

Clinical and Laboratory Profile of Central Nervous System Tuberculosis

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Abstract

Introduction: Eight million people worldwide die each year from tuberculosis (TB), which is caused by Mycobacterium tuberculosis. In underdeveloped and developing countries, TB continues to be a primary cause of morbidity and mortality. About 10% of cases of TB are in the central nervous system (CNS), which has the highest mortality rates. The present work intends to investigate the prevalence of various CNS TB manifestation patterns, the clinical features of those who have tuberculous meningitis, and abnormalities in cerebrospinal fluid related to tuberculous meningitis.

Materials and methods: In this cross-sectional study, 41 cases of CNS TB with a variety of involvement

patterns were included. The clinical, laboratory and treatment results of these patients were assessed.

Results: Anemia greatly increased the risk of meningitis. HIV cases had significantly higher rates of mortality and abscess cases. At the time of presentation, 51.2% of patients had multiple patterns. The most frequent presentation with the greatest number of complications was meningitis alone, followed by meningitis with tuberculoma and tuberculoma alone. In 37.5% of instances, tuberculoma was present in various phases of development, and in 37.5% of cases, lesions were in the liquid caseating stage.

Conclusion: The most severe extrapulmonary TB presentation, with a high mortality rate and ongoing

neurologic effects even after effective therapy, is CNS infection.

Keywords: Central Nervous System Tuberculosis, CSF, Leptomeninges's, Meningitis, Pachymeningitis, TB, Tuberculoma.

Introduction

Tuberculosis (TB), caused by Mycobacterium tuberculosis accounts for eight million annual, worldwide deaths [1]. TB remains a leading cause of morbidity and mortality in the developing world. It may account for 1/6th of the 3 million of global mortality. Central nervous system (CNS) involvement is thought to occur in 2-5% of patients with tuberculosis and up to 15% of those with AIDS-related tuberculosis [2,3]. Clinical presentation depends on the particular manifestation, although in all cases symptoms and signs are nonspecific and include fever, seizures, meningism and focal neurological deficits (e.g., altered sensorium, hemiparesis). Fever, headache, vomiting, and altered consciousness level are the most common symptoms at presentation. Neck rigidity, cranial nerve palsies, and papilledema are the most common signs observed [4].

Risk factors for CNS tuberculosis include age (children > adults), HIV-coinfection, malnutrition, recent measles in children, alcoholism, malignancies, the use of immuno suppressive agents in adults and disease prevalence in the community [5]. Lab analysis is inevitable in CNS TB with cerebrospinal fluid analysis being an important diagnostic aid in TBM. Various studies have seen CSF smear positivity for AFB in 10% to 90% of cases [6].

Neuro tuberculosis can present in various patterns, which can be identified on MRI. The meningeal forms include lap to meningitis and pachymeningitis. Parenchymal forms of neuro tuberculosis include

tuberculoma in its various stages, tubercular cerebritis and abscess, tubercular rhomb encephalitis, and tubercular encephalopathy.

Each pattern has characteristic MRI appearances and differential diagnoses on imaging. Complications of neuro tuberculosis, usually of tubercular meningitis, include hydrocephalus, vasculitis, and infarcts as well as cranial nerve palsies [7].

The current study aims to examine the prevalence of various central nervous system TB manifestation patterns, the clinical characteristics of individuals with tuberculous meningitis, and abnormalities in cerebrospinal fluid associated with tuberculous meningitis.

Materials and Methods

Study Design

This cross-sectional study was carried out at the Department of General Medicine, Government Medical College, Kozhikode, Kerala, India.

Inclusion Criteria

All patients with clinically suspected central nervous system tuberculosis with supportive lab parameters such as cerebrospinal fluid (CSF) findings suggestive of Tb meningitis, raised CSF protein (normal CSF protein: 15 to 60 mg/100 mL), elevated cell count with lymphocytosis (normal count: 0 to 5 white blood cells), low CSF glucose (50 to 80 mg/100 mL), CSF culture positivity for tuberculosis. CSF acid fast bacilli positivity, GeneXpert positivity in sputum or CSF and Biopsy proved cases of tuberculosis were included in the study.

Exclusion Criteria

Patients with meningitis, abscess, hydrocephalus, infarcts, and myelitis caused by non-tubercular causes, as well as those with tuberculous involvement of the

vertebrae or disc (spondylodiscitis/potts spine), were excluded from the study.

Methods

In this observational study, we included 41 cases of CNS tuberculosis, including various involvement patterns. We studied the clinical and laboratory parameters and outcomes of these patients.

Results and Discussion

The current investigation highlights the various clinical and laboratory factors of CNS TB as well as its presenting patterns. The clinical and laboratory features of 41 patients with CNS TB were studied. Among the 41 patients, 51.2 per cent (21/41) were men and 48.8 (20/41) per cent were women (Figure 1). The mean age of the patients in this study was 36.44 ± 22.15 years. A maximum number of patients (22%) were in the 31 to 40 years of age group (Figure 2). The youngest patients included in our study were of 1 year of age and the eldest was 86 years old. In the follow-up, death was found to be significantly higher in the elderly with a mean age of 51.25 ± 21.94 .

