Diagnostic and Therapeutic Challenges in the Surgical Management of CNS Tuberculosis

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ABSTRACT

Background: Tuberculosis of the central nervous system is very common in South East Asia region and particularly in India. Despite of various diagnostic modalities and treatment options the outcome remains poor. Clinicians face many challenges in management of tubercular infections of the brain and spine.

Material & Methods: Twenty five patients with CNS tuberculosis who had undergone neurosurgery were included in this study. All the patients were evaluated with CT scan or MRI or both. After neurosurgical interventions a close observation and regular follow up over a period of two years was done to evaluate the radiological and clinical outcome. Results: The commonest presentation of CNS tuberculosis was hydrocephalus followed by Pott's spine. Radiological investigations and close clinical observation guided the timing of the surgical intervention. All patients showed significant clinical and radiological improvements during follow up. Conclusion: Various investigations provide little support for the management of sequela of post tubercular meningitis and tuberculosis of the spine. Vigilant clinical observations and imaging studies are required in the early follow up period to identify the worsening or new emerging signs. Imaging studies are becoming the major decisive tools for the diagnosis and evaluation of outcome.

KEYWORDS: CNS Tuberculosis, Surgical management

INTRODUCTION

Central Nervous System Tuberculosis (CNS TB) is caused by Mycobacterium tuberculosis. This is one of the most devastating clinical manifestations of tuberculosis (TB), noted in 5 to 10 percent of extra pulmonary TB cases, and accounts for approximately 1 percent of all TB cases[1]. Global burden of TB is still high, particularly in developing countries, and globally, there were an estimated 9.27 million new cases (139 per 100,000 population) of TB in 2007, and the
number of prevalent cases was 13.7 million (206/100,000 population)[2].

CNS TB is very common in South-East Asia Region particularly in India. India, China, Indonesia, South Africa and Nigeria rank first to fifth in terms of the incidence. South East Asia Region accounts for 31 percent of total cases whereas the African Region accounts for 85 percent of total TB with HIV[3]. CNS TB results from hematogenous dissemination of the Mycobacterium from the primary pulmonary infection and the formation of small subpial and subependymal foci (Rich foci) in the brain and spinal cord[4].

Central nervous system tuberculosis has wide clinical spectrum of neurological manifestations. The CNS TB can be classified as intracranial and spinal tuberculosis. Intracranial CNS TB may be tuberculous meningitis, tuberculous encephalopathy, tuberculous vasculopathy, CNS tuberculomas (single or multiple) and tuberculous brain abscess whereas the spinal tuberculosis may be Pott’s spine and Pott’s paraplegia; non-osseous spinal tuberculoma and spinal meningitis. [1]

Clinical diagnosis of TBM is difficult as the clinical features are nonspecific and vary widely, and is often diagnosed when brain damage has already occurred [2, 5]. Involvement of spine occurs in less than 1 percent of TB patients and it can be secondary to Pott’s spine or as non-osseous spinal cord tuberculosis meningitis. The thoracic spine is involved in about 65 percent of cases, and the lumbar, cervical and thoraco-lumbar spine in about 20 percent, 10 percent and 5 percent respectively[1, 6].

Vertebral body tuberculosis ( Pott’s disease) with cord impingement account for the majority of all cases with spinal involvement and most commonly presents with pain, a gibbus, and signs of extrinsic cord compression.[7]. Extradural cord tuberculomas cause more than 60% of cases of non-osseous paraparesis, although tuberculomas can occur in part of the cord [8].

CNS TB is still a diagnostic and therapeutic challenge despite the availability of antitubercular therapy and a battery of tests which have variable sensitivity and specificity. Hence we felt it is imperative to study the profile of these patients presenting in the Neurosurgical setting.

MATERIALS AND METHODS

The present study was done at IHBAS, tertiary care neuropsychiatry hospital at Delhi, India. Twenty five patients of CNS TB who underwent surgery in the Neurosurgery department were included in the study by non-probability convenience sampling from March 2009 to Dec 2011. Study design was descriptive case series.

