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Original Research Article

Clinico-radiological and Laboratory Profile of Patients with Central Nervous System Tuberculosis (CNS TB): An Observational Study

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Abstract

Aim: The aim of the present study was to assess the clinical features, complications and outcome in patients with central nervous system tuberculosis (CNS TB) and to correlate the clinical, laboratory and radiological findings of CNS TB.

Methods: The present study was conducted in the Department of Medicine, DMCH Darbhanga, India, over a period of two years and 100 patients were included in the study. Written informed consent were taken from patients or relatives in this hospital based study.

Results: Out of 100 patients, 84 patients had TBM (tuberculous meningitis) and 16 patients had tuberculoma. Mean age of patients was 34.6 years with male preponderance. Common symptoms were fever, headache and vomiting. The most common signs were neck stiffness followed by Kernig's sign and Brudzinski's sign.Cerebrospinal Fluid (CSF) staining was positive in 9.52% patients and mean CSF protein was 157 mg%. 64 patients had CSF lymphocytosis (count >90%). CSF Polymerase Chain Reaction(PCR) was positive in 78 patients and CSF ADA levels were high (> 10 U/L) in 52 patients. 63% patients had meningeal enhancement and 10 patients had tuberculomas.

Conclusion: Diagnosis of CNS TB should be based on clinical features and 3 or more supportive criteria rather than CSF positivity on staining or culture which may be negative many times. Hence supportive criteria like CSF examination (raised proteins, lymphocytosis, low sugar) along with positive CSF PCR, raised CSF ADA levels(>10IU/L), positive Computed Tomography(CT) and Magnetic Resonance Imaging (MRI) findings, evidence of culture positive, histologically proved or radiological tuberculosis anywhere in the body and response to treatment should be considered for the diagnosis of CNS TB. Rapid and early diagnosis by positive CSF PCR and CT/MRI findings should replace CSF AFB staining and culture for the diagnosis of CNS TB. After completion of cat I regime of treatment (RNTCP) for 6 months,duration of treatment should be decided by treating physician, neurophysician.

Keywords: central nervous system tuberculosis, clinical findings, laboratory findings, radiological findings

Introduction

Tuberculosis (TB) in all its forms remains a challenging clinical problem and a public health issue of considerable importance and magnitude world over. Tuberculosis meningitis is the most devastating manifestations of TB. The World Health Organization (WHO) has estimated an annual incidence of 9.27 million new cases of TB worldwide, and the number of prevalent cases of about 13.7 million. Most of the disease burden is in Africa and South East Asia, where annual incidence rate is 356 and 182 cases per 10,000 population respectively.[1] Tuberculosis has reemerged in

industrialized countries, largely because of increase in travel from endemic countries to developed nations.[2] This emergence is due in part to infection with human immunodeficiency virus (HIV), development of multidrug resistant M. tuberculosis, and reduced resources for treatment and surveillance of patients.[2,3] The occurrence of extrapulmonary TB is directly proportional to the prevalence of TB infection. Tuberculosis of the central nervous system (CNS) accounts for approximately 10% of extrapulmonary cases of or about 0.7% of all cases of TB.[4]

The response to tuberculous infection inside the nervous system varies from person to person, depending upon the immune status, concurrent illness, predisposing risk factor, disease burden and many other comorbid factors.[5] Virtually, all tuberculous infection of CNS is caused by the human tubercle bacillus, M. tuberculosis, an obligate aerobic bacteria, whose only natural reservoir is human. This organism is nonmotile, nonspore forming and slow growing, with a generation time of 15 to 20 hours. The complex antigenic structure of the cell wall includes polysaccharides, proteins, peptides, lipids and glycolipids with specific immunologic properties. These molecules determine the characteristic immune response to tuberculous infection and its resultant pathology.[5,6] Less commonly, other mycobacteria may be involved.