Meningitis (66.75%) and tuberculoma (57.1%) were found to have similar incidence rates in our study's female participants despite meningitis (66.75%) being the most prevalent presentation in males. Males were shown to have higher rates of abscess, rhombencephalitis, and cerebritis than females (Table 1). The most common symptom was fever (80.5%) followed by headache (75.6%), altered sensorium (53.7%), weight loss (48.8%) and seizure (41.5%). Meningeal signs (56.1%) were the most common sign followed by cranial nerve involvement (26.8%). The most common cranial nerve involved was the facial nerve (72.7%) followed by oculomotor (9.1%) and abducens (9.1%) (Figure 3).

Based on laboratory test results, the average hemoglobin among patients was 11.62 ± 1.88 gm/dl, and 65.9% of patients had anemia. Meningitis cases were significantly greater in anemia patients (77.8%) than in non-anemia cases (35.7%), showing a significant relationship between meningitis and anemia. The average ESR for our study's subjects was 66.51 ± 23.8 mm/hr and was elevated in 39 (95.1%) patients. ESR and presentation type did not, however, correlate in any way. Nineteen individuals (46.3%) tested positive for Mantoux.

In this investigation, CSF was evaluated in 18 patients. The mean value of CSF count was 204.8 ± 92.51 and 70% of patients had lymphocytic predominant cells. The mean CSF protein value was 189.28 ± 71.71 (above the normal limit) and high protein was seen in 17 (94.4%) patients. The mean sugar value was 30.22 ± 10.38 mg/dl (lower than normal) and a low sugar value was seen in 77.8% of patients. GeneXpert positivity was seen in 66.7% of patients (Table 2).

There were 13 diabetics, 4 retroviral infected, 1 cancer patient (lymphoma), 9 people with pulmonary TB, 4 people with extrapulmonary TB, 12 smokers, and 10 alcoholics among the subjects in our study. There is no relationship between the type of presentation and diabetes ie, the types of presentation are almost the same in cases with and without diabetes. The correlation between abscess and HIV is strong; specifically, the prevalence of abscess is much higher in HIV-positive cases (50.0%) compared to HIV-negative cases (2.7%). This is consistent with the study conducted by Rana et al. [8]. Additionally, there is a strong correlation between HIV and death, with cases of death being substantially more common in HIV-positive cases

(74.0%) than in HIV-negative cases (13.5%) (Figure 4). This complies with the WHO Fact Sheet [9]. It is agreed that CNS TB is almost never a primary infection of this organ. The organism in the large majority of cases is conveyed from the primary site in the lungs, gastrointestinal tract, bone and lymph nodes by the bloodstream. As such, the patient is already in an allergic state or has developed a certain state of immunity before the brain is infected. The initial tuberculous lesions (Rich focus) may be present in the meninges, the subpial and subependymal surface of the brain, or the spinal cord [10,11, 12]. Our results show that most patients (51.2%) had more than one pattern at the time of presentation. Among the 41 cases, 26 (63.4%) patients had meningitis, 24 (58.5%) had tuberculoma, 3 (7.3%) had an abscess, 4 (9.8 %) each had rhombencephalitis and spinal TB and 1 (2.4 %) had cerebritis at presentation. Meningitis alone 12/41 (29.21%) was the most common presentation [13] followed by meningitis with tuberculoma 10/41 (24.3 %) and tuberculoma alone 8/41 (19.51%). Cerebritis 1/41 (2.4%) was the least common presentation. Meningitis was the presentation associated with the maximum number of complications (hydrocephalus, infarct, ventriculitis). The most common complication was hydrocephalus followed by intracranial infarct. Most patients had tuberculomas at more than one location. 8 patients out of 41 expired during the follow-up period. Among meningitis patients 73.1% patients had leptomeninges's, 11.5% had pachymeningitis and 15.4% patients had both lep to and pachy meningitis. The association between hydrocephalus, infarct, ventriculitis and meningitis is significant and is significantly higher in cases with meningitis (53.8%, 42.3% & 23.1%) as compared to the cases with no meningitis (6.7%, 0.0% &

0.0%). Therefore, meningitis is the presentation associated with the maximum number of complications. However, the follow-up findings are almost the same in cases with and without meningitis.

Conclusion

CNS TB was shown to be more common in those between the ages of 31 and 40, and men slightly more than in women. The most frequent symptom was fever, followed by headache, and the facial nerve was most frequently affected. Anemia greatly increased the risk of meningitis. HIV cases had significantly higher rates of mortality and abscess cases. At the time of presentation, 51.2% of patients had several patterns. The most frequent presentation was meningitis alone, followed by meningitis with tuberculoma and tuberculoma alone. Meningitis was the presentation linked with the greatest number of complications (hydrocephalus, infarct, ventriculitis). In our study, most had tuberculomas at more than one location followed by frontal lobe as the single most common location. 37.5% of cases had tuberculoma in multiple stages of evolution while 37.5% had lesions in the liquid caseating stage. Complications were significantly lower in cases with tuberculoma. However, resolution cases were significantly lower in cases with tuberculoma. Infection of the CNS is the most severe extrapulmonary manifestation of TB, with a high mortality rate and residual neurologic sequelae, even with adequate treatment.

