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# Tuberculoma of Cavernous Sinus - An Atypical Presentation of Neurotuberculosis with Review of Existing Literature

Medical Science

KEYWORDS :Neurotuberculosis, cavernous sinus, extracranial sites

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## ABSTRACT

*Tuberculoma is one of the commonest intracranial masses, particularly so in developing countries. Occurrence of central nervous system (CNS) tuberculoma in the cavernous sinus area is extremely rare. Even, the diagnosis of the condition is very challenging as the presentations are often misleading and mimic that of some intracranial tumors, thus often requires a neurosurgical procedure. Only sixteen cases have been reported in previous literature, of which two cases presented in pediatric age group. Here we report the third pediatric case of cavernous sinus tuberculoma. A four year old boy presented with progressive cavernous sinus syndrome without any history of exposure to tuberculosis. Laboratory results were nonspecific with normal chest radiography. His cervical lymph node biopsy showed caseating granuloma, rapid bacteriological confirmation was possible and was treated successfully. Although the diagnosis of the condition is very difficult, careful search for extracranial sites of the disease in can lead to early histopathological confirmation and better outcome.*

**Introduction:**

Tuberculosis (TB) is capable of a wide variety of intracranial presentations including meningeal and intracerebral or parenchymal disease[1]. Intracranial tuberculomas are common lesions, mainly in developing countries accounting for 10-30% of all intracranial masses[2, 3]. Tuberculoma of the CNS can occur at any site in any age group. Despite the propensity to affect the hemispheres, unusual locations of CNS tuberculoma continue to be reported, including the cerebropontine angle, the sellar and suprasellar regions, and, the cavernous sinus (CS) [1, 4]. Only sixteen cases of CS tuberculomas have been reported in the various literatures and journals since 1992[1].

Out of 16 cases, pulmonary TB was detected in three cases and it was localized to Meckel's cave in three patients. Cervical lymph node involvement was seen in one patient and in another case, subcarinal lymph node biopsy proved the diagnosis[1]. Extra-neural TB was reported in six patients and the initial diagnosis was meningioma in seven cases. In all cases, tuberculous bacilli were absent in the cerebrospinal fluid (CSF). It is interesting to observe that none of the biopsied intracranial tumors had reported acid fast bacilli (AFB) smear positivity and none had culture positivity for *Mycobacterium tuberculosis* (MTb).

Here we report a new case of CS tuberculoma, probably the third case in pediatric age group where rapid diagnosis including bacteriological confirmation was possible by BACTEC culture of biopsied tissue material.

**Case Report:**

A four-year-old boy from lower socioeconomic status with the body weight of 8 kg (< 3rd percentile of WHO growth chart) was admitted with history of sudden onset of high grade fever with severe headache along with periorbital edema, bilateral proptosis and ptosis of both eyes [Fig. 1], with retro orbital pain and two episodes of generalized tonic-clonic convulsions for last two days. There was no history of contact with tuberculosis.

**Fig. 1: Ocular manifestations in the patient at initial presentation showing bilateral ptosis, proptosis and periorbital edema**

On examination, the patient was semiconscious (Glasgow Coma Scale score - 9/15), highly febrile (103ºF), moderately pale and four significantly enlarged cervical lymph nodes were palpable. He had tachycardia (pulse rate 116/min), tachypnea (respiration rate 46/min) with normal blood pressure (90/64 mm of Hg). Chest auscultation was normal and CNS examination revealed signs of meningeal irritation along with bilateral IIIrd & VIth cranial nerve palsy. Plantar response was bilateral extensor, all jerks were brisk. Motor and sensory system could not be elicited properly.

Investigations revealed Hemoglobin -7.9gm/dl, total leucocyte count -13700/cmm, Neutrophils 68%, Lymphocytes 36%, Eosinophils 4%, Basophils 1%, Monocytes1%; ESR – 56mm. CSF study showed 16 cells/cmm (all lymphocytes), protein -69 mg/dl, glucose-60 mg/dl, ADA 6U/L, Ziehl–Neelsen (ZN) stain did not show any tubercular bacilli. Chest x-ray was normal with a negative tuberculin test. Other baseline investigations were normal. Considering the clinical diagnosis of CS thrombosis, initially empirical treatment with ceftriaxone and vancomycin was started along with anticonvulsant, mannitol and other supportive care.

After initial treatment, improvement in consciousness level was observed but fever and the ophthalmological ailments persisted and the patient developed left sided incomplete hemiplegia. Blood culture came sterile and HIV serology was non-reactive. MRI brain suggested granulomatous lesions most likely tuberculoma involving right basal ganglia, periventricular and medial temporal region and both CS area [Fig. 2].

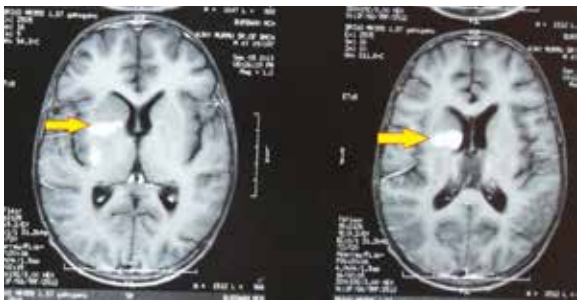

**Fig. 2: T2 weighted MRI showing thrombosis involving right basal ganglia, periventricular and medial temporal region and both cavernous sinus areas (as indicated by arrows)**

FNAC of the cervical lymph node showed AFB on ZN stain. Biopsy of the lymph node showed caseating granuloma suggestive of tuberculosis and BACTEC culture for *MTb* became positive.

Category I anti-tubercular drugs (ATD) with Isoniazid (H), Rifampicin (R), Pyrazinamide (Z) and Ethambutol (E) was started as per schedule along with steroid (Inj. Dexamethasone for seven days followed by prednisolone, for seven weeks).

We observed a dramatic & rapid response within five days by gradual reduction of periorbital edema with regression of proptosis and patient remained afebrile from the third day of starting of ATD. The signs of cranial nerve affection resolved within two weeks. The left sided weakness persisted but was gradually improving on physiotherapy.

The patient was discharged after three weeks of hospital stay. He attended follow up visit at our OPD regularly and was improving. Repeat MRI after one year of treatment with ATD was planned but he did not turn up.

**Discussion:**

Despite the considerable advancement in medical sciences, tuberculosis still remains a challenge and a public health issue worldwide, particularly in developing countries. There is increasing incidence of CNS tuberculosis, mostly due to human immunodeficiency virus and population migration, and development of multi-drug resistant strains[4].

Common presentations of CNS tuberculosis are tuberculous meningitis, tuberculoma, abscess or Pott's disease. In developing and endemic countries nearly 20% of brain masses have a tuberculous origin[5]. Intracranial tuberculomas are mostly located in cerebral hemispheres and basal ganglia in adults, and in cerebellar hemispheres in children[3]. Rare locations like brainstem, cerebellopontine angle, hypothalamic region, meckel's cave, pituitary gland and intraventricular spaces have been reported[1, 4]. The CS is an exceptional location for intracranial tuberculomas as in our case.

Review of literature found 16 reported cases of CS tuberculosis other than our own and only two cases were reported among children. Most cases of CS tuberculomas presented with variable degrees of CS syndrome without any history of TB, nonspecific laboratory & chest radiographic findings, and thus, not considering this diagnosis[4]. Nine of the 17 total cases were found to be HIV negatives including ours. The diagnoses of eleven cases were based on operative removal of the tumor and resultant pathology. Other cases, including our case, were diagnosed after testing revealed evidence of tuberculosis at extra-CNS sites.

The diagnose CS tuberculoma based on radiological features is often very difficult as there are no pathognomonic radiological findings. CT scans of a tuberculoma reveal an iso – to – hyperdense lesion with varying contrast enhancement pattern[6]. T1-weighted MRI demonstrates an iso – to – hypointense lesion. On T2-weighted images, it can appear as a hyperintense lesion or a hyperintense center surrounded by a hypointense rim[7]. A recent paper also suggests that diffusion-weighted MRI and MRI spectroscopy help in the diagnosis of tuberculoma[8]. One case demonstrated the utility of positron emission tomography (PET) -CT in finding an alternative site of disease[1]. Our case, once-again demonstrated the utility of BACTEC culture in rapid diagnosis of tuberculosis. ATD was started empirically in four cases with satisfactory resolution. All patients received a three or four drug regimen for a 12-month period; only five patients were administered steroids including ours. Resolution was achieved in all patients.

Mainstay of treatment in intracranial tuberculomas is medical. Surgery is reserved for large, solitary lesions with significant mass effect and unresponsive to medical treatment. Treatment of tuberculoma follows that of CNS tuberculosis in general: 4-drug antitubercular therapy (HRZE) in a 2-month intensive phase followed by 2 drug therapy (HR) for a continuation phase to complete a 9–12 month course[9], although shorter and longer courses have also been proposed. The rationale for corticosteroid treatment includes possible reduction of symptoms as well as prevention of paradoxical expansion of the tuberculoma[1, 4, 10], although there were no proved benefits of adjunctive steroids in the treatment of CNS tuberculoma in controlled trials[9].

In conclusion, intracranial tuberculomas can be situated in every location and can mimic any lesion. A careful search for extracranial sites of disease can lead to earlier and safer histopathological confirmation and thus, difficulty and delay in diagnosis can be avoided. Pulmonary involvement is not always present and radiological studies are not always conclusive. Biopsy is often required for definite diagnosis, still treatment is essentially medical. A high index of suspicion should be maintained, particularly in presence of risk factors. Antitubercular therapy is highly effective, and adjunctive steroids must be considered in order to expedite the recovery. A long-term clinical and radiologic follow-up are very much essential in securing a good outcome.

**Table 1: Characteristics of various reported cases in existing literature**

| Authors and year | Age (years)/ gender/ ethnic origin | Symptoms/ presentation | Pulmonary involvement | Extra Neural Sites involvement | Immunological status | Diagnostic method | AFB* smear/ culture positivity | Treatment | Outcome |
|---|---|---|---|---|---|---|---|---|---|
| Morris et al., 1992 | 42, F "Filipino „ | Orbital pain, ptosis, facial numbness, vision blurred | No | No | HIV† -ve | Operative removal revealing granulomas | AFB -ve | HRZ & Pyridoxine | Complete resolution of eye deficits, Continued CN § VII palsy |

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|---|---|---|---|---|---|---|---|---|---|
| Phookan et al., 1995 | 33 M, "Asian" | Headache, Orbital pain, diplopia, facial pain, ptosis, opthalmoplegia | No | No | NR ‡ | Operative removal revealing granulomas | AFB –ve, Culture not mentioned | HRZE \|\| + Pyridoxine | Improved eye deficit at 2yrs but not resolved |
| Bafna et al.,, 1997 | 65 F, NR | Periorbital pain, Ptosis and ophthalmoplegia on right | No | Yes (Cervical LN ¶ ) | DM **+ve | Cervical LN biopsy | AFB -ve, Culture +ve for MTb †† | HRZE + Methyl prednisolone | Partial improvement of ptosis and motility at 6 weeks, imaging improvement |
| Rebai et al., 2001 | 44 F, NR | Headache for 1 month, right ptosis, horizontal diplopia, right CN III, CN V, CN VI deficit | Yes | Yes (Encapsulated Pleurisy) | NR | Biopsy of lesion performed revealing tuberculoma | Not commented on both | HRE for 1year | Complete resolution with improved imaging |
| Al Soub et al., 2001 | 44 M, Thai | Headache, periorbital pain, ptosis, ophthalmoplegia | Yes | Yes (lung infiltrate on chest radiography) | HIV -ve | Sputum culture revealed Mtb | AFB –ve, Culture +ve for MTb | HRZE + Pyridoxine for2months, Then HR for 10 months, Prednisolone-1month | Complete resolution with improved imaging |
| Hui, 2002 | 48 M, NR | Headache and double vision x 2 weeks, R eye abduction deficit, absent right corneal reflex, right eye ptosis, R CN III, IV, V, VI deficit | No | No | NR | Operative removal revealing granuloma | Both -ve | ATD ‡‡ treatment for 12 month | Residual right abducens nerve palsy |

**Table 1 continued……**

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|---|---|---|---|---|---|---|---|---|---|
| Grayeli et al., 1998 | 48 M, "Black African" | Headache & orbital pain for 2 months, left eye ptosis, left upward and medial gaze deficit, hemifacial hypethesia | Yes | Yes (Apical Macronodular hypodensities) | HIV -ve | Operative removal revealing granuloma, CxR¶¶ with sequelae of old TB | AFB –ve, Culture -ve | HRE | Complete resolution with improved imaging |
| Goel et al., 1999 | 35 F, NR | Headache for 1 year, left facial paresthesia, left gaze diplopia, wasting of temporalis and masseter on left, left CN V, VI deficit | No | No | HIV -ve | Operative removal revealing tuberculoma | AFB –ve, Culture – not mentioned | ATD for 18 months | Complete resolution with improved imaging |
| Yanardag et al., 2005 | 36 M, NR | Headache for 2 months, ptosis, diplopia, medial, upward and lateral left gaze deficit, left hemifacial hypoaesthesia in CN V1 area | No | No | HIV -ve | Operative removal revealing granuloma | Both -ve | HRE | MR improved at 2 months, symptoms improved at 4 months |
| Intusoma et al., 2006 | 3 F, Thai | Ptosis & medial gaze palsy of R eye for 7 day, mild proptosis and 4 mm non reactive pupil | Yes | Yes (lung infiltrate on chest radiography) | Healthy HIV status not mentioned | Presumed diagnosis, Abnormal CxR, +ve MT, | +ve MTb Culture from gastric content | ATD for 12 months | Complete recovery. |
| Kesavadas et al., 2007 | 29 M, Asian | Left sided facial numbness, decreased taste, RUE RLE weakness, L CN V sensory deficit, left temporalis and masseter wasting, right uvula, RUE RLE hypotonia | No | No | HIV - ve | CSF lymphocytosis, operative removal revealing granuloma | Both -ve | ATD for 4 month at the time of reporting | Complete resolution with improved imaging |
| Boutarbouch et al., 2009 | 45 M, NR | Headache, periorbital pain, left hemifacial neuralgia, diplopia, ptosis, lateral gaze palsy | No | No | NR | Operative removal revealing granulomas | Both -ve | HRZS for 3 month, then HR for 9 month | Complete resolution with improved imaging |

**Table 1 continued……**

| Authors and year | Age (years)/ gender/ ethnic origin | Symptoms/ presentation | Pulmonary involvement | Extra Neural Sites involvement | Immunological status | Diagnostic method | AFB smear/ culture positivity | Treatment | Outcome |
|---|---|---|---|---|---|---|---|---|---|
| Haque et al., 2012 | 35 M, Asian | Headache for 1 year and right sided ptosis for 1 month. 3rd nerve palsy of right side | No | No | NR | Operative removal & histopathological confirmation | Not commented about both | ATD for 18 month | Ocular symptoms improved within 4 wks with improved imaging at 18 months) |
| Jaimovich et al.,2013 | 42 F, Argentina | Headache, right ptosis, right hemifacial hypoesthesia, right ophthalmoplegia | No | No | HIV -ve | Operative removal revealing granuloma | AFB not mentioned, culture -ve | HRZE for 2month, then HR for 4 month + Dexamethasone for 8 wks | Complete resolution with improved imaging |
| Kumar et al., in 2014 | 11 F, Asian | right hemicranial headache, diplopia, numbness of the right side of her face – 2m Right ear purulent discharge & hearing loss – 2yrs | No | Yes (Mastoid air cells) | NR | Operative removal revealing granuloma | Not commented about both | HRZE Total 18months treatment | Complete resolution with improved imaging |
| Kapadia et al., 2014 | 48 F, Asian | Diplopia – 2 months, Headache & photophobia – 1month, ptosis, lateral gaze palsy, diminished medial & downward gaze, Facial hypothesia | No | Yes (Subcarinal lymph node involvement) | HIV - ve | Quantiferon1-GOLD test – positive, Biopsy of the subcarinal lymph node revealed granulomas & +ve culture for Mtb | AFB not mentioned, culture +ve for MTb | HRZ + Levofloxacin (L) for 3 month, HR+ L for 1month, HR for 8month, Prednisolone | Ocular symptoms improved rapidly with near complete resolution on MR at 1 months |

Abbreviations: *AFB=Acid Fast Bacilli, † HIV= Human Immunodeficiency Virus, ‡ NR= Not Reported, § CN = Cranial Nerve, || [H = Isoniazid, R = Rifampicin, Z = Pyrazinamide, E = Ethambutol], ¶ LN= Lymph Node, ** DM= Diabetes Mellitus, †† MTb = *Mycobacterium tuberculosis*, ‡‡ ATD =Antitubercular drugs, ¶¶ CxR= Chest X-ray

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