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Clinical Profile of Tuberculosis Meningitis in a Tertiary Care Hospital

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Abstract: ***Background: Tuberculosis (TB) is a major global problem and a public health issue of considerable magnitude. Approximately, eight million new cases of TB and three million deaths are reported annually. In recent times, there has been a resurgence of tuberculosis in both developing and developed countries. Among Extra - pulmonary TB, tuberculous meningitis (TBM) leads to multiple central nervous system (CNS) complications and remains a major health problem. Tuberculous Meningitis (TBM) remains an important cause of morbidity and mortality, especially in the developing world, where it accounts for 7 - 12% of the tuberculosis cases. Materials and Methods: Study Setting: This study was carried out in Dept. of General Medicine in BGS GIMS Source: A total of 70 patients of meningitis who were admitted during the study period were taken as study subjects, who fulfilled the inclusion criteria Type of Study: This is a descriptive and case control study. Inclusion Criteria: 1. All Patients presenting with fever and signs of meningeal irritation 2. Age > 18years Exclusion Criteria: 1. Any intracranial bleed or sub dural hematoma 2. Patients already on ATT Results: Total of 70 patients were included in the study, 30 were TB meningitis, 13 were pyogenic meningitis, 26 were viral meningitis, 1 was fungal meningitis. The age of TB meningitis ranged from 18 to 75 years, with a mean age of 41.8years. In TB meningitis group, male: female ratio was 1: 1. The most common symptom was fever followed by headache, altered sensorium and seizures. All the patients had neck stiffness. Papilledema was seen in 33.3%, cranial nerve palsies in 30%, hemiplegia in 16.7% and 10% of the patients were comatose. Cranial nerve palsies, especially oculomotor nerve palsies and hemiplegia were seen only in TB meningitis patients and not observed in other groups of meningitis. Conclusions: The clinical presentation of TBM is vague with non specific symptoms that are hard to distinguish from other types of meningitis. Nested PCR was found to be more sensitive, as compared to smear microscopy. As false negative results are reported on PCR, PCR alone should not be used as a criterion, It should be supported by clinical, radiological, cytological and other microbiological for guiding the clinicians in the decision making for the appropriate therapy.***

Keywords: Adenosine Deaminase, Cerebrospinal Fluid, Cranial Nerve Palsy, Meningitis, Pyogenic, Viral, Tuberculosis, Tbm - Tuberculous Meningitis

1. Introduction

Tuberculosis (TB) is a major global problem and a public health issue of considerable magnitude. Approximately, eight million new cases of TB and three million deaths are reported annually. In recent times, there has been a resurgence of tuberculosis in both developing and developed countries. The attributing risk factors include the increasing prevalence of HIV infection, overcrowding in the urban population and in abnormal communities (such as prisons), poor nutritional status, appearance of drug - resistant strains of tuberculosis and ineffective tuberculosis control programs. India has about 1.8 million new cases of TB annually, accounting for a fifth of new cases in the world a greater number than in any other country.

Among Extra - pulmonary TB, tuberculous meningitis (TBM) leads to multiple central nervous system (CNS) complications and remains a major health problem. Tuberculous Meningitis (TBM) remains an important cause of morbidity and mortality, especially in the developing world, where it accounts for 7 - 12% of the tuberculosis cases. Due to its relative rarity and the protean nature of the symptoms, tuberculosis of the CNS remains a formidable diagnostic challenge. In view of varied clinical manifestations and the existing diagnostic dilemma, the present study is designed to assess the clinical profile of tubercular meningitis

Aims and Objectives:
To study the clinical profile of TB meningitis

2. Methodology

Study Design: Descriptive case control study
Study Duration: 12 months
Study Setting: Department of General Medicine, BGS GIMS Hospital, Bengaluru
Study Population: Patients with meningitisin admitted medical wards, Department of General Medicine, BGS GIMS Hospital, Bengaluru

Inclusion Criteria
1) All Patients presenting with fever and signs of meningeal irritation
2) Age >18years

Exclusion Criteria
1) Any intracranial bleed or sub dural hematoma
2) Patients already on ATT

Study Procedure
After obtaining clearance from institutional ethics committee, 70 patients were enrolled in our study as per the inclusion and exclusion criteria. An informed consent was obtained from the patients/ local guardian enrolled in the study. Detailed history from patients/bystanders was taken and clinical examination and required investigations was done on patients admitted with Meningitis and the findings are recorded in a pretested proforma.

Patients are divided into two groups after detailed clinical assessment and initial laboratory reports
1) Tubercular meningitis
2) Non tubercular meningitis

Pyogenic meningitis
Viral meningitis
Others: fungal meningitis
Diagnosis of TBM and non - TBM was based on criteria described below.