Diagnosing CNS TB is troublesome because it has a variety of clinical manifestations. CNS TB may be categorized into three groups: tuberculous meningitis (TBM), an intracranial space-occupying lesion (SOL) or tuberculoma/abscess, and tuberculous myelitis or spinal cord tuberculosis. CNS TB involving immunodeficient populations is challenging. One study demonstrated that even though an HIV infection did not alter the clinical manifestations of TBM, it dramatically reduced the survival rate of HIV individuals who developed TBM.[7] A recent study from China demonstrated that younger age, agricultural work, and miliary form of TB are decisive risk factors associated with TBM. However, the recent study does not focus on clinical findings of CNS TB stratified by different immune statuses.[8]

The aim of the present study was to assess the clinical features, complications and outcome in patients with central nervous system tuberculosis (CNS TB) and to correlate the clinical, laboratory and radiological findings of CNS TB.

Materials and Methods

The present study was conducted in the Department of Medicine, DMCH Darbhanga, India over a period of two years(January 2020 to December 2021) and 100 patients were included in the study. Written informed consent were taken from patients or relatives.The patients were evaluated in detail and were grouped in three stages according to severity of illness at presentation as per the criteria of modified British Medical Research Council[9] as stage I (Nonspecific symptoms, few or no clinical signs of meningitis), stage II(Signs of meningitis, drowsy, cranial nerve palsies) and stage III (Stupor or coma, systemic toxicity, paralysis).

Diagnosis of CNS TB was done on the basis of clinical features like fever >2 wks, headache, vomiting, convulsions, signs of meningeal irritation with or without neurological deficit and positive CSF studies (staining or culture) OR clinical features and supportive criteria (3 or more criteria) such as I (CSF examination suggestive of TBM i.e. proteins >60 mg%, sugar <40 mg%, cells >50 cumm, lymphocytosis > 60 %), II (CSF PCR positive for TB and CSF ADA >10u/L), III CT/MRI findings (one or more) showing meningeal enhancement, infarcts, basal exudates, obstructive hydrocephalus, tuberculomas, IV(evidence of additional culture positive or histopathologically proved and radiologically proved extra pulmonary TB or miliary TB) and V(Response to treatment). All patients were thoroughly investigated with routine tests as well as specific tests for TB like Erythrocyte Sedimentation Rate(ESR), Mantoux test, sputum and aspirate from lymph node for ziehl neelsen stain and CSF analysis for microscopy and biochemistry,Adenosine Deaminase (ADA), CSF and serum Enzyme Linked Immunosorbent Assay (ELISA) for IgM antibody using A60 antigen and a CT scan of brain. All patients received antituberculous therapy as per Revised National Tuberculosis Control Programme(RNTCP) guidelines. Steroids were given to stage 2 and 3 patients for 4 to 6 weeks with tapering of doses as recommended. Follow up was done for 6 months after completion of chemotherapy. Statistical evaluation was done using chi square test and p value calculated using student's t test.

Results

Table 1: Patient characteristics

Gender	**N (%)**
Male	70 (70)
Female	30 (30)
Symptoms	
Fever	100 (100)
Loss of weight	82 (82)
Headache	72 (72)
Vomiting	65 (65)
Altered sensorium	55 (55)
Convulsion	24 (24)
Coma	32 (32)
Weakness in limbs	38 (38)
Diplopia	2 (2)
Deviation of angle of mouth	7 (7)
Signs	
Neck stiffness	85 (85)
Kernig's sign	78 (78)
Bridzinski's sign	74 (74)
Pallor	72 (72)
Cervical lymph nodes	9 (9)
Papillodema	55 (55)
Cranial nerve palsy	34 (34)
Hemiplegia	25 (25)
Quadriplegia	10 (10)
Cerebellar signs	2 (2)
Decerberate posture	17 (17)

Out of 100 patients, 84 patients had TBM (tuberculous meningitis) and 16 patients had tuberculoma. Mean age of patients was 34.6 years with male preponderance. Common symptoms were fever, headache and vomiting. The most common signs were neck stiffness followed by Kernig's sign and Brudzinski's sign.

