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CLINICAL PROFILE OF PATIENTS WITH CENTRAL NERVOUS SYTEM TUBERCULOSIS

Medicine

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ABSTRACT

Introduction: World-over, tuberculosis (TB) remains as a major public health issue, mostly affecting the lesser privileged. TB involving the central nervous system (CNS) contributes to less than 1% of infections caused by it. Early recognition of CNS TB with early treatment is of paramount importance to optimum outcome.

Objectives: The objectives were to study the clinical profile of patients with central nervous system tuberculosis and to study the socio-demographic and clinical risk factors that predispose to its development. It was a retrospective descriptive chart-based study on 30 patients of CNS TB admitted from 1st January 2016 to 31st December 2017.

Results: Among the 30 patients included, there were 22 males and 8 females. Fever, headache and vomiting were the most common presenting features. The median time of presentation was 3 days. Neck stiffness and Kernig's test were the most common signs. CSF analysis showed lymphocyte predominance, with low glucose; elevated protein and ADA levels. Leptomeningeal enhancement and vasculitic infarcts were common neuroimaging features. The mean duration of stay was 15.23 days. Partial recovery was noted in 22 and death in two.

Conclusion: CNS TB can occur in all ages with a male preponderance. It continues to pose challenges, both in diagnosis and management, with significant morbidity and mortality

KEYWORDS

Central nervous system tuberculosis; CNS TB; clinical profile; CSF analysis; leptomeningeal enhancement.

Introduction:

World-over, tuberculosis (TB) remains as a major public health issue affecting the lesser privileged. (1) In this world-wide epidemic, 80% of new cases occur among the poor, malnourished and immune compromised individuals; and the remaining associated with HIV. (2) TB involving the central nervous system (CNS) contributes to less than 1% of infections caused by it. The occurrence of extra-pulmonary TB is directly proportional to the prevalence of TB infection, and the neurological involvement of TB infection constitutes approximately 5 -15% of the cases of extra-pulmonary TB. (3) It is associated with significant neurological sequelae and mortality; especially in immune compromised. (2, 3) Outcome in CNS tuberculosis is associated with the stage of disease at presentation. Early recognition of CNS TB with early treatment is of paramount importance to optimum outcome. (4) We attempted to study the clinical profile of patients having CNS TB.

Aims and objectives:

1. To study the clinical profile of patients with central nervous system tuberculosis
2. To study the various socio-demographic and clinical risk factors which predispose to development of CNS tuberculosis

Materials and methods:

Study design and source of data:

This retrospective chart-based descriptive study included patients admitted in the wards and intensive care departments of a tertiary care hospital in South India for a period of 2 years from 01st January 2016.

Methodology:

Data was obtained from the in-patient and out-patient records available at the medical records department. Data collected included standard demographic details, history regarding the current illness, timeline of progression, details of haematological and biochemical investigations; which included CSF analysis, Computerised tomographic or Magnetic resonance neuro-imaging features; and duration of hospital stay with outcome.

Selection criteria:

Inclusion criteria: (1) Patients diagnosed with CNS tuberculosis and treated as in-patients from 1st January 2016 to 31st December 2017. (2) Patients referred from other hospitals for management of CNS tuberculosis.

Exclusion criteria: (1) History of CNS tuberculosis. (2) Patients who were empirically treated for CNS tuberculosis without evidence.

Statistical analysis:

Data collected was analysed using SPSS v20.0 and it was interpreted as frequencies and percentages using the Chi-square test.

Results:

The study included 30 patients out of which 22 were males and 8 were females. The mean age was 41.03 ± 18.03. The median age was 35 years. The age group of the study population ranged from 14 to 87 years. Among these patients 10 (33.3%) were below 30 years, 16 (53.3 %) were in the age group between 31 to 60 years and 4 (13.3%) were aged more than 60 years.

Table-1: Frequency and percentage of symptoms at presentation.

Symptoms	Frequency	Percentage
Fever	24	80%
Headache	21	70%
Vomiting	10	33.3%
Photophobia	9	30%
Altered sensorium	9	30%
Hemiparesis	3	10%
Seizures	1	3.3%

The most common symptoms were fever, headache and vomiting. Other symptoms were seizures, hemiparesis and altered sensorium (table-1). Among the 30 patients, 24 (80%) presented with fever, 21 (70%) presented with headache, 10 (33.3%) presented with vomiting, 9 (30%) presented with altered sensorium, 3 (10%) presented with hemiparesis and 1 (3.3%) presented with seizures. The median time of presentation was 3 days. Three patients (10%) were at risk for CNS TB as they had concurrent human immunodeficiency virus infection (n=2) and pulmonary tuberculosis (n=1).

Table 2: Frequency and percentage of clinical signs.

Signs	Frequency	Percentage
Neck stiffness	25	83.33
Hemiparesis	7	23.3
Gaze palsy	5	15.67
Diplopia	4	13.3
Febrile	3	10
Kernig's test	15	50
Brudzinski's test	4	13.33
Papilledema	1	3.3

The most common neurological sign was neck stiffness (25, 83.33%); followed by hemiparesis (7, 23.3%), gaze palsy (5, 15.67%) and diplopia (4, 13.3%). Only 3 (10%) had fever at presentation (table-2). Also,15 (50%) had positive Kernig's sign; four had Brudzinski's sign and 1 had papilloedema Three patients had a GCS of less than 8 at the time of presentation. Thirteen patients had a GCS between 9-14. Fourteen patients had a GCS of 15.