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Legend Graph and Tables

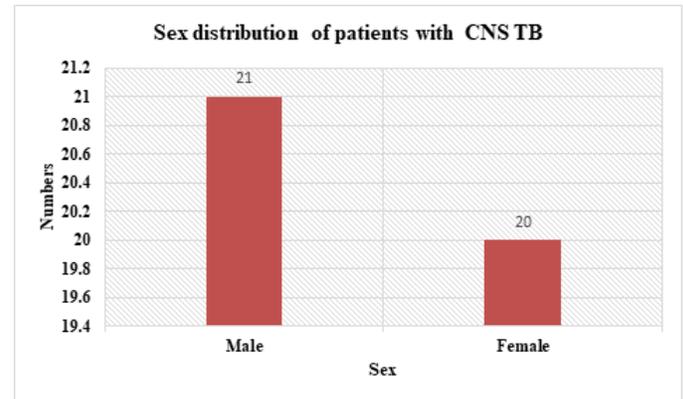


Figure 1: Sex distribution of patients with CNS TB

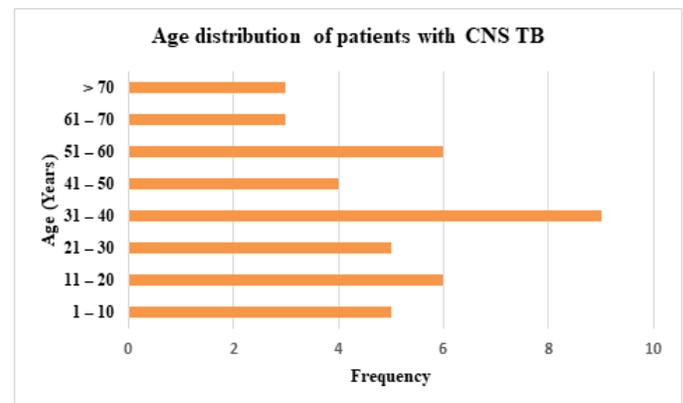


Figure 2: The age distribution of CNS TB patients

Type of Presentation	Male (N = 21)	Female (N = 20)	Total (N = 41)
Meningitis	14 (66.7%)	12 (60.0%)	26 (63.4%)
Tuberculoa	12 (57.1%)	12 (60.0%)	24 (58.5%)
Abscess	2 (9.5%)	1 (5.0%)	3 (7.3%)
Cerebritis	1 (4.8%)	0 (0.0%)	1 (2.4%)
Rhombencephalitis	3 (14.3%)	1 (5.0%)	4 (9.8%)
TB Spine	2 (9.5%)	2 (10.0%)	4 (9.8%)

Table 1: The pattern of presentations in CNS TB

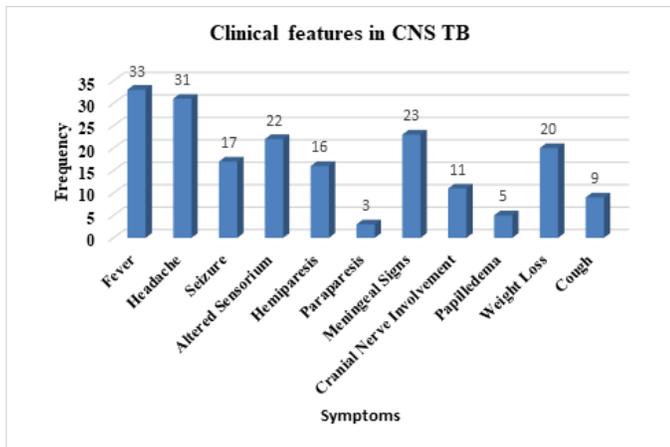


Figure 3: Clinical features in CNS TB

Cerebro Spinal fluid	Mean Value
Total Count in CSF (Cells/Microliter)	204.8±92.51
Protein (mg/dl)	189.28±71.71
Sugar (mg/dl)	30.22±10.38

Table 2: CSF Findings in CNS TB

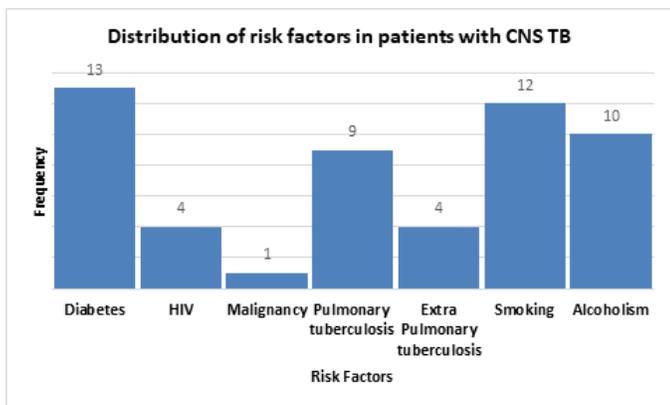


Figure 4: Distribution of risk factors in patients with CNS TB