Patient groups

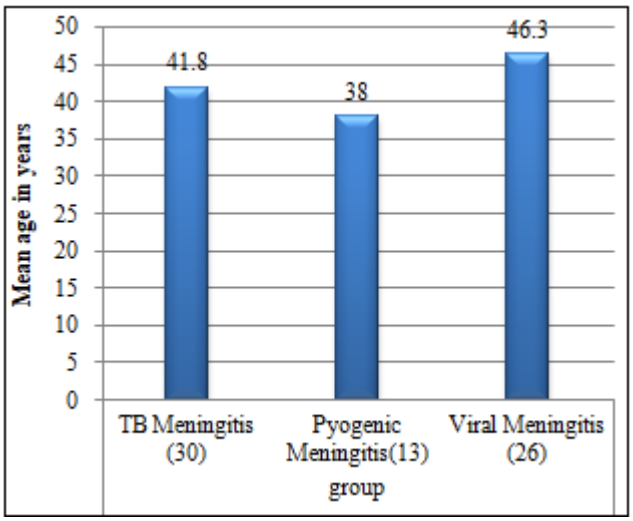
1) Tuberculous meningitis patients
a) Sub - acute or chronic fever with features of meningeal irritation such as headache, neck stiffness and vomiting, with or without other features of CNS involvement.
b) CSF samples showing raised protein levels, and/or decreased glucose (CSF: blood glucose ratio < 0.5), and/or pleocytosis with lymphocytic predominance. (100 to 500 cells)
c) CT or MRI features suggestive of Tuberculosis
d) Positive ADA

2) Non - TBM patients
A) Pyogenic meningitis:
- Acute Fever and/or signs of meningeal irritation
- CSF findings showing increased proteins, decreased glucose (CSF: blood glucose ratio < 0.2), and/or pleocytosis with a predominance of polymorphonuclear cells.

B) Viral meningitis patients: This group included suspected patients with the following observations
- Acute onset of fever and symptoms and signs of meningeal irritation.
- CSF samples showing mild or no increase in protein, glucose levels often normal, and pleocytosis, predominantly lymphocytic. (cells 10 - 100)
- No clinical evidence for extra cranial tuberculosis

3. Results

Total of 70 patients were included in the study, 30 were TB meningitis, 13 were pyogenic meningitis, 26 were viral meningitis, 1was fungal meningitis



Age distribution:
The age of TB meningitis patients ranged from 18 to 75years with the mean age of 41.8 years, in pyogenic meningitis it ranged from 18 to 76years with the mean age of 38.0years, in viral meningitis, it ranged from 20 to 75years with the mean age of 46.3years

Gender:
In TBM group, 50% were males and 50% were females.

In pyogenic meningitis group, 76.9% were males and 23.1% were females. In viral meningitis group, again 50% were males and 50% were females.

Symptoms and signs:
All the patients in the 3 groups had fever.

86.7% patients had headache in TB meningitis group, 100% patients had headache in pyogenic and viral meningitis.

Altered sensorium at the time of presentation was seen in 73.3% of patients in TBM group, 69.2% in pyogenic meningitis group, 73.1% in viral meningitis group.

Seizures were present in 30% of the patients in TBM group, 46.2% in pyogenic meningitis group, 38.5% in viral meningitis group.

Papilloedema was present in 33.3% of the patients in TBM group, 23.1% in pyogenic meningitis group, 11.5% in viral meningitis group.

Neck stiffness was present in all the patients in the 3 groups.

Cranial nerve palsies were present in 30% of the patients in TBM group, where as they were not seen in pyogenic and viral meningitis.

Hemiplegia was present in 16.7% of the patients in TBM group, where as it was absent in pyogenic and viral meningitis.

So, neurological deficits were seen only in TBM group. 10% of the patients were comatose in TBM group and 7.7% were

comatose in pyogenic meningitis group, where none of the patients in viral meningitis were comatose.

Total WBC Count, Platelets & Creatinine: High in pyogenic compared to viral and TB. Total count was elevated in 43.3% of the patients in TBM group, in 100% of the patients in pyogenic meningitis group, 30.8% of the patients in viral meningitis group. It was reduced in 3.8% of the patients in viral meningitis group.

Thrombocytopenia was present in 13.3% of patients in TBM group, 53.8% of the patients in viral meningitis group where as it was absent in pyogenic meningitis group. Thrombocytopenia was mainly seen in viral meningitis group.

Creatinine was elevated in 10% of the patients in TBM group, 23.1% in pyogenic meningitis group, 15.4% in viral menigitis group.

ESR:
Mean ESR was 66 in TBM group, 38.15 in pyogenic meningitis group, 43.08 in viral meningitis group. TBM group has higher ESR than both pyogenic and viral meningitis.

Mantoux test:
It was positive in 86.7% of the patients in TBM group, 38.5% in pyogenic meningitis group, 42.3% in viral meningitis group.

HIV:
HIV was positive in 6.7% of the patients in TBM group, 7.7% of the patients in viral meningitis group where as it was negative in all the patients in pyogenic meningitis group.

Pulmonary TB
Co existing Pulmonary TB was present in 13.3% of the TBM patients.

CSF Analysis:

CSF blood glucose ratio< 0.6. TBM vs Viral is significant . CSF Glucose was reduced in 86.7% of the patients in TBM group, 100% patients in pyogenic meningitis group, 15.4% of the patients in viral meningitis group. CSF glucose is usually not reduced in viral meningitis group.

CSF Protein CSF Protein was elevated in all the patients in TBM group, 92.3% in pyogenic meningitis group, 53.8% in viral meningitis group.

ADA: TBM is significantly higher than pyogenic and viral. ADA was elevated in 83.3% of the patients in TBM group, 3.8% in viral meningitis group and it was normal in all patients in pyogenic meningitis group.

CSF Cell Count Mean cell count was high in pyogenic group. Neutrophilic predominance in pyogenic group, Lymphocytic predominance in other two groups. Cell count was significantly high in TBM group compared to viral meningitis group.

CT Head: Basal exudates and infarcts were present in 16.7% of TBM patients, where as they were absent in other two groups. Hydrocephalus was present in 16.7% of TBM patients, 7.7% of pyogenic meningitis patients and it was absent in viral meningitis patients. Cerebral edema was present in 26.7% of TBM patients, 23%of pyogenic meningitis patients and 15.3% of viral meningitis patients. Tuberculoma/tubercular abcess was present in 6.7% of TBM patients.

4. Discussion

Before *M. tuberculosis* was identified by Robert Koch in 1882, TBM was clinically described by Robert Whytt in 1762 for the first time in children with acute hydrocephalus.[10]Until the discovery of antituberculosis drugs in the second half of the 20th century, TBM was a fatal disease for everyone. However, its mortality can still reach 60% today particularly in developing countries. Sequelae can be seen in 25% of survivors despite five major and numerous minor drug options available.[10, 11, 12]

The clinical presentation of TBM is vague with non specific symptoms that are hard to distinguish from other types of meningitis. A total of 70 patients were included in the study, out of which 30 were TB meningitis, 13 were pyogenic meningitis, 26 were viral meningitis and one was fungal meningitis. The age of TB meningitis ranged from 18 to 75 years, with a mean age of 41.8years. In TB meningitis group, male: female ratio was 1: 1.

The most common symptom was fever followed by headache, altered sensorium and seizures.

All the patients had neck stiffness. Papilledema was seen in 33.3%, cranial nerve palsies in 30%, hemiplegia in 16.7% and 10% of the patients were comatose. Cranial nerve palsies, especially oculomotor nerve palsies and hemiplegia were seen only in TB meningitis patients and not observed in other groups of meningitis.

Thrombocytopenia was present in 13.3% of the patients in TB meningitis group and 53.8% of the patients in viral meningitis group, where as it was not seen in pyogenic meningitis patients. The presence of renal failure was less in TB meningitis patients compared to other groups. Mantoux test was positive in 86.7% of the patients with TB meningitis, but it is not specific because it was positive in 38.5% of pyogenic meningitis patients and 42.3% of viral meningitis patients. However it is known that mantoux can be positive in patients with latent infection or previous history of BCG vaccination. Mean ESR was high in TB meningitis patients when compared to other groups. Since active TB is more common in people infected with HIV, it must be stressed that HIV testing should always be performed in conjunction with diagnosing TBM. In our study, HIV was positive in only two patients (6.7%) in TB meningitis group and in 7.7% of the patients in viral meningitis group. It was negative in all the patients in pyogenic meningitis group.

TBM is one of the common clinical manifestations of extra - pulmonary tuberculosis. There has been a rising trend of

TBM in developing countries like India in the past two decades. The detection of TBM is difficult to establish because of its pleomorphic clinical presentation and variable CSF cellular content and biochemical parameters, similar to that of partially treated pyogenic meningitis cases. Delayed diagnosis and treatment may be associated with many serious CNS complications.

5. Conclusions

TBM is an insidious disease, but it can also have an atypical presentation as acute or sub acute meningitis. In conclusion, the diagnosis of TBM is often difficult due to the atypical clinical presentation and the paucibacillary nature of the sample. Nested PCR was found to be more sensitive, as compared to smear microscopy. We suggest that nested PCR deserves a place in the laboratory diagnosis of TBM, but a careful adherence to the test protocol is mandatory. As false negative results are reported on PCR, PCR alone should not be used as a criterion for initiating or terminating the therapy. It should be supported by clinical, radiological, cytological and other microbiological findings (smear microscopy and culturing by conventional and automated systems) for guiding the clinicians in the decision making for the appropriate therapy, whenever it is possible.

Conflict of Interest: Nil

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