

## Clinical management of tuberculous meningitis: experiences of 42 cases and literature review

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**Abstract** Tuberculous meningitis (TBM) is common infectious disease. Early diagnosis and timely treatment are critical for the cure of the disease. Thwaites standard is widely accepted but not the golden standard. Here, we analyzed 42 cases of TBM patients in local hospital and combined with literature review to provide more information in TBM management.

**Keywords** Tuberculous meningitis · Case report · Literature review

### Introduction

The tuberculous disease showed world-wide increase since 1985, and has become a serious problem for public health [1, 2]. One-third of the population were infected, in which 95 % cases were in developing countries. Tuberculous meningitis (TBM) is caused by *Mycobacterium tuberculosis* infection to the meninges, which surrounds the central nervous system. TBM could lead to high mortality rate (100 % if untreated) [3–6]. Even with anti-tuberculous treatment, 30 % TBM patients would still die.

Thwaites standard has been developed for early diagnosis of TBM [2, 3, 7–9]. Yet in different countries and with different population, the TBM patients were found to be with different symptoms. In the present study, we retrospectively reviewed 42 cases of TBM patients from 2009

to 2011 in our hospital to provide more information in clinical management of TBM patients.

### Clinical data

42 Cases of TBM patients (23 male, 19 female) were retrospectively analyzed. Five cases aged <20, nine cases aged 20–40, 11 cases aged 40–60 and 17 cases aged >60 years. The time interval between disease symptom and the hospitalization was 5–10 days 7 cases, 10 days to 1 month 12 cases, and more than 1 month 14 cases.

No specific clinical symptoms were found. The common symptom included headache (39/42), fever (40/42), nausea/vomit (16/42), sleepiness/coma/unconsciousness (18/42), urinary retention (4/42), decreased vision (4/42), psychiatric symptoms (1/42), hemiparalysis (1/42), paraplegia (1/42), epilepsy (1/42).

On cerebrospinal fluid (CSF) examination, 36 cases showed normal CSF while six cases showed yellow color. For the CSF pressure: ten cases more than 300 mmH<sub>2</sub>O, 11 cases 200–300 mmH<sub>2</sub>O, and 21 cases less than 200 mmH<sub>2</sub>O. For the white blood cell count, 14 cases <100 × 10<sup>6</sup>/L, ten cases 100–200 × 10<sup>6</sup>/L, and 18 cases >200 × 10<sup>6</sup>/L. With biochemical examination of CSF: 20 cases showed normal glucose level, four cases with increase and 18 cases with decreased levels. 32 cases showed decrease in chloride level: four cases were less than 100 mM/L, 12 cases were 100–110 mM/L and 16 cases were 110–120 mM/L. The CSF protein levels showed increase: eight cases were 0.5–1.0 g/L, 17 cases were 1–2 g/L and 17 cases were more than 2 g/L.

Radiological examinations included MRI or head CT scan. 14 Cases demonstrated typical tuberculosis infected sites in multiple brain areas, including frontal cortex and

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ganglia. Two cases showed hydrocephalus, and nine cases showed no clear abnormality. Nine cases showed other types of diseases: seven cases were ischemia, one cases degeneration and 1 case of cystic lesion.

The peripheral ESR and CRP levels were measured. 25 Cases showed ESR less than 20 mm/h, nine cases 20–40 mm/h and seven cases >40 mm/h. For CRP, 30 cases showed normal range, while 12 cases showed increase.

The CSF culture of tuberculosis bacteria was negative for all cases. Six patients went for T-SPOT examination, and four cases showed positive signs, including two cases in the central nervous system, 1 case in spleen and 1 case in lung.

For the clinical management, the patients were treated with HRZE and DXM, with or without fluoroquinolone. 35 Cases were cured, four cases showed no change and three cases left hospital with no improvement.

Surprisingly, according to Thwaites standard, no patients were diagnosed as TBM. 13 Cases were suspected as TBM and 26 cases were only showing such possibility.

## Discussion

The authors believe that the diagnosis of tuberculous meningitis should be based on combined examinations of clinical symptoms, CSF, radiology as well as the existence of tuberculous in the body. The detection of *Mycobacterium tuberculosis* (MTB) from CSF was considered as critical criteria for the diagnosis, which was not found in all cases described here. It is also believed that the CSF from TBM patients demonstrated increased protein levels, decreased glucose and chloride levels, increased cells such as lymph cells. In the present study, we found that no clear CSF transition was reported, leading to the early diagnosis as other infection diseases to the central nervous system.

In the radiological examinations, enhanced MRI showed better results compared to the CT examination, with bigger lesion revealed. Previous study showed that the MTB invasion into the head with blood circulation caused early edema in the cranial base (pial and ependymal), with multiple symptoms following such as tuberculous formation [10–12]. In the early phase, MRI examination would show enhanced signal and asymmetric signals, while in the middle or late phase the signal is strong in the meningitis. This should be differentiated from other brain diseases such as tumor. Therefore, MRI examination should be a critical examination for TBM patients, and need to be performed repeatedly to follow the dynamic changes of the disease.

The erythrocyte sedimentation rate (ESR) has been found to be increased in TBM patients [3, 4, 13–15], while

in the present study 61 % patients showed normal ESR. Among the patients showing the increase, the percentage of increase did not correlate with the disease state, sex and progression ( $P > 0.05$ ). Therefore, we conclude that the ESR has limited value as the diagnosis factor.

We also employed enzyme-linked immunospot assay (ELISPOT) to detect antibody or cytokine secretion at cellular level. We found the IFN secretion by T cells when induced by T-SPOT TB test, with high sensitivity and specificity [16]. This also brings lower costs compared to flow cytometry, and we consider this as a useful technique for TBM diagnosis.

Last but not least, we treated all 42 cases of TBM patients with standard HRZE protocol, with fluoroquinolone supplemented for some patients. If the patient did not show significant improvement after 1 month, the drug-resistant TBM should be considered and Zyvox (linezolin) should be considered according to our own experiences.

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**Conflict of interest** None declared.

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