



TUBERCULAR MENINGITIS - A CASE SERIES

General Medicine

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ABSTRACT

Tuberculosis (TB) has affected humanity since the beginning of the recorded time and is associated with various other aspects like poverty, malnutrition, overcrowding, and immunosuppression. Objective: To study the clinical, pathological and radiological profile in cases of Tubercular Meningitis. **Material And Methods:** A retrospective case series of five cases of Meningeal TB who presented to the Medicine and Pulmonary Medicine department of Dr. D.Y. Patil Hospital, Navi Mumbai, India, over a period of two months (October - November 2021). The data regarding the demographic details, clinical course and outcome of the patients was collected from the hospital database. Utmost care was taken to maintain the privacy and confidentiality. **Results:** Five cases of TBM were studied over a period of 2 months. Fever was the most common symptom in these cases, followed by headache, neck rigidity and altered mental status. Out of five cases, in 2 cases Tuberculoma was found in MRI (P+C) and in 2 cases Miliary Kochs was found on HRCT Chest (P+C). All patients were started on ATT via DOTS. 1 patient was brought back to the hospital with stroke as a complication. **Conclusion:** For patients with EPTB, bacteriological evaluation of the response to treatment is often limited by the difficulty in obtaining follow-up specimens. It is important to use both clinical and radiographic findings to judge the effectiveness and response of the on-going treatment. Even though there has been some progress, the need of the hour is the availability, accessibility and affordability of more sensitive diagnostic tests and better drug therapy.

KEYWORDS

Tubercular Meningitis, Extrapulmonary TB, Mycobacterium tuberculosis, ATT, DOTS.

INTRODUCTION

Tuberculosis (TB) has affected humanity since the beginning of the recorded time and is associated with various other aspects like poverty, malnutrition, overcrowding, and immunosuppression. Since its discovery, the infectious nature of the disease has advanced, and it remains a leading cause of death globally.^{1,2}

Clinically, Tuberculosis can manifest as pulmonary TB (PTB) and extrapulmonary TB (EPTB).³ The most frequent clinical presentations of EPTB are often lymphadenitis, pleuritis and osteo-articular TB. 4-6 It is observed that young age, female gender, Asian and African origin, and human immunodeficiency virus (HIV) infection are independent risk factors for EPTB.⁷

The incidence rate of EPTB has increased worldwide, causing a renewed interest in the extrapulmonary forms of tuberculosis among the scientific community. Dissemination of TB to the brain results in the most severe form of extrapulmonary tuberculosis, Tubercular Meningitis (TBM). TBM has high rates of mortality and disability, hence represents a medical emergency. Although the occurrence of TBM is relatively rare in children, but it is associated with higher rates of mortality and continues to be a common cause of neuro-morbidity.^{8,9}

Cultures of *M. tuberculosis* obtained from specimens (collected from patients), play a vital role in the definitive diagnosis of TB. However, diagnosis of EPTB often becomes challenging as the clinical samples obtained from relatively inaccessible sites may be paucibacillary, which can decrease the sensitivity of diagnostic tests. Anti-TB treatment remains the mainstay treatment in the management of EPTB, though the optimal duration of therapy is still debatable. Six months of standard anti-TB medical therapy is generally considered adequate for most forms of EPTB, but longer treatment is often suggested in a case of TB meningitis.³

The frequency and kinds of evaluation depends on the sites involved, severity of disease, and the ease with which specimens can be obtained. Due to lack of availability of smear microscopy or culture to monitor patients with EPTB, clinical monitoring is the usual way to assess the response to treatment. In contrast with PTB treatment, cure for EPTB is difficult to define due to lack of established data, regimens and criteria for the end of treatment.

CASE 01

A 16 year old female presented with fever, neck rigidity and altered mental status. She was subjected to radiological investigations, and on HRCT Chest (P+C), it was observed that she had Miliary Kochs. She was started on ATT via DOTS. Definitive diagnosis of TBM was made with the help of CSF Studies. She gradually improved clinically and was discharged home.

CASE 02

A 27 year old female presented with fever, neck rigidity, headache and altered mental status with a history of 1 episode of seizure. On examination, it was observed that she had photophobia and papilledema. Clinically, Kernig's Sign was positive. Definitive diagnosis of TBM was made with the help of CSF Studies. She was started on ATT via DOTS. She gradually improved clinically and was discharged home.

CASE 03

A 54 year old female presented with fever, neck rigidity, headache and altered mental status with a history of 2 episode of seizure. On examination, it was observed that she had photophobia and papilledema. Clinically, Kernig's Sign and Brudzinski's Sign were positive. On subjecting her to radiological investigations, Tuberculoma was found on MRI (P+C). Definitive diagnosis of TBM was made with the help of CSF Studies. She was started on ATT via DOTS. She seized once during her course of treatment at the hospital. She gradually improved clinically and was discharged home. She had a stroke and was brought back to the hospital. She passed away after 2 days of arrival.

CASE 04

A 23 year old male presented with fever, neck rigidity, headache and altered mental status with a history of 1 episode of seizure. Clinically, Kernig's Sign and Brudzinski's Sign were positive. On subjecting him to radiological investigations, Tuberculoma was found on MRI (P+C). Definitive diagnosis of TBM was made with the help of CSF Studies. He was started on ATT via DOTS. He patient gradually improved clinically and was discharged home.

