Tuberculous brain abscesses: Case series and review of literature

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ABSTRACT

Introduction: Tuberculous brain abscess (TBA) is a rare but serious condition. It resembles a pyogenic brain abscess clinically and radiologically and poses a problem in diagnosis and treatment. A final diagnosis is established by smear or culture demonstration of acid fast bacilli (AFB) within the abscess. Here, we report four such cases in our five-year study on brain abscesses, along with the different diagnostic modalities used. Materials and Methods: A total of 75 brain abscess pus specimens were collected during neurosurgery, either by burr hole or by craniotomy. These specimens were further subjected to Gram stain, Ziehl-Neelsen (ZN) stain, and conventional microbiological culture. Only those cases which showed presence of AFB on ZN stain along with the growth of Mycobacterium tuberculosis were considered as TBAs. Such TBA cases were further presented along with their In vitro Proton Magnetic Resonance (MR) Spectroscopic findings. Results: Of these four patients, three were males. Though this condition is more commonly seen in immunocompromised patients, three of the patients in this study were immunocompetent. All the four pus specimens showed presence of AFB in the ZN stain. Three of them grew M. tuberculosis as sole isolate. The fourth case was of concomitant tuberculous and pyogenic brain abscess. In vitro Proton MR spectroscopy of the pus specimens showed absence of multiple amino acids at 0.9 ppm, which was found to be hallmark of TBA. One patient died of four. Conclusions: TBA always poses a diagnostic dilemma. ZN stain and conventional microbiological culture for Mycobacteria always help to solve this dilemma. In vitro Proton MR Spectroscopy also seems to have the diagnostic utility.

Key words: Brain abscess, pyogenic, tuberculous MR Spectra

Introduction

Tuberculous brain abscess (TBA) is a rarely reported form of central nervous system (CNS) tuberculosis.[1] TBA is a focal collection of pus containing abundant acid fast bacilli (AFB) surrounded by a dense capsule consisting of vascular granulation tissue.[2] TBA always poses a diagnostic dilemma as they are difficult to differentiate from pyogenic brain abscesses, tuberculous meningitis, and tuberculoma on the basis of clinical, laboratory, and roentgenographic information.[1] Whitener,[1] in his excellent review, had laid down the diagnostic criteria for TBA. The present study reports four cases of TBA along with comparative analysis of other TBA cases from the available literature.

Materials and Methods

During the 5-year study on brain abscesses, pus specimen was collected during neurosurgery either by burr hole or by craniotomy. This was then sent to Department of Microbiology for the subsequent workup after obtaining proper consent. This study was performed after obtaining necessary ethical clearance from the institutional ethical committee.

Gram and Ziehl-Neelsen (ZN) stains were performed immediately. Aerobic, anaerobic, and fungal cultures were put up using conventional methods.[3] Pus specimens were also inoculated on Lowenstein Jensen’s medium and incubated at 37°C for 6 to 8 weeks. Colonies obtained were confirmed to be acid fast by ZN and then were identified by conventional methods such as rate
of growth, pigment production, niacin accumulation, nitrate reduction test, and sensitivity to paranitrobenzoic acid (500µg/ml).

In three TBA cases, 100 µl of pus sample was loaded in 5 mm NMR tube and deuterium oxide (D₂O) (Armar Chemicals, Switzerland) was added to make approximate volume of 0.6 ml, and then subjected to In vitro Proton MR Spectroscopy (¹H MRS) using Mercury plus Varian 300 MHz (7.05 T) nuclear MR spectrometer. After the NMR analysis (256 scans), the different peaks obtained were noted. Referencing was done with the water peak at 4.8 ppm. The interpretation of peaks was done according to the available literature.[4,5] The spectra of pus which yielded Mycobacterium tuberculosis were further compared with spectra of pus that yielded pyogenic organisms.

**Results**

Of 75 pus specimens, ZN stain revealed presence of AFB in four (5.3%). Three pus specimens grew M. tuberculosis as the sole pathogen causing the brain abscess. In one case, along with M. tuberculosis, pus specimen showed growth of Enterococcus avium and Proteus vulgaris. Table 1 shows all the details of the patients encountered in the present study. Of these four cases, three were immunocompetent, while one patient was infected with Human Immunodeficiency Virus (HIV). Two of the pus specimens which yielded pure growth of M. tuberculosis subjected to in vitro ¹H MRS showed complete absence of multiplet of amino acids-lipids at 0.9 ppm and lactate + lipid at 1.3 ppm [Figure 1a]. Pus from pyogenic brain abscesses (anaerobic) showed presence of multiplet of amino acids-lipids at 0.9 ppm along with presence of lactate + lipid at 1.3 ppm, acetate at 1.92 ppm, and succinate at 2.4 ppm [Figure 1b]. However, the pus specimen which yielded M. tuberculosis along with E. avium + P. vulgaris showed spectra similar to pyogenic brain abscess.

![Figure 1a: In vitro ¹H MRS of the pus specimen which grew Mycobacterium tuberculosis on culture](image1a)

![Figure 1b: In vitro ¹H MRS of the pus specimen which grew anaerobe on culture](image1b)

### Table 1: Details of the patients from the present study

<table>
<thead>
<tr>
<th>Age/Sex</th>
<th>Presenting signs and symptoms</th>
<th>Immune status</th>
<th>Lobe involved</th>
<th>Extra CNS TB</th>
<th>ZN stain</th>
<th>Culture results</th>
<th>In vitro MR spectroscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>47/M</td>
<td>Fever, loss of consciousness, lt hemiparesis, History of fall, convulsions</td>
<td>Immunocompetant</td>
<td>Frontal</td>
<td>Nil</td>
<td>AFB seen M tuberculosis</td>
<td>Absence of amino acids at 0.9 ppm, lactate –lipid at 1.3 ppm</td>
<td></td>
</tr>
<tr>
<td>23 years/M</td>
<td>Decrease in vision, headache, fever, giddiness</td>
<td>Immunocompetant</td>
<td>Multiple</td>
<td>Pulmonary</td>
<td>AFB seen M tuberculosis</td>
<td>Not done as specimen was inadequate</td>
<td></td>
</tr>
<tr>
<td>25 years/M</td>
<td>Headache, convulsions</td>
<td>Immunocompromised : HIV infected</td>
<td>Parieto-occipital</td>
<td>Pulmonary</td>
<td>AFB seen M tuberculosis</td>
<td>Absence of amino acids at 0.9 ppm, lactate –lipid at 1.3 ppm</td>
<td></td>
</tr>
<tr>
<td>15 years/F</td>
<td>Headache, vomiting, fever, CSOM</td>
<td>Immunocompetant</td>
<td>temporal</td>
<td>Nil</td>
<td>AFB seen M tuberculosis, Enterococcus avium and Proteus vulgaris</td>
<td>Multiplet of amino acids at 0.9 ppm, lactate –lipid at 1.3 ppm, acetate at 1.92 ppm</td>
<td></td>
</tr>
</tbody>
</table>
Discussion

*M. tuberculosis* is a rare cause of brain abscess; however, this organism should be considered in patients with disseminated *tuberculosis* or in individuals from areas where *tuberculosis* is endemic.[2] The present study noticed four (5.4%) TBA cases in five-year study on brain abscesses. In all these four cases, there was an evidence of pus within the brain and bacteriological proof of AFB in the pus by microscopy as well as by culture. In 1978, Whitener[1] reported a case of TBA and reviewed 57 similar cases in the world literature. He found that only 16 of the 57 cases could be considered as verified TBAs in terms of the following three criteria: 1. Macroscopic evidence from surgical or autopsy material of true abscess formation within the brain substance, characterized by cavity formation with central pus; 2. Sufficient histological description to assure that the inflammatory reaction in the abscess wall was composed predominantly of vascular granulation tissue containing acute and chronic inflammatory cells particularly polymorphonuclear leukocytes; and 3. Proof of *tuberculosis* origin by either a positive culture of the pus for *M. tuberculosis* or demonstration of acid-fast organisms in the pus or abscess wall. After Whitener[1] reviewed the world literature, isolated cases of TBAs have been reported.[6-17] In most of these cases, proof of *tuberculosis* origin was by either a positive culture of the pus for *M. tuberculosis* or demonstration of acid-fast organisms in the pus, except in the study by Kaushik et al.,[15] the diagnosis was confirmed by Polymerase chain reaction (PCR) for *M. tuberculosis* MPB64. Thus, newer techniques like PCR may provide useful tool for diagnosis of *tuberculosis* from paucibacillary specimens like pus in which conventional methods may show low sensitivity. Even in the present study, a new technique, *In vitro* HMRS, was evaluated for the diagnosis of TBA. Absence of multiplet of amino acids-lipids at 0.9 ppm seems to be a hallmark of TBAs. Similar findings have been reported in the literature.[18,19] An attempt was made to compare these spectra with the pus specimen, which showed pure growth of anaerobe (pyogenic brain abscess). Pus specimens which showed the presence of anaerobes on culture revealed the presence of multiplet at 0.9 ppm, along with lactate-lipid at 1.3 ppm, acetate at 1.92 ppm, and succinate at 2.4 ppm [Figure 1a and b].

The case of concomitant tuberculous and pyogenic brain abscess showed spectra similar to pyogenic brain abscess. However, succinate (marker for anaerobes) peak was absent suggesting that the pus specimen may have facultative anaerobes. As there are no major peaks in TBA except that of lactate-lipid, the total spectra were masked by the pyogenic abscess spectra. However, the

Gram stain, ZN stain, and gold standard conventional culture gave the complete etiological diagnosis.