The patients were recruited in an out-patient department setting, who were either initially treated somewhere else as a TBM case or presented to the Neurosurgery OPD as a new case of CNS TB. The Neurosurgery department at IHBAS is a new department and at present does not have neurosurgical emergency facility hence the presentations of the patients were mainly sub acute or chronic. All the patients were treated under the supervision of the Neurosurgeon.

All the patients were investigated systematically through various diagnostic tests. Blood profile was evaluated with complete blood count with ESR and ELISA for TB. Two Sputum smears for acid fast bacilli (AFB) were done for each patient. Cerebrospinal fluid (CSF) examination comprising of the entire battery of Biochemistry (proteins, sugars), Cytology, Gram stain, AFB smear, India ink stain, PCR and Culture were done for all the patients. Biopsy of the granulomatous tissue was done in whichever case granulomas were surgically accessible. Radiological investigations like X-Ray Chest, CT scan /MRI or both were done for all the patients.

Complying with the chemotherapeutic guidelines of antitubercular therapy, all the patients received two phase anti tubercular medication. In all the patients, Neurosurgical procedure was done as per the required intervention according to the neurosurgical diagnosis of the patient and the evidence based practice. After neurosurgical interventions the patients were assessed in the follow up both radiologically and clinically over a period of two years.

The data of the patients was entered , compiled and analysed in MSExcel and the statistical output was represented as frequencies and
percentages. The tables representing the frequencies and percentages of presenting complaints and clinical features were made to summarise the findings.

RESULTS

Of total 25 cases, 12 were males and 13 were females i.e., 48% and 52% respectively. The mean age of patients was 20.9 years; the minimum age was 6 months while maximum was 80 years. At presentation to the hospital, the mean duration of illness was seen to be 6.9 months; the minimum was 15 days and the maximum 4 yrs. Past history of tuberculosis was present in 3 cases (12%) out of total 25 cases.

Table1: Clinical features of the study group

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>No. of Patients</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>Weakness in limbs</td>
<td>9</td>
<td>36</td>
</tr>
<tr>
<td>Headache</td>
<td>8</td>
<td>32</td>
</tr>
<tr>
<td>Anorexia</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>Visual symptoms</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>Altered consciousness</td>
<td>4</td>
<td>16</td>
</tr>
</tbody>
</table>

Table 2: Diagnostic profile of the study group

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Patients</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocephalus</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>Potts Spine with cord compression</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Spinal Arachnoiditis*</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Calvarial tuberculosis with extradural lesion</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

*1 patient of Pott’s spine and 1 patient with hydrocephalus had associated Spinal Arachnoiditis

The history of close contact of tuberculosis was present in 2 cases (8%) of patients. The diagnostic profile of the study subjects is presented in Table 2. Various clinical features and patterns of CNS TB were observed. Table 1 shows the clinical features observed at the time of presentation in the Neurosurgical department. The commonest diagnosis of the patients was post tubercular hydrocephalus. Hydrocephalus was mostly obstructive type for which ventriculo-peritoneal shunt surgery was commonest modality of treatment. Second common diagnosis was Potts spine, 1 patient of Pott’s spine and 1 patient with hydrocephalus had associated spinal arachnoiditis. There was one patient of calvarial tuberculosis with extradural lesion. 72% of patients were
anemic. ESR was highly variable (mean 52 mm at end of 1st hour by Westergren method. Normal chest radiograph was seen in 22 cases (88%), while 3 cases (12%) had Chest X-ray suggestive of Pulmonary TB.

Figure: 1 MRI Brain with Contrast (axial view) showing Brain stem Tuberculoma

Figure: 2 MRI Brain with Contrast (sagittal view) showing Posterior fossa conglomerate Tuberculoma
Figure: 3 MRI Thoracolumbar spine showing collapse of the vertebra and compression of the spinal cord due to granulation tissue in the sagittal view.

Sputum smear examination was done in all the patients and only 3 cases (12%) were sputum positive. Various biochemical and bacteriological investigations of the ventricular cerebrospinal fluid collected at the time of surgery did not reveal any evidence of Acid Fast Bacillus. AFB stain, culture, histopathology and PCR for tuberculosis was positive in patients where the granulomatous tissue was found i.e. in 3 cases of spinal tuberculosis and 1 case of extradural brain abscess with osteomyelitis.

