



TUBERCULOUS BRAIN ABSCESS: RARE PRESENTATION OF A COMMON DISEASE

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ABSTRACT

Introduction: Tuberculous brain abscess is a rare form of central nervous system tuberculosis. It needs to be differentiated from pyogenic brain abscess which is a close mimic on radiology and histopathology.

Material and methods: Retrospective review of case records of histologically confirmed brain abscess and tuberculomas from 1987 to 2014 was done and cases fulfilling the criteria by Whitener were included. The clinical, imageologic, histologic and microbiologic findings were noted. Zeihl Neelson (ZN) stain and additional stains as appropriate were performed.

Results: There were 8 patients with TBA accounting for 2.67% of brain abscess and 2.88% of tuberculomas in the study period (28 years). There were 5 males and 3 females in the age range 10-45 (median 26.5) years. CT scan showed ring enhancing lesions with central hypodensity in all of them. The histopathology showed granulation tissue with palisading histiocytes and necrotic material with tinctorial properties of caseation. ZN stain revealed acid fast bacilli which were further confirmed on culture examination. The unusual findings were atypical mycobacteria in one and concomitant *Nocardia* spp in another. **Conclusion:** Histopathology with appropriate additional stains and culture confirmation help in identifying concomitant pathogens. Correct diagnosis and differentiation from pyogenic abscess is essential for management.

KEYWORDS : Tuberculous brain abscess, Histopathology, Culture, Atypical mycobacteria, *Nocardia* spp.

Introduction:

Tuberculous brain abscess (TBA) is a rare manifestation of central nervous system (CNS) tuberculosis. It is uncommon even in countries where tuberculosis is endemic. The criteria for the diagnosis of TBA are pus / necrotic material in the abscess cavity, evidence of acute and chronic inflammatory cells in the abscess wall, absence of epithelioid granulomas and presence of acid fast bacilli (AFB) or *Mycobacterium tuberculosis* on culture.^[1] Menon et al reviewed all reported cases of TBA and added 4 cases of their own.^[2] Only few small case series of TBA were reported from India since then.^[2,5] In this paper, we report a case series of eight TBA in immunocompetent patients from a tertiary care center from south India seen over a period of 28 years. We also highlight the importance of additional stains and culture confirmation for concomitant pathogens.

Material & Methods:

This was a retrospective study of the case records of all the intracranial tuberculomas and brain abscesses diagnosed on histology in the department of pathology from our institute between 1987 and 2014. The cases of brain abscess fulfilling the criteria of Whitener as TBA were included in the study.^[1] The demographic data, clinical, imaging and surgical findings were retrieved from the medical records. Predisposing conditions if any were noted. Culture reports were obtained from microbiology department. The histology sections were reviewed with hematoxylin and eosin (H & E), Zeihl Neelson (ZN), reticulin and Masson trichrome stains. Additional stains like 1% AFB or Gomori's methanamine silver (GMS) and periodic acid Schiff (PAS) were done wherever indicated.

Results:

In the study period of 28 years, 300 brain abscess and 278 intracranial tuberculomas were diagnosed on histology in our department. There were eight TBA which constituted 2.67% of brain abscess and 2.88% intracranial tuberculomas. There were five males and three females including two children with age ranging from 10 to 45

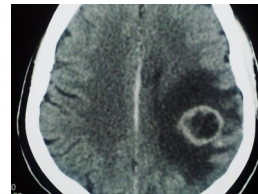


Figure 1: Computerised tomographic image shows ring enhancing lesion with peri-lesional edema in left temporo-parietal area with mass effect.

Stereotactic aspiration of pus and biopsy of the abscess wall was done in three and excision of abscess was done in all the other patients. All the patients were started on anti tuberculous treatment (ATT) with isoniazide, rifamycin, ethambutol and pyrizinamide. One patient died in the post operative period due to sepsis. No follow up details were available for two patients. Five patients improved with ATT at 6 months follow up. Long-term follow-up details were not available.

The aspirated pus in all the cases showed AFB on ZN stain. Culture was available in all; *Mycobacterium tuberculosis* in six,

Mycobacterium fortuitium in one and a mixed infection of Mycobacterium tuberculosis and Nocardia brasiliensis in one.

Histopathology showed fibrous capsule, granulation tissue and necrotic material (Fig.2). The capsule did not show epitheloid granulomas or giant cells. There were neutrophils, and

lymphomononuclear cells . The necrotic material had tinctorial properties of caseation which prompted us to do the ZN stain and it revealed moderate to numerous AFB in all the cases. The atypical mycobacteria were positive with PAS stain in addition to ZN stain. In one patient there were slender filaments of Nocardia spp on GMS and 1% AFB stains in addition to AFB (Fig. 2).

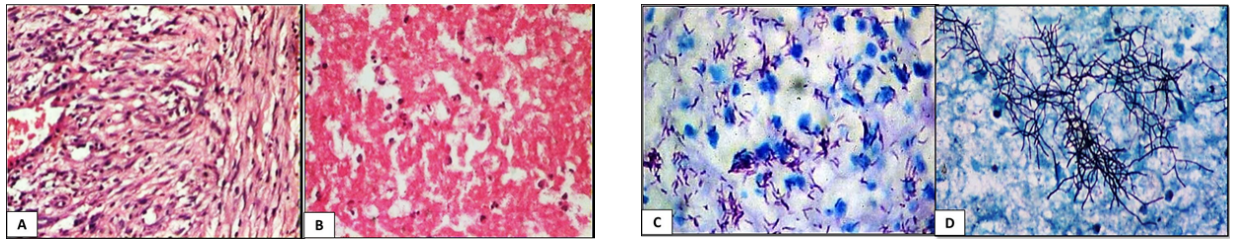


Figure 2: Photomicrograph shows (A) Thick fibrous capsule with granulation tissue H&Ex400; (B) Necrotic material with tinctorial property of caseation H&Ex100. The necrotic material showing (C) Acid fast bacilli ZNx1000; (D) Nocardia spp SMx100.

Table 1 shows the clinical, imageological, surgical, microbiological and pathology findings.

Table 1: Tuberculous brain abscess: demographic, clinical, imageological, operative, culture and pathology features

| S No | Age/ gender | Clinical presentation | Imageology | Surgery | Culture/ Pathology |
|------|-------------|---|--|--|--|
| 1 | M/25 years | Headache and vomiting 20 days; swaying while walking 7days; no papilloedema; left cerebellar signs + | CT: Well defined hypodense irregular walled lesion with good contrast enhancement, mass effect, distortion of 4th ventricle, hydrocephalus | Circumscribed well defined abscess with frank yellow pus with well formed wall in left cerebellar hemisphere. Excised totally | Pus: ZN stain positive Culture: Mycobacterium tuberculosis Pathology: Thick fibrous wall with granulation tissue, lymphomononuclear infiltrates, palisading histiocytes and necrotic material; ZN stain revealed numerous AFB |
| 2 | M/25 years | Fever 2 months; seizures 1 month; headache, vomiting, right side weakness; altered sensorium 20 days; right UMN facial palsy, right hemiplegia, meningeal signs+; know case of pulmonary tuberculosis on irregular treatment; | CT: ring enhancing lesion with peri-lesional edema in left temporo-parietal area with mass effect | Burr hole was made and pus was aspirated and ATT was started; patient developed drug induced hepatitis; excision performed and left frontal reservoir placed with EVD; put on ventilator; developed hypo-natremia, SIADH, sepsis and died. | Pus: Zn stain positive; PAS stain positive; Culture: Mycobacterium fortuitium (atypical mycobacteria) after 5 days Pathology: fragment of abscess wall with granulation tissue and necrotic material |
| 3 | M/10 years | Headache, vomiting: 15 days; fever 1 month; swaying while walking 15 days; cerebellar signs+ | CT: multi-loculated cerebellar abscess with thick irregular wall; hydrocephalus+ | Total excision of the abscess | Pus: ZN stain positive Culture: Mycobacterium tuberculosis Pathology: palisading histiocytes around multiple foci of necrotic material; ZN stain positive |
| 4 | F/45 years | Headache, vomiting: 1 month seizures 2 months; altered sensorium 1 week; papilloedema | CT: ring enhancing lesion with irregular thick wall and central hypodense area in right parietal area with mass effect | Encapsulated abscess with thick wall and central purulent necrotic material, was excised | Pus: Zn stain positive Culture: Mycobacterium tuberculosis Pathology: Thick fibrous wall with lympho-mononuclear infiltrate, neutrophilic debris and necrotic material; ZN stain revealed moderate number of AFB |
| 5 | M/10 years | Fever 3 months; left hemiparesis 10 days; seizures 10 days | CT: multi-loculated abscess with irregular wall in right frontal region with contrast enhancement and peri-lesional edema; MRI: irregular ring enhancing lesion with peri-lesional edema and mass effect | Total excision of the abscess | Pus: ZN stain positive Culture: Mycobacterium tuberculosis Pathology: granulation tissue with neutrophilic debris, lymphomononuclear cells and necrotic material; ZN stain revealed moderate number of AFB |
| 6 | F/35 years | Headache, vomiting 15 days; fever 1 month; known case of pulmonary tuberculosis in the past | CT:irregular enhancing lesion in the left parietal region with central hypodense area; MRI: irregular ring enhancing lesion with peri-lesional edema X-ray chest : fibro-cavitary lesion in left upper lobe | Total excision of the abscess | Pus: ZN stain positive; Culture: Mycobacterium tuberculosis + Nocardia brasiliensis Pathology: Fibrotic wall with granulation tissue, and necrotic material; tiny granules positive with 1% AFB and thin filaments on GMS stain in addition to AFB on ZN stain |

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| 7 | F/28 years | Fever, headache, vomiting 2 months; seizures 1 month | MRI: contrast enhancing ring lesion in the left temporo-parietal region; peri-lesional edema, mass effect | Excision of the abscess | Pus: ZN stain positive Culture: Mycobacterium tuberculosis Pathology: palisading histiocytes, foamy macrophages, lympho-mononuclear infiltrates, and necrotic material; ZN stain revealed AFB |
| 8 | M/42 years | Fever, headache, vomitings and seizures 1 month | MRI: ring enhancing lesion in right frontal region with mass effect | Excision of the abscess | Pus: ZN stain positive Culture: Mycobacterium tuberculosis Pathology: granulation tissue, foamy macrophages, lympho-mononuclear infiltrate and necrotic material; ZN stain revealed numerous AFB |

Abbreviations: CT: computed tomography; MRI: magnetic resonance imaging; ZN: Zeihl Neelson; PAS: periodic acid Schiff; GMS: Gomori's methenamine silver; AFB: acid fast bacilli

Discussion:

The exact incidence of TBA is unknown. It is reported that TBA occurs in 4-8% of patients with CNS tuberculosis who do not have HIV infection and in 20% of patients with HIV infection.^[6,7] In our series, TBA constituted 2.67% of brain abscess and 2.88% of tuberculomas in histologically verified samples over a period of 28 years. All our patients were immunocompetent and negative for HIV infection. The rarity of TBA and its occurrence in immunocompetent patients as seen in our series was reported in earlier studies from India.^[3-5] Though HIV epidemic rendered tuberculosis more prevalent, TBA associated with HIV is rarely reported from India.^[2-3] Associated tuberculous pathology in lung, bone or CNS is reported earlier as seen in two of our patients.^[2,5] The diagnosis of TBA is challenging as the clinical, radiological and pathological findings are very similar between pyogenic abscess and TBA.^[2] Definitive diagnosis of TBA is histological study of wall of the abscess complemented by ZN stain or culture studies. All our patients were diagnosed on histology of the excised brain abscess, with demonstration of AFB in the necrotic material. We observed that the tinctorial properties of the necrotic material in addition to palisading histiocytes provide important clue to suspect tuberculous etiology on histology. Chakraborti et al suggested that palisading epithelioid cells, sheets of foamy histiocytes, neutrophilic exudate rich in fibrin and nuclear debris provide important clues to diagnosis.^[4] Additional stains with 1% AFB and GMS identified thin filaments of *Nocardia* spp in addition to AFB, and confirmed on culture (Fig.3). A second concomitant pathogen in TBA is rare.^[2,9] Atypical mycobacteria (*Mycobacterium fortuitum*) are rarely reported in TBA[9]. TBA differs from tuberculoma with central caseation by lacking epithelioid granulomas and from pyogenic brain abscess by the presence of AFB in the pus.

Treatment options for TBA include stereotactic aspiration or total excision followed by medical treatment.^[5,7] Mohindra et al recommended surgical excision of TBA measuring >3 cm in size to promote the efficacy of ATT.^[5] Stereotactic aspiration and biopsy of cyst wall as a useful alternative modality of management in select group of patients was highlighted by Mohanty et al.^[10] Three of our patients had stereotactic aspiration of pus with biopsy of the abscess wall and all other patients had excision of the abscess.

The exact pathogenesis of TBA is uncertain. It develops either by hematogenous spread from lung or parenchymal tuberculoma/tuberculous focus from the meninges.^[4] The tissue reaction depends on the immune status of the host and the size of the inoculum and hence a large inoculum of bacilli in a sensitized host may lead to an exaggerated exudative phase with extensive caseation.^[1,4]

Conclusions: Tuberculous brain abscess is rare occurring in immunocompetent patients. The diagnosis is essentially on histological examination of abscess wall, tinctorial properties of necrotic material, complemented by ZN stain and / or culture. Additional histochemical stains and culture help in identifying concomitant and unusual pathogens.

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