Table 2: CSF findings in cases of TBM

CSF examination	**N=84**
CSF AFB staining	
Positive	8
Colour	
Clear colour	68
Straw coloured	16
Cobweb	40
Proteins Mean=157 mg%	
>60 mg%	20
>100 mg%	64
Blood sugar <40 mg%	84
Chlorides Mean=118 mmol/L	
<120 mmol/L	80
Total cells 220 cells/cumm Lymphocyte mean= 179.5	
>60%	20
>90%	64
CSF PCR	78
CSF ADA	
>10 IU/L	52
10-20 IU/L	24

CSF staining was positive in 9.52% patients, mean CSF protein was 157 mg%. 64 patients had CSF lymphocytosis (count >90%) and CSF PCR was positive in 78 patients.CSF ADA levels were high (> 10 U/L) in 52 patients.

Table 3: CT/MRI Findings

CT/MRI Findings	N (%)
Meningeal enhancement	63 (63)
Basal exudates	7 (7)
Hydrocephalus	7 (7)
Infarcts	13 (13)
Tuberculomas	10 (10)

63% patients had meningeal enhancement and 10 patients had tuberculomas.

Discussion

Central nervous system (CNS) tuberculosis (TB) is a devastating infection with high rates of morbidity and mortality worldwide and may manifest as meningitis, intracranial tuberculoma, spinal arachnoiditis and rarely tuberculous encephalopathy. In the order of frequency pathological changes are seen in meninges, ependyma, choroid plexus, blood vessels and brain parenchyma.[10,11] Tuberculous meningitis (TBM) presents as acute meningitis syndrome, as insidious subacute demyelinating process or tuberculous encephalopathy. Risk factors for the development of TBM are extremes of age, alcoholism, diabetes, malignancy, recent corticosteroid use and HIV infection.[12] The early and exact diagnosis of TBM is important but difficult due to time taken in definitive microbiological procedures.[13] Diagnosis on pure clinical ground is impossible necessitating the importance of CSF studies and neuroimaging, CSF studies are the principle diagnostic tool in TBM. CSF shows pleocytosis with lymphocytes, elevated protein ranging from 60 mg% to 400 mg% or even higher, sugar between 20 mg%-40 mg%. It is sterile on routine bacterial culture. Demonstration of tubercle bacilli by AFB staining or culture remains the most important step of CSF study but its yield is much low.[14]

In our study,out of 100 patients, 84 patients had TBM (tuberculous meningitis) and 16 patients had tuberculoma. Mean age of patients was 34.6 years with male preponderance. Common symptoms were fever, headache and vomiting. The most common signs were neck stiffness followed by Kernig's sign and Brudzinski's sign. The incidence of hemiplegia, quadriplegia and cranial nerve palsies mentioned in various studies varies from 20-30 %.[15,16]

The rapid diagnosis of TBM is fundamental to clinical outcome. Clues to diagnosis of TBM include TB elsewhere in the body, a positive family history of TB, recent exposure to cases with active TB, a history of head trauma, alcoholism, immunocompromised state, including diabetes, chronic renal disease, HIV infection, etc.[17] On general physical examination, careful attention should be given to presence of lymphadenopathy, spinal or other joint lesion, scrotal mass, draining sinuses, nonhealing vaginal ulcers, etc. Abnormalities of chest X-ray include miliary infiltration, hilar lymphadenopathy and upper lobe infiltrates.[17] Mantoux positivity may also help, if the suspicion is strong. The key to diagnosis lies in CSF analysis and radiological investigations.In our study, CSF staining was positive in 9.52% patients. Mean CSF protein was 157 mg% and 64 patients had CSF lymphocytosis (count >90%). CSF PCR was positive in 78 patients and CSF ADA levels were high (> 10 U/L) in 52 patients. 63% patients had meningeal enhancement and 10 patients had tuberculomas.

Conclusion

Diagnosis of CNS TB should be based on clinical features and 3 or more supportive criteria rather than CSF positivity on staining or culture which may be negative many times and takes more time too. Hence supportive criteria like CSF examination (raised proteins, lymphocytosis, low sugar) along with positive CSF PCR, raised CSF ADA levels (>10IU/L), positive CT / MRI findings, evidence of culture positive, histologically proved or radiological tuberculosis anywhere in the body and response to treatment should be considered for the diagnosis of CNS TB. Rapid and early diagnosis by positive CSF PCR and CT/MRI findings should replace CSF Acid Fast Bacilli(AFB) staining and culture, in further, for the diagnosis of CNS TB. After completion of cat I regime of treatment (RNTCP) for 6 months, duration of treatment should be decided by treating physician, neurophysician.

References

1. World Health Organization (WHO). Frequently asked questions about TB and HIV. 2010.
2. Reider HL, Canthen GM, Kelly GD. Tuberculosis in the United States. Am J Epidemiol 1979;109:205-209.
3. Selwyn PA, Hartel D, Lewis VA, Schoenbaum EE, Vermund SH, Klein RS, Walker AT, Friedland GH. A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. New England journal of medicine. 1989 Mar 2;320(9):545-50.
4. Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC. Consensus statement. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. WHO Global Surveillance and Monitoring Project. Jama. 1999 Aug 1;282(7):677-86.

5. Garg RK. Tuberculosis of the central nervous system. Postgraduate medical journal. 1999 Mar;75(881):133-40.
6. Zuger A. Tuberculosis. In: Scheld WM, Whitley RJ, Marra CM, editors. Infection of the central nervous system, 3rd edition. Lippincot Williams and Williams 2004;441-460.
7. Thwaites GE, Duc Bang N, Huy Dung N, Thi Quy H, Thi Tuong Oanh D, Thi Cam Thoa N, Quang Hien N, Tri Thuc N, Ngoc Hai N, Thi Ngoc Lan N, Ngoc Lan N. The influence of HIV infection on clinical presentation, response to treatment, and outcome in adults with tuberculous meningitis. The Journal of infectious diseases. 2005 Dec 15;192(12):2134-41.
8. Ma Y, Ji X, Jiang H, Liu F, Chu N, Li Q. A study of risk factors for tuberculous meningitis among patients with tuberculosis in China: An analysis of data between 2012 and 2019. Frontiers in Public Health. 2023 Jan 27;10:1040071.
9. British Medical Research council. Streptomycin in treatment of Tuberculous meningitis. Lancet 1948; 1:582-496.
10. AR R. The pathogenesis of tuberculous meningitis. Bull John Hopkins Hosp. 1933;52:5.
11. Dastur DK, Lalitha VS. The many facets of neurotuberculosis: an epitome of neuropathology. Progress in neuropathology. 1973;2:351-408.
12. Thwaites G, Chau TT, Mai NT, Drobniewski F, McAdam K, Farrar J. Tuberculous meningitis. Journal of Neurology, Neurosurgery & Psychiatry. 2000 Mar 1;68(3):289-99.
13. Andronikou S, Wieselthaler N, Smith B, Douis H, Fieggen AG, van Toorn R, Wilmshurst J. Value of early follow-up CT in paediatric tuberculous meningitis. Pediatric radiology. 2005 Nov;35:1092-9.
14. Ahuja GK, Mohan KK, Prasad K, Behari M. Diagnostic criteria for tuberculous meningitis and their validation. Tubercle and lung disease. 1994 Apr 1;75(2):149-52.
15. Karstaedt AS, Valtchanova S, Barriere R, Crewe-Brown HH. Tuberculous meningitis in South African urban adults. QJM: monthly journal of the Association of Physicians. 1998 Nov 1;91(11):743-7.
16. Bayındır C, Mete Ö, Bilgic B. Retrospective study of 23 pathologically proven cases of central nervous system tuberculomas. Clinical neurology and neurosurgery. 2006 Jun 1;108(4):353-7.
17. Prabhakar S, Thussu A. CNS tuberculosis. Neurology India 1997;45(3):132-140