Ventriculo-peritoneal shunt surgery was planned and done in all 20 hydrocephalus cases, laminectomy and decompression was done in four cases. In one patient of extradural brain abscess, craniectomy and evacuation of extradural granulation tissue was done. These patients were periodically followed up for 2 years after the surgery and all the patients exhibited significant neurological improvement following surgery.

DISCUSSION

Various diagnostic modalities and treatment options are available for CNS TB still the outcome remains poor and clinicians face many challenges in the management of the tubercular infection of the brain and spine. In our study sample, the mean age of patients was 20.9 years; the minimum age was 6 months while maximum was 80 years. Malik Z. I. et al in their study reported the mean age of their study subjects as 29.67 years [9]. Kalita J et al quoted in his different studies as the mean age of 28 years and 25.6 years, which are nearly similar to our study [10]. Of total 25 cases, 48 % were males and 52% were females.

At presentation to the hospital, the mean duration of illness was seen to be 7 months; the minimum was 15 days and the maximum 4 yrs. These cases were actually the sub-acute presentation as
sequelae of tuberculous infections. Various studies available in the literature depict lesser mean duration of illness as they were usually studies of acute onset CNS TB. Malik Z. I. et al and Grigis NI et al in their studies reported the mean duration of illness at presentation as 29.13 days and 29.5 days respectively [9, 11].

Past history of tuberculosis was present in 3 cases (12%) out of total 25 cases. Cherian A and Thomas S.V. also reported that history of tuberculosis is elicited in 10% of the patients[1]. The most common presentation was hydrocephalus. Rajeshekar V. reported in his study that hydrocephalus is common in the later stage of CNS TB[12]. Malik Z. I. et al observed in their study that most common features were hydrocephalus[9]. Hydrocephalus could be seen in different studies as major complication by Davis LE et al as 52%, 71.4% by Tariq M et al and Kalita J et al as 91% [10, 13,14].

72% of patients were anemic .ESR was highly variable (mean 52 mm at end of 1st hour by Westergren method. Similar results were reported by Malik Z. I. et al and Kalita J et al[9,10]. Normal chest radiograph was seen in 22 cases (88%), while 3 cases (12%) had Chest X-ray suggestive of Pulmonary TB. Grigis NI et al reported that 60% of the patients who underwent chest radiography had features suggestive of pulmonary TB[11]. Malik Z. I. et al reported 50% of his patients showed positive chest radiograph[9]. Other studies have shown positive X-rays in 35% and 40 % [13, 15]. Venugopal in his study quoted that 20% of his study subjects had abnormal chest X ray[16].

Sputum smear examination was done in all the patients and only 3 cases (12%) were sputum positive. Alsoub H et al [14] also reported a yield of 15%, whereas Malik Z. I. et al reported 6.6% of his study subjects had sputum positivity[9,15].Various biochemical and bacteriological investigations of the ventricular cerebrospinal fluid collected at the time of surgery did not reveal any evidence of Acid Fast Bacillus. AFB are less commonly found in the CSF of patients with cerebral tuberculoma or spinal tuberculosis and tissue examination is usually required to confirm the diagnosis[17]. Thwaites G et al have concluded that once the anti-tuberculosis medication is commenced the sensitivity of smear and culture falls rapidly. The search for the AFB in CSF and tissue remains the most preferred diagnostic test for the CNS TB. However, practically the things are not that simple as once the anti-tuberculosis medication is commenced the sensitivity of smear and culture falls rapidly[7].

Thwaites and coworkers suggested in their research that the culture is too slow to help in initial treatment decision. There are various other tests like tubercular skin test, CSF adenosine deaminase, nucleic acid amplification (NAA) assay, IGRA and polymerase chain reaction (PCR) which also are part of diagnostic workup of CNSTB. However their diagnostic accuracy are highly variable[7, 11, 18,19,20,21].