CASE 05

A 15 year old female presented with fever. On examination, it was

observed that she had photophobia and papilledema. Clinically, Brudzinski's Sign was positive. She was subjected to radiological investigations, and on HRCT Chest (P+C), it was observed that she had Miliary Kochs. She was started on ATT via DOTS. Definitive diagnosis of TBM was made with the help of CSF Studies. She gradually improved clinically and was discharged home.

SUMMARY

TABLE 01: SUMMARY

	CLINICAL SIGNS AND SYMPTOMS	DIAGNOSIS	COMPLICATIONS
CASE 01 16/F	Fever Neck Rigidity Altered Mental Status/Drowsy	Miliary Kochs on HRCT Chest (P+C). Definitive diagnosis of TBM with CSF Studies.	-
CASE 02 27/F	Fever Neck Rigidity Headache Altered Mental Status/Drowsy Photophobia Seizure Papilledema Kernig's Sign	Definitive diagnosis of TBM with CSF Studies.	-
CASE 03 54/F	Fever Neck Rigidity Headache Altered Mental Status/Drowsy Photophobia Seizure Papilledema Kernig's Sign Brudzinski's Sign	Tuberculoma on MRI (P+C). Definitive diagnosis of TBM with CSF Studies.	Stroke
CASE 04 23/M	Fever Neck Rigidity Headache Altered Mental Status/Drowsy Seizure Kernig's Sign Brudzinski's Sign	Tuberculoma on MRI (P+C). Definitive diagnosis of TBM with CSF Studies.	-
CASE 05 15/F	Fever Photophobia Papilledema Brudzinski's Sign	Miliary Kochs on HRCT Chest (P+C). Definitive diagnosis of TBM with CSF Studies.	-

DISCUSSION

Tubercular meningitis is the most severe form of TB, associated with significant mortality and morbidity. Yet, it is difficult to diagnose and treat these patients. Despite the treatment, morbidity and mortality in these cases remain unacceptably high. Diagnosis of TBM is often delayed by the insensitive and lengthy culture technique required for disease confirmation; hence, empirical ATT should be started if clinical suspicion is high.

It is often observed that around 10% to 50% cases of EPTB have concomitant pulmonary involvement. Therefore, it is suggested that all suspected cases of EPTB should be assessed for concomitant PTB to determine whether the case is infectious and to assist with diagnosis. In EPTB cases, there are chances to have positive sputum culture results despite normal chest radiography findings.¹⁰ The sensitivity of sputum culture is found to be 24% to 29% for TBM.¹¹

A previous study reported that AFB smears and culture positivity approached 87% and 83% respectively, in four serial CSF samples. 12 Examination of the CSF typically reveals

- leucocytosis (10-1000×103 cells/mL; mostly lymphocytes)
- raised protein (0.5-3.0 g/L)
- CSF:plasma glucose <50%

However, atypical CSF findings are well described, particularly in immune-suppressed patients, and the CSF can be acellular or contain a predominance of neutrophils.¹³

The antibiotic regimens for TBM are based on those used to treat PTB.

This can result in suboptimal drug levels in the CSF, due to poor blood-brain barrier penetrance. The role of various other therapies like adjunctive anti-inflammatory, host-directed therapies (including corticosteroids, aspirin and thalidomide) has not been extensively explored. In TB meningitis, recent randomized controlled trials and meta-analysis revealed that corticosteroids can significantly improve the disability-free survival and help in decreasing the mortality rates. Thus, adjunctive corticosteroids like dexamethasone/prednisolone are recommended to all cases, regardless of disease severity.^{14,15}

There is scant information regarding drug-resistant EPTB in the medical literature. A recent study of EPTB in Korea reported that the overall resistance rate to at least one anti-TB drug was 8.9%, and multidrug resistance rate was 1.8%, which were similar/slightly lower than those in the entire TB patients. 16 If the patient has symptoms suggestive of CNS involvement and is infected with drug-resistant TB, the regimen should use drugs that have adequate penetration into the CNS.

TBM has the propensity to cause secondary vasculitis through various mechanisms, which can lead to development of cerebrovascular complications. Tubercular vasculitis can be detected by VWI (vessel wall imaging) in the form of nodular or smooth segmental enhancement of vessel wall with or without stenosis. Incorporation of VWI (vessel wall imaging) in routine MR imaging can play a significant role in^{17,18}

- early detection of the disease
- management of cerebrovascular complications
- improve prognosis of the disease.

Optimal management regimens of neurological complications (eg. hydrocephalus and paradoxical reactions) and of hyponatraemia, which frequently accompanies TBM, remain to be elucidated. The emergence of multi and extreme drug resistant strains of M. tuberculosis further challenges the standard therapy.

CONCLUSION

Bacteriological evaluation of the response to the treatment of TBM is often limited because of the difficulty faced in obtaining the follow-up specimens. It is important to use both clinical and radiographic findings to judge the effectiveness and response of the on-going treatment.

Clinical trials are required to provide robust evidence guiding the most effective supportive, therapeutic, and neurosurgical interventions for TBM that will improve morbidity and mortality. Paediatric clinical trials on larger scale are needed to determine the appropriate place of various diagnostic and treatment methods in paediatric TBM.

Even though there has been some progress, the need of the hour is the availability, accessibility and affordability of more sensitive diagnostic tests and better drug therapy.

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