Whitener’s[1] review of 16 cases also revealed the following common features in TBA: 1. Frequent occurrence of TBA in the third and fourth decade of life; 2. A 35% incidence of multiple brain abscesses; 3. Predominant supratentorial location of the abscess in the frontal lobe; 4. Evidence of extra CNS *tuberculosis* in 85% cases; and 5. Occurrence of TBA despite antituberculous treatment and presentation with rapidly progressive neurological deficit.

Contrary to Whitener’s[1] observations, one of our patients was a 15-year-old girl. Table 2 clearly shows that TBA can occur at any age. Of four cases in the present study, one (25%) of the patients presented with multiple brain abscesses involving temporal, parietal, and occipital lobe. Remaining three cases had a solitary abscess involving frontal, temporal, and parietal lobe. Multiple TBA is rare, with only a few reports appearing in the literature.[17,20]

Table 2 also shows that TBA can occur in any part of brain involving the ventricles.[10]

In the present study, the coexistence of pulmonary *tuberculosis* was seen in two patients. CNS *tuberculosis* occurs secondary to hematogenous spread of *M. tuberculosis* from pulmonary Koch’s.[15]

Among the laboratory diagnostic modalities used, ZN stain and culture were found to detect the presence of AFB in all the four cases. Table 1 shows that three of the pus specimens grew *M. tuberculosis* as sole isolate. The fourth case was of concomitant tuberculous and pyogenic brain abscess. A second concomitant pathogen with TBA is rare.[21] There are very few reports of concomitant tuberculous and pyogenic brain abscess that appeared in the literature, namely dual infection due to *Toxoplasma*,[21] *Echinococcus*,[22]

TBAs are an unusual clinical presentation of central nervous system tuberculosis occurring extremely infrequently in developed countries, and almost always in immunocompromised patients. TBA is an uncommon clinical entity, even in countries where *tuberculosis* is endemic.[23] It occurs in only 4 to 8% of patients with CNS TB who do not have HIV infection[1] but in 20% of patients who do have HIV infection.[22,23] We encountered one such case which yielded a pure growth of *M. tuberculosis*. Fischl et al.[21] described a case of TBA and toxoplasma encephalitis in a Haitian woman with AIDS. Farrar et al. reported TBA in a 43-year-old man with a history of intravenous drug use. Vidal et al.[25] (2003) reported a case of TBA in a patient with AIDS. They also reviewed the
Table 2: Details of tuberculous brain abscess patients from the available literature