In our study 4 (16%) cases revealed granulation tissue which was surgically accessible hence could be biopsied and were conclusive of tubercular pathology. A tissue biopsy has much higher diagnostic yield than CSF for the diagnosis of tuberculoma and spinal tuberculosis. Rajeshekar et al in their study reported stereotactic biopsy was diagnostic in 94% of their cases[12].

On radiological investigations ,CT/MRI or both, hydrocephalus was seen in 20 cases(80%), Potts spine was observed in 4 cases (16%) .3 cases (12%) had Tuberculomas ,2 cases(8%) had spinal arachnoiditis , and extradural collection, skull osteomyelitis ,cold abscess was seen in one case (4%). The Brain of the patient with TBM should be imagined with contrast enhanced CT either before the treatment (as part of the diagnostic work up) or within the first 48 hours of treatment. Early brain CT can help to diagnose the TBM and will provide important baseline information particularly when considering surgical intervention for the hydrocephalus [7].All patients with suspected cerebral TB or Spinal cord TB should be investigated by MRI as it is critical to demonstrate whether surgery is indicative and to follow the subsequent response to therapy[7].

We observed radiological imaging studies have maximum contribution in establishing the CNS TB diagnosis. These are becoming the major decisive tools for the empirical therapy and early follow up of the patients to evaluate the therapy. An extra neural of TB should be sought clinically
and radiologically in all patients with CNS TB as it may indicate safer and more accessible site for the diagnostic sampling. All the patients received two phase anti tubercular medication. The literature suggests that the empirical ATT should be started even before the result of AFB culture and sensitivity are available. A close follow-up is necessary to assess the response to ATT and a repeat radiological investigation.

A systematic review and meta-analysis concluded that six months of treatment were probably sufficient for the TBM, provided the drug resistance is low [22]. However, most studies recommend the treatment for the year as it may be under influence of disease severity, CNS drug penetration, undetected drug resistance and partial compliance on the response to therapy[23, 24].

In six of our study subjects steroids were also administered along with ATT. The British Guidelines also recommend that all TBM patients must be given the adjunctive Corticosteroid regardless of the disease severity at presentation. [7]. In the patients with TB without meningitis or spinal cord TB corticosteroid may be helpful if symptoms are not controlled or getting worsening on ATT or spinal cord compression secondary to vertebral TB. Early VP shunt should be considered in those cases that are with non-communicating hydrocephalus and in case of communicating, if medical treatment fails [7].

20 cases in the present study underwent ventriculo-peritoneal shunt surgery, laminectomy and decompression was done in 4 cases and craniectomy was done in 1 patient. Urgent surgical decompression should be done in all those cases with extra-dural lesion causing paraparesis. Delay in ATT in CNSTB is strongly associated with death and neurological sequelae. The low sensitivity of all currently available rapid diagnostic test mean empirical therapy may need to be started in many patients with suspected CNS TB, although it is difficult to stop treatment once started. The ATT regimen should be the same as that recommended for the HIV uninfected individuals; whenever possible the regimen should include rifampicin. Adjunctive corticosteroids are recommended for those with TBM and infection HIV. The risk of drug resistance must be assessed individually for all patients with CNS TB. The presence of risk factors prompt rapid susceptibility testing or diagnostic specimen and additional drug must be strongly considered. New or working neurological signs in patients on treatment for CNS TB should be prompt imaging and neurological review. [7].All the patients were followed up for a period of 2 years post surgery at regular intervals and all the patients exhibited significant neurological improvement following surgery.

CONCLUSION

The tuberculin test, biochemical investigations and AFB stain and culture of the cerebrospinal fluid or granulation tissue provide little support for the management of sequelae of post tubercular meningitis and tuberculosis of the spine. There should be high index of suspicion for the CNS TB in a patient who is from an endemic region. There may be extensive tubercular involvement of CNS even in absence of the history of pulmonary diseases, tubercular contact or any other neurological deficit. It is difficult to assess the therapeutic response in the early follow up period in view of the lack of sensitive and specific tests. Vigilant clinical observation and imaging studies is required in the early follow up period to identify the worsening or new emerging signs in the patients of CNS TB. Imaging studies are becoming the major decisive tools for the empirical therapy and early follow up of the patients to evaluate the therapy.

REFERENCES


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