CSF analysis showed a lymphocyte predominant picture with elevated protein; low to normal glucose; and elevated adenosine deaminase (ADA). One third of the patients had an ADA < 5 (10, 33.3%) and remaining had ADA > 5 (66.7%). Computerised tomography and/or magnetic resonance imaging of the patients revealed predominantly leptomeningeal enhancement, exudates, vasculitic infarcts, hydrocephalus and cerebral oedema.

The mean duration of hospital stay was 15.23 ± 12.98 days. The clinical recovery was measured as partial recovery, complete recovery and death. Partial recovery was defined as improvement in the presenting symptoms without full recovery. Complete recovery was defined as complete resolution of symptoms. Among the study population, 22 (73.3%) showed a partial recovery and 6 (20%) showed a complete recovery. Death was noted in 2 out of the 30 patients studied.

Discussion:

Central nervous system (CNS) disease caused by Mycobacterium tuberculosis is not uncommon and is a devastating manifestation of tuberculosis. We studied the clinical profile of patients with CNS TB and the socio-demographic risk factors that lead to its development.

The mean age of the study population was 41.03 ±18.03 years; and ranged from 14 to 87. A study from Iran on older children and adults had age ranging from 9 to 80. [5] A Vietnamese study demonstrated an age group of 16 to 70 years. [6] A Canadian study demonstrated a mean age group of 37.14 among its study population. [7]

In this study, the most common symptoms were fever, headache and vomiting. The other symptoms being seizures, hemiparesis and altered sensorium. This was similar with studies which found fever, headache and diplopia to be the common presenting features. [3] A study on CNS TB in Minnesota, USA, showed fever, headache, meningismus and altered consciousness as presenting features. Clinical manifestations of tuberculoma or tuberculous brain abscess depend largely on their location. They often presented with headache, seizures, papilledema, or features of increased intracranial pressure. [2]

The risk factors found in this study were HIV infection in two and pulmonary TB in one. Cherian et al noted the presence of younger age group, malnutrition, alcoholism and malignancies. [9] The signs suggestive of CNS involvement were neck stiffness,hemiparesis, cranial nerve palsies and altered consciousness. In 50% (n=15) patients had a positive Kernig's sign and 4 had a positive Brudzinski's sign. This was significantly lower than a study from Chicago, where meningeal stiffness was found in 88% of the study population. [8] A study done in Kerala had cranial nerve palsies, behavioural changes and papilledema to be the common presenting signs. Another study demonstrated cranial nerve palsies in 20-30% of their patients; and 6th nerve being the most affected. [9]

The CSF analysis showed lymphocyte predominance with elevated protein, low to normal glucose and elevated ADA. ADA, a marker of cell mediated immunity, is associated largely with lymphocytic proliferation and differentiation. The sensitivity and specificity of ADA in CSF range from 44 to 100% and 71 to 100%, respectively. [2] A study on non-HIV-infected adults with CNS tuberculosis in Turkey found CSF lymphocyte predominance in 85%, neutrophil predominance in 15% and high proteins in 77%. [10] In another study, lymphocyte predominant CSF was seen in 72% of the patients while 25% had acellular fluid. [8] Thwaites postulated five features to be predictive for the diagnosis of TBM, namely; the age, duration of illness, blood white cell count, total CSF white cell count and CSF neutrophil proportion. [6]

Neuroimaging features identified in the present study were leptomeningeal enhancement, exudates, vasculitic infarcts, hydrocephalus and cerebral oedema. Similar findings were demonstrated by Rock et al as basal leptomeningeal enhancement, hydrocephalus and infarctions in the supratentorial region and brain stem. [2]

The CT criteria for the diagnosis of CNS tuberculosis by Kumar et al were basal meningeal enhancement, ventriculomegaly, tuberculoma, and infarcts. He proposed these characteristics to distinguish CNS TB from pyogenic meningitis and found basal meningeal enhancement, tuberculoma, or both were 89% sensitive and 100% specific for TBM. [11] Andronikou et al suggested specific characteristics of basal meningeal enhancement, which may be seen in up to 90% of TBM cases. [12] Cherian et al demonstrated that choroid plexus enhancement with ventricular enlargement on imaging is highly suggestive of TBM.

MRI images in CNS TB shows diffuse thickening of leptomeninges and meningeal enhancement. Cerebral infarcts were seen in nearly 30% of cases. [9] Vasculitic infarct was the most serious consequence of TBM. [13] MRI brain was the imaging of choice in detecting brain infarcts that typically revealed multiple lesions in the territories of the middle cerebral artery and its perforating branches. [14] Early diagnosis and treatment of TBM are the most important factors in determining the outcome of the disease. [15]

The mean duration of hospital stay was 15.23 ± 12.98 days. Mortality was noted in 2 out of the 30 patients. In-hospital mortality in CNS TB was 69.1% in a study South Africa was not related to the neurological illness. [16] A Study at University of Chicago showed that poor outcomes were largely confined to cases presenting at an advanced stage or at the extremes of age. [17] Most deaths were attributed to neurological deterioration, nosocomial pneumonia, septic shock, and multiorgan failure in CNS TB. [8] The data available on the recovery and hospital stay among CNS TB patients are limited.

Conclusion:

CNS TB has a male preponderance and can occur in all ages. The most common clinical features were fever, headache and vomiting with neck stiffness, hemiparesis and cranial nerve palsies. The CSF analysis had lymphocyte predominance, low to normal glucose; and with elevated protein and ADA levels. Common neuro imaging features were leptomeningeal enhancement, exudates, vasculitic infarcts and hydrocephalus. The varied clinical presentation of CNS TB poses a challenge in its diagnosis and management; any delay would adversely affect the outcome.

Conflicts of interest:

Authors have not received any grants from funding agencies.

Disclosure:

Authors have no disclosures to make.

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