 3 of illness and gradually became more disoriented. He was admitted to our hospital on day 10, as he appeared to be aggravated with abnormal speech and behavior. The patient had no relevant medical history or any contact with patients with tuberculosis. Although he worked for the Japan Self-defense Forces, he had no history of overseas missions.

He had clouding of consciousness and a Glasgow Coma Scale (GCS) of 10 (E4V1M5). The body temperature was 38.8°C, and chest sounds were clear. Laboratory findings revealed a mild inflammatory reaction indicated by a white blood cell count of $6,600 \times 10^3/\text{mL}$ and C-reactive protein level of 1.42 mg/dL. Cerebrospinal fluid (CSF) examination showed a pressure of 30 cmH₂O, cell count $139 \times 10^3/\text{mL}$ ($129 \times 10^3/\text{mL}$ mononuclear cells), protein level 142 mg/dL, sugar level 20 mg/dL (117 mg/dL simultaneous blood glucose), and chlorine level 104 mEq/L. The acid-fast bacteria smear culture test of CSF and India ink staining were both negative. The total score of Thwaites' criteria was 1. Chest X-ray and chest and abdominal CT showed no abnormal findings. Brain diffusion-weighted magnetic resonance

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imaging (MRI) showed a high-intensity spotty lesion at the splenium of the corpus callosum (Fig. 1A).

The patient was diagnosed with meningitis and treatment was started with intravenous meropenem hydrate at 2 g every 8 h as well as aciclovir at 10 mg/kg every 8 h. On day 14, an emergency external ventricular drainage (EVD) system was inserted to treat acute hydrocephalus with a GCS score of 8 (E2V4M2) (Fig. 1B). The next day, tuberculous meningitis was suspected, and the patient was treated with the following four antitubercular drugs: 5 mg/kg/day isoniazid (INH), 600 mg/day rifampicin (RFP), 2 g/day pyrazinamide (PZA), and 1 g/day ethambutol (EB). In addition, the patient was treated with 13.2 mg/day dexamethasone sodium phosphate. On day 18 of illness, brain MRI revealed multiple high-intensity spotty lesions with diffusion-weighted imaging and abnormal gadolinium enhancement and thickening of the meninges with T1-weighted imaging. Brain magnetic resonance angiography showed multiple stenoses of the bilateral internal carotid arteries (Fig. 1C–E).

Following EVD, the patient's consciousness improved to a GCS score of 11 (E3V3M5). The dose of dexamethasone sodium phosphate was gradually reduced and changed to 1 mg/kg/day prednisolone, which was also gradually

reduced. Acyclovir was discontinued on day 28 as the CSF polymerase chain reaction (PCR) test was negative for herpes, and the EVD tube was removed the next day. However, on day 29, spinal drainage was carried out secondary to worsening consciousness due to the reaggravation of hydrocephalus.

On day 33, treatment with meropenem hydrate was discontinued because the CSF PCR test was positive for tuberculosis. Furthermore, the PCR test of the sputum was negative for tuberculosis. On day 40, CSF findings improved with a cell count of $11 \times 10^3/\text{mL}$ ($6 \times 10^3/\text{mL}$ mononuclear cells), protein level 70 mg/dL, and sugar level 47 mg/dL. A VP shunt was surgically placed on day 48.

Eventually, on day 61, the patient was relocated to a rehabilitation hospital with a modified Rankin Scale score of 3 with attention and memory impairment (Fig. 2). He returned to work with only mild weakness of the left lower limb (modified Rankin Scale score of 1) 10 months after illness.

DISCUSSION

It is important to promptly diagnose patients with suspected tuberculous meningitis and to begin appropriate treatment

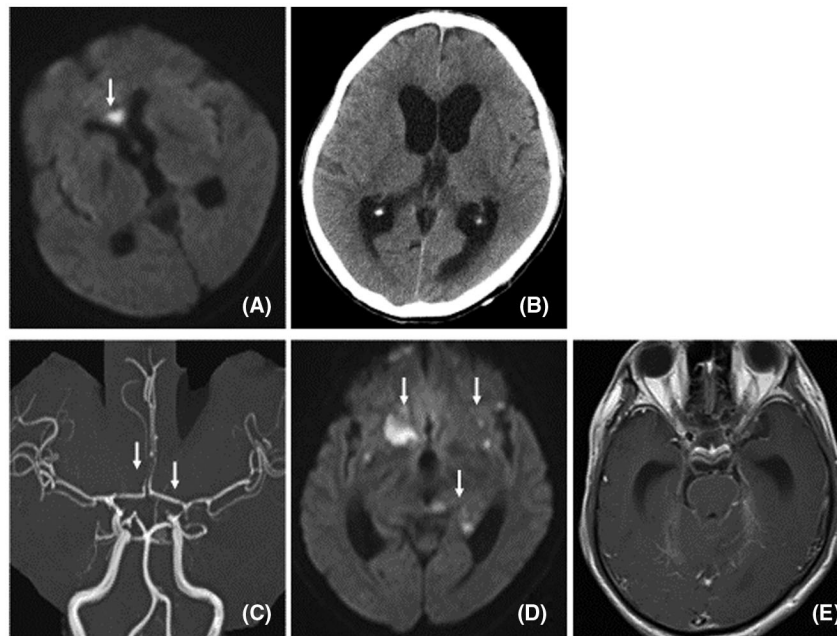


Fig. 1. A, Diffusion-weighted (DW) magnetic resonance imaging (MRI) of the brain on admission of a 43-year-old man with tuberculous meningitis. Brain DW-MRI showing a high-intensity spotty lesion at the splenium of the corpus callosum (arrow). This lesion is most likely an acute infarction. B, Computed tomography (CT) scan of the brain on day 14 of illness. CT showing the expanded lateral ventricles due to acute hydrocephalus. C–E, MRI and magnetic resonance angiography (MRA) of the brain on day 18. MRA of the brain showing multiple stenoses of bilateral internal carotid arteries (arrows) (C). MRI of brain showing multiple high-intensity spotty lesions with DW imaging (arrows) (D) and abnormal enhancement of meninges with MR-T1-weighted image using contrast medium (E).

early to promote good outcomes.³ In our case, CSF smear test was negative, but the tuberculosis smear examination has a true positive rate (sensitivity) of only 5%–40% with a specificity of approximately 80%.⁴

Thwaites *et al.* have proposed diagnostic criteria for tuberculous meningitis (Thwaites' diagnostic scoring indexes [TDSI]) with an emphasis on rapidity.⁵ A point system is utilized for diagnosis, and a score of 4 or less is suggestive of tuberculous meningitis. Patients aged 36 years or older are assigned 2 points, and those under 36 years of age are given 0. Laboratory findings of white blood cell counts of $15,000 \times 10^3/\text{mL}$ or more are given 4 points, while lower counts are given 0 points. Cerebrospinal fluid cell counts of $900 \times 10^3/\text{mL}$ or more are assigned 3 points, and lower counts are given 0 points. Furthermore, the amount of neutrophils found in CSF is given 4 points when the number of spheres is 75% or more, and 0 points when the percentage is lower. The clinical course is -5 points within 6 days of onset and 0 points following this specified onset time. Tuberculous meningitis is diagnosed when the total score is 4 or lower.

Similarly, the Marais' scoring indexes (MDSI) have been found to be useful for rapid diagnosis.^{6–8} The MDSI include more detailed clinical and imaging findings compared to the TDSI. Imaging is particularly important, with hydrocephalus and basal meninges contrast effects being characteristic. Contrast enhancement of the basal meninges is seen in 89% of cases of tuberculous meningitis.⁶ Furthermore, the presence of cerebral infarction is also considered a highly

specific finding. In our case, the cerebral imaging criteria were 6 points, for a total of 16 points, which is considered possible tuberculous meningitis (Table 1).

By using readily available clinical and laboratory findings, clinicians might suspect tuberculous meningitis from the day of admission and can start treating patients in a timely manner. The specifics of drug therapy for tuberculous meningitis have not yet been established. For example, the World Health Organization recommends INH, RFP, PZA, and EB for the first 2 months and INH and RFP for the next 7–10 months for extrapulmonary tuberculosis, including tuberculous meningitis.⁹

Gadolinium enhancement of the basal meninges and hydrocephalus and multiple cerebral infarctions caused by cerebral artery stenosis, which are typical imaging characteristics of tuberculous meningitis, were observed in our case.¹⁰ Delay in the treatment of hydrocephalus associated with tuberculous meningitis greatly affects the prognosis. Therefore, it is important to appropriately treat hydrocephalus at an early stage.^{11,12} Singh *et al.* proposed an indication for shunt placement when any one of the following conditions is satisfied: (i) presence of symptoms of intracranial hypertension, such as headache, vomiting, stasis papilla, consciousness disorder, and walking disorder; (ii) brain CT or MRI revealing expansion of the ventricle accompanied by edema around the cerebral ventricle; (iii) a CSF cell count of $\leq 5/\text{cm}^3$; or (iv) improvement of intracranial hypertension symptoms following EVD.^{13,14} In this study, EVD was used to address acute hydrocephalus but was then changed to

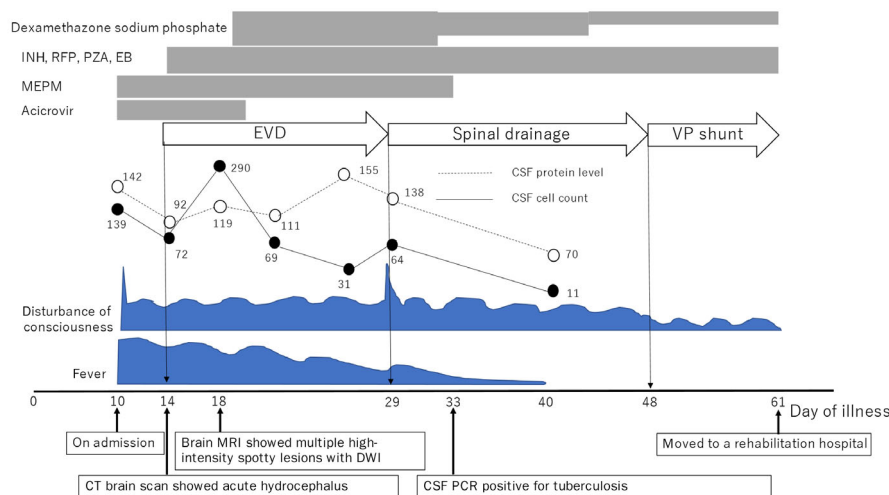


Fig. 2. Summary of course after admission of a 43-year-old man with tuberculous meningitis. The schema shows symptoms, cerebrospinal fluid (CSF) findings, and treatment over time. CT, computed tomography; DWI, diffusion-weighted imaging; EB, ethambutol; EVD, external ventricular drainage; INH, isoniazid; MEPM, meropenem hydrate; MRI, magnetic resonance imaging; PCR, polymerase chain reaction; PZA, pyrazinamide; RFP, rifampicin; VP, ventriculoperitoneal.

Table 1. Diagnostic scoring indices for tuberculous meningitis

(A) Thwaites' diagnostic scoring index ^a		
Age (years)	≥36	2
	<36	0
WBC (× 10 ³ /mL)	≥15,000	4
	<15,000	0
History of illness (days)	<6	0
	≥6	−5
Cells in CSF (× 10 ³ /mL)	≥900	3
	<900	0
Neutrophils in CSF (%)	≥75	4
	<75	0
(B) Marais' diagnostic scoring index ^b		
Clinical criteria	Symptom duration >5 days	4
Max. score 6	Systemic symptoms suggestive of Tb: weight loss, night sweats, or persistent cough for >2 weeks	2
	History of recent close contact with an individual with pulmonary Tb or a positive TST or IGRA	2
	Focal neurological deficit	1
	Cranial nerve palsy	1
	Altered consciousness	1
CSF criteria	Clear appearance	1
Max. score 4	Cells: 10–500 × 10 ³ /mL	1
	Lymphocytic predominance (>50%)	1
	Protein concentration > 100 mg/dL	1
	CSF to plasma glucose ratio < 50% or an absolute CSF glucose concentration < 39.6 mg/dL	1
Cerebral imaging criteria	Hydrocephalus	1
Max. score 6	Basal meningeal enhancement	2
	Tuberculoma	2
	Infarction	1
	Precontrast basal hyperdensity	2
Evidence of Tb elsewhere	Chest radiograph suggestive of active Tb (signs of Tb, 2; miliary Tb, 4)	2, 4
Max. score 4	CT/MRI/ultrasound evidence for Tb outside the CNS	2
	AFB identified or MTB cultured from another source (sputum, lymph node, gastric washing, urine, blood culture)	4
	Positive commercial MTB NAAT from extraneural specimen	4

Abbreviations: AFB, acid-fast bacilli; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; IGRA, interferon-gamma release assay; Max., maximum; MRI, magnetic resonance imaging; MTB, *Mycobacterium tuberculosis*; NAAT, nucleic acid amplification test; Tb, tuberculosis; TST, tuberculin skin test; WBC, white blood cell.

^aTuberculous meningitis is diagnosed when the total score is ≤4.

^bProbable tuberculous meningitis: a diagnostic score of ≥12 is required when imaging is available, and a score of ≥10 when imaging is not available. Possible tuberculous meningitis: a diagnostic score of 6–11 is required when imaging is available, and a score of 6–9 when imaging is not available.

spinal drainage. Due to the persistence of hydrocephalus, we successfully placed a VP shunt on day 48.

Potential adverse effects of early shunt surgeries include shunt infection or occlusion.¹⁵ Ambekar et al. reported that shunt dysfunction was unrelated to CSF cell count and

glucose level but was related to CSF protein level. Furthermore, they reported that the risk of shunt dysfunction in cases with ≥200 mg/dL of CSF protein is quadruple that of cases with ≤100 mg/dL.¹⁵ As we were able to control the cell count and CSF protein levels through EVD and spinal

drainage, the VP shunt was completed without shunt dysfunction.

CONCLUSION

For patients with tuberculous meningitis, antitubercular medications should be given promptly according to the proposed measurements of the TDSI and MDSI. When hydrocephalus is a complication, it is important to determine the appropriate shunt timing while confirming the properties of CSF. The clinical course of hydrocephalus secondary to tuberculous meningitis varies from case to case and so does the timing of VP shunting; however, if hydrocephalus is not treated quickly, it results in poor prognosis. On the other hand, a treatment completed too early runs the risk of dysfunction. Although it is difficult to discuss definitive events in this single case report, the appropriate timing of shunting for each case should not be overlooked.

DISCLOSURE

Approval of the research protocol: N/A.

Informed consent: Written informed consent was obtained from the patient for publication of this case report.

Registry and registration no. of the study/trial: N/A.

Animal studies: N/A.

Conflict of interest: None.

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