<table>
<thead>
<tr>
<th>Study</th>
<th>Age/ Sex</th>
<th>Presenting symptoms</th>
<th>Immune status</th>
<th>Lobe involved</th>
<th>Extra CNS TB</th>
<th>ZN stain results</th>
<th>Culture results</th>
<th>Other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whitener, 1978</td>
<td>25/M</td>
<td>Sore throat, throat pain, fever, swelling of the left side of neck, and jaw pain</td>
<td>Immuno-competant</td>
<td>Frontal</td>
<td>Nil</td>
<td>AFB seen</td>
<td>M. tuberculosis</td>
<td></td>
</tr>
<tr>
<td>Mohanty and Rao, 1978</td>
<td>20/F</td>
<td>History of progressive impairment of memory, and insomnia, intermittent headaches, vomiting, right-sided focal convulsions, several attacks of brief unconsciousness.</td>
<td>Immuno-competant</td>
<td>Frontal</td>
<td>Nil</td>
<td>No AFB seen</td>
<td>M. tuberculosis</td>
<td></td>
</tr>
<tr>
<td>Chandramuki et al, 1981</td>
<td>37/M</td>
<td>Headache, giddiness, vomiting, blurring of vision, fever, bilateral papilloedema</td>
<td>Immuno-competant</td>
<td>Cerebellar</td>
<td>Pulmonary</td>
<td>AFB seen</td>
<td>----------------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>13/F</td>
<td>Bifrontal headache, convulsions, neck stiffness, bilateral papilloedema, facial palsy</td>
<td>Immuno-competant</td>
<td>Fronto-temporal Abdominal</td>
<td>AFB seen</td>
<td>M. tuberculosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inbasekaran and Natarajan, 1991</td>
<td>4/F</td>
<td>Headache, vomiting, unsteady walking</td>
<td>Immuno-competant</td>
<td>Cerebellar</td>
<td>Pulmonary</td>
<td>Bacteriological examination showed</td>
<td>M tuberculosis</td>
<td></td>
</tr>
<tr>
<td>Farrar et al, 1997</td>
<td>43/F</td>
<td>Intravenous drug user, Focal seizure, involuntary movement of leg,</td>
<td>HIV infected</td>
<td>Fronto-parietal</td>
<td>Nil</td>
<td>AFB seen</td>
<td>M. tuberculosis</td>
<td></td>
</tr>
<tr>
<td>Vajramani et al, 1999</td>
<td>26/F</td>
<td>Fever, neck pain, double vision, neck stiffness</td>
<td>Immuno-competant</td>
<td>Intraventricular</td>
<td>Nil</td>
<td>AFB seen</td>
<td>----------------------</td>
<td></td>
</tr>
<tr>
<td>Babu and Shavinder, 2001</td>
<td>40/M</td>
<td>Fever, headache, vomiting</td>
<td>CT showed hypodense lesions surrounded by enhancing ring</td>
<td>Parietal</td>
<td>Nil</td>
<td>AFB seen</td>
<td>M. tuberculosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>35/F</td>
<td>Fever, headache, vomiting</td>
<td>HIV infected,</td>
<td>Frontal</td>
<td>Nil</td>
<td>AFB seen</td>
<td>M. tuberculosis, Streptococci</td>
<td></td>
</tr>
<tr>
<td>Siddiqui et al, 2001</td>
<td>55/M</td>
<td>Headache, vomiting, altered conscious-ness, neck rigidity, left sided hemiparesis</td>
<td>Diabetic</td>
<td>Parietal</td>
<td>Nil</td>
<td>AFB seen</td>
<td>M. tuberculosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>42/F</td>
<td>Occipital headache, fever, left sided weakness, bilateral papilloedema, lt sided motor deficit</td>
<td>Immuno-competant</td>
<td>Occipital</td>
<td>Nil</td>
<td>No AFB seen</td>
<td>M. tuberculosis, Streptococci</td>
<td></td>
</tr>
<tr>
<td>Vidal, et al, 2003</td>
<td>34/F</td>
<td>Headache, seizures</td>
<td>HIV infected,</td>
<td>Frontal</td>
<td>Nil</td>
<td>AFB seen</td>
<td>----------------------</td>
<td></td>
</tr>
<tr>
<td>Chatto-padhyay and Kundu, 2006</td>
<td>15/M</td>
<td>Fever, headache, vomiting, convulsions, double vision, left sided hemiparesis</td>
<td>Immuno-competant</td>
<td>Frontal</td>
<td>Nil</td>
<td>AFB seen</td>
<td>----------------------</td>
<td></td>
</tr>
<tr>
<td>Kaushik et al, 2007</td>
<td>26/M</td>
<td>Fever, headache, altered sensorium, neck stiffness, papilloedema</td>
<td>HIV infected</td>
<td>Parietal</td>
<td>Pulmonary</td>
<td>No AFB seen</td>
<td>Negave for pyogenic organisms, M tuberculosis and fungi</td>
<td>PCR + MPB64</td>
</tr>
<tr>
<td>Somale et al, 2009</td>
<td>11/F</td>
<td>Headache, blurring vision, vomiting, left eye prominent, seizure in the past, unilateral proptosis</td>
<td>Immuno-competant</td>
<td>Parieto-temporo-occipital</td>
<td>Tubercular lymphadentis: cervical and abdominal</td>
<td>AFB seen</td>
<td>No growth</td>
<td></td>
</tr>
</tbody>
</table>
Table 2: (Contd..)

<table>
<thead>
<tr>
<th>Study</th>
<th>Age/ Sex</th>
<th>Presenting symptoms</th>
<th>Immune status</th>
<th>Lobe involved</th>
<th>Extra CNS TB</th>
<th>ZN stain results</th>
<th>Culture results</th>
<th>Other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narang et al, 2010</td>
<td>2/F</td>
<td>Fever, paroxysmal cough, decreased movement of Right side of body, drowsiness, decreased acceptance of food, papilloedema</td>
<td>Immuno-competant</td>
<td>Multiple</td>
<td>Bilateral military motting in chest X-ray</td>
<td>No AFB seen</td>
<td>M. tuberculosis</td>
<td>PCR + for M. tuberculosis</td>
</tr>
</tbody>
</table>

literature from 1981 to 2002 and found eight cases of TBAs in HIV infected patients. Kaushik et al.18 also reported TBA in a 26-year-old male who was HIV seropositive.

Of these four patients, from the present study, patient no. 1 died who also had an altered level of consciousness at the time of admission. He also gave history of fall but no history of extra CNS tuberculosis. Rest three patients were put on anti-Koch’s treatment and being followed up regularly.

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References


Commentary

It is not uncommon to encounter tuberculous infection of central nervous system (CNS) in developing countries. Majority of these cases are either tuberculous meningitis or tuberculosis. Tuberculous brain abscess (TBA) is a rare condition.