

# INTRACRANIAL TUBERCULOMAS AND CARIES SPINE: AN EXPERIENCE FROM CHILDREN'S HOSPITAL ISLAMABAD

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**Background:** Pulmonary tuberculosis in infants and children in Pakistan is quite common. However, there is limited data about uncommon forms of tuberculous infection of central nervous system. Tuberculosis of nervous system is a serious disease and if not treated adequately, carries high morbidity and mortality. This study was undertaken to highlight the occurrence of relatively uncommon forms of tuberculosis in children. **Methods:** This was a retrospective review of the case records of the patients who were admitted in Children's Hospital, Islamabad with the diagnosis of cerebral tuberculoma or tuberculosis of spine between January, 1994 and August, 2002. Diagnosis was based on clinical features, history of contact with tuberculous patient, abnormalities on chest X-rays and neuroimaging studies of brain and spine. **Results:** Nine children had cerebral tuberculomas, six more than one and in five were bilateral. Eight had caries spine, 2 cervical, 4 thoracic and 2 lumbar regions. Three had been vaccinated with Bacillus-Calmette-Guerin and family history of tuberculosis was positive in 7 (41%) children. Nine (53%) patients had evidence of pulmonary tuberculosis on chest x-ray. Ten computed scan brain, four magnetic resonance imaging, two spinal scan and two myelographic studies were performed. Three patients with tuberculomas and five with caries recovered and 8 were left with neurological deficit. One child with cerebral tuberculomas died. **Conclusion:** Intracranial tuberculomas and spinal tuberculosis are not rare problems in children. Early diagnosis and prompt antituberculous therapy are the most important factors for the favourable outcome.

**Key words:** Tuberculosis, Tuberculoma, tuberculous spondylitis, Caries spine

## INTRODUCTION

Tuberculosis (TB) is a serious health problem in poor countries and a leading cause of death. Approximately eight millions new cases of TB and three millions deaths are reported annually.<sup>1</sup> However, TB of central nervous system (CNS) is the most severe and life-threatening form of disease in children. Early diagnosis and prompt antituberculous therapy is important for optimal outcome, but diagnosing tuberculosis in young patients remains difficult.<sup>2</sup> The incidence of CNS TB is closely related to the prevalence of tuberculous infection in general. Initial focus of infection is usually in the lungs and through haematogeneous route tubercle bacilli spread to extra pulmonary sites. Tuberculous infection of CNS usually presents over weeks or months and because of insidious onset of symptoms, diagnosis may be delayed. Common clinical features of tuberculosis are fever, anorexia, weight loss, pallor, cough and night sweats. As the disease progresses, symptoms attributable to CNS appear. In case of tuberculomas features are headache, vomiting, seizures, cranial nerve palsies, weakness of one or more limbs and coma. Typical features of caries spine are backache, walking difficulty, weakness of one or more limbs and urinary and bowel problems. Although, TB is a widespread problem, data about intracranial tuberculomas and spinal spondylitis in children is limited.<sup>3</sup> This study was undertaken to highlight the presence of relatively uncommon forms of CNS tuberculosis in young patients.

## MATERIAL AND METHODS

Case records of children admitted in Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad between January 1994 and August 2002 and diagnosed as cerebral tuberculoma or caries spine were reviewed. Those children who in addition also had tuberculous meningitis were excluded from the study.

Diagnostic criteria required for the diagnosis of tuberculomas was: consistent signs and symptoms for  $\geq 4$  weeks and cranial CT scan showing single or multiple post contrast lesions with enhancing ring or uniform density with or without surrounding cerebral oedema and one of the following:

- a. History of TB in the family
- b. Chest x-ray (CXR) consistent with tuberculous infection of lungs

- c. Induration of > 10 mm with Tuberculin skin testing after 48 to 72 hours irrespective of prior Bacillus-Calmette-Guerin (BCG).
- e. Response to antituberculous therapy OR Mycobacterium tuberculosis (MTB) detected on polymerase chain reaction (PCR) OR Isolation of MTB from CSF or gastric aspirate on acid-fast stain or culture.

**Criteria for the diagnosis of caries spine was:**

- Signs and symptoms consistent with tuberculosis
- Clinical features of spinal cord compression,
- Complete or partial collapse of one or more vertebrae on X-ray spine and
- One of the criteria (a to e) used as above and
- Magnetic resonance imaging (MRI) or CT spine showing destruction of intervertebral disc and adjoining vertebrae causing compression of spinal cord or myelography with obstruction at the level of vertebral collapse as seen on plain X-ray of the spine. Children younger than 12 years were included.

Laboratory evaluation included complete blood picture with erythrocyte sedimentation rate (ESR), CSF analysis and culture, CXR, tuberculin skin test, serum electrolytes, liver and renal functions. Pre and post contrast CT scan of brain were performed on patients with suspected intracranial pathology. In children with vertebral involvement, spine was X-rayed in frontal and lateral views followed by either MRI/CT or myelography. Gastric aspirate for acid-fast stain and culture and blood or CSF PCR studies for MTB were obtained whenever possible. Gastric aspirates were obtained by either aspiration or lavage with 15 to 20 ml of distilled water for 3 consecutive mornings. Gastric aspirate specimens were sent for acid-fast staining and cultures. Sibs were screened in Outpatients with Mantoux test, ESR and CXR. Parents and other adult members of family had CXR whenever indicated.

Treatment was initiated with antituberculous therapy (ATT) and dexamethasone. Isoniazid (10-20 mg/kg), rifampicin (10-20 mg/kg) and pyrazinamide (30-40 mg/kg) was given orally in single daily dose and continued for twelve months. Streptomycin (20-30 mg/kg) was administered as intramuscular injection for the initial two months. Dexamethasone was administered intravenously or orally in full doses for three months and then tapered over the next 2 weeks. No surgical procedure was performed on children with intracranial tuberculomas irrespective of size, number or location and none of the Para vertebral abscess was drained.

## **RESULTS**

17 children were diagnosed as having tuberculous infection of CNS during 9 years. Nine had cerebral tuberculomas and eight Pott's disease. 11 were boys and age of the patients ranged from 10 months to 12 years with a mean of 5.5 years. Duration of symptoms before admission ranged from 1 to 12 months. Family history of TB was positive in 7 (41%) family members, mostly parents or grandparents. In patients with cerebral tuberculomas, common features were headache, vomiting, motor weakness of one or more limbs, cranial nerve palsies (3, 6 and 7<sup>th</sup>) and abnormal movements. Presenting symptoms in case of caries spine were backache, neck pain, walking difficulty and frequent falls. On examination had gibbus, restricted movements of spine and pyramidal signs in lower limbs. Two patients had loss of sensations and a sensory level. Three children had been vaccinated against tuberculosis. Majority of children received ATT in inappropriate doses and duration with poor compliance before coming to the hospital. Hospital stay ranged from 2 to 5 weeks. Ten (58%) were malnourished and lived in overcrowded slums with unhygienic living environment.

CXRs were abnormal in 9 children and included diffuse infiltrates, hilar lymphadenopathy, consolidation and calcification. Eight patients had involvement of vertebrae, thoracic 4, cervical and lumbar region 2 each. Five of these had Paravertebral abscess, 3 thoracic and 2 cervical region. Some patients had more than one abnormality on CXR (Fig-1). ESR varied from 10 to 55 mm and in 5 (27%) patients Tuberculin skin test had induration of > 10 mm after 48 hours. Seven out of nine patients had positive PCR for MTB. Pre and post contrast CT scan brain were performed on 10 children. All but one scan were abnormal: 6 showed more than one tuberculomas and in 5 were bilateral (Fig. 2AB). Three had single tuberculoma and in two appeared as uniform density (Fig. 2C). Four patients with vertebral spondylitis had MRI showing cord compression with vertebral collapse (Fig. 3A) and myelography in two showed obstruction (Fig. 3B) and 2 CT scan spine also showed destruction of vertebrae and paravertebral abscess (Fig. 3C). Gastric aspirate results (twelve patients) were negative

**Fig-1: Chest X-Ray showing large paravertebral abscess in cervicothoracic region and consolidation in left upper lobe. Lower vertebrae are affected as well (not shown)**

Eight children, 3 with cerebral tuberculomas and five with vertebral spondylitis recovered completely or with minimal neurological deficit. Five children had paravertebral abscess, three of them quite large, and depending upon the size these abscesses resolved 6 to 18 months after the initiation of ATT.

**Fig-2: Intracranial tuberculomas (A) Bilateral multiple with round enhancing rings (B) Unilateral multiple with irregular enhancing margins and (C) a large single as uniform opacity in right frontal lobe with extensive brain oedema and shift to the left**

**Fig-3 (A) MRI spine showing collapse of 10th thoracic vertebra and small abscess anteriorly, (B) Myelogram showing paravertebral abscess and obstruction at the level of 8<sup>th</sup> thoracic vertebra and (C) CT Scan showing paravertebral abscess and destruction of vertebral body**

Three patients were left with lower limb weakness and two of them also had kyphosis. Five children with tuberculomas were left with one or more of the neurological sequelae such as paraparesis, hemiparesis, seizures, blindness and cranial nerve palsies. One child died with cerebral tuberculomas.

## DISCUSSION

Childhood tuberculosis is a serious health problem and an important cause of morbidity and mortality.<sup>4</sup> Despite WHO's universally recommended Directly Observed Treatment Strategy, Pakistan is one of the several developing countries where tuberculosis remains an highly endemic disease.<sup>5</sup> Despite the fact that disease is widespread in Pakistan, culture-positive cases of TB in children are rare.<sup>3</sup> Therefore, most cases are diagnosed on the basis of clinical features, family history and radiological abnormalities.<sup>6</sup> In present series diagnosis was based upon epidemiological and clinical criteria. An effort was made to exclude other lesions, which can mimic cerebral tuberculomas and caries spine. In the presence of consistent clinical picture, one or more of the epidemiological evidence of tuberculosis such as family history of tuberculosis, abnormal CXR, neuroimaging abnormalities consistent with tuberculous infection of CNS, positive Tuberculin test and response to ATT was prerequisite to make the diagnosis of CNS tuberculosis.

Several reports of pulmonary tuberculosis and tuberculous meningitis in adults have appeared in recent years.<sup>7, 8</sup> however; data about tuberculous infection of CNS in general and intracranial tuberculomas and vertebral spondylitis in particular in children is limited. To authors' knowledge, this is the first case series about cerebral tuberculomas and caries spine in Pakistani children. In present series 9 patients had cerebral tuberculomas, in majority they were multiple and bilateral. CT scan brain with and without contrast was a very useful investigation. Intracranial tuberculomas are rare and their diagnosis is often delayed or overlooked. They are solid avascular nodular lesions with central caseation and on contrast CT brain are characterized by intense nodular or ring enhancement.<sup>9</sup> The "target sign" defined as central calcification is nonspecific finding and is not pathognomonic of CNS tuberculomas.<sup>10</sup> Histologically central core is caseation necrosis surrounded by Langhans giant cells and epithelioid cells. Outer layer is capsule and consists of collagenous fibres. Histological findings correlate well with Gd-DTPA enhanced MRI abnormalities.<sup>11</sup> High index of suspicion is important, however, current neuroimaging techniques can differentiate other lesions which may simulate intracranial tuberculomas.<sup>12</sup> Intracranial tuberculomas usually do not require surgery and respond well to ATT and dexamethasone. If diagnosed early and treated promptly, are potentially curable tumours of CNS.<sup>13</sup> If for some reasons neuroimaging studies cannot be performed urgently, ATT and steroids may be initiated on empirical basis and final decision may be made when all relevant investigations are available.

Tuberculous osteomyelitis occurs in only 1 to 6 % of children with tuberculosis.<sup>14</sup> Vertebrae are the most commonly affected bones,<sup>15</sup> though, rarely cervical spine.<sup>16</sup> Infection starts in the cancellous bone or anterior part of the vertebral body. Destruction of vertebral body leads to collapse and wedging anteriorly. Spinal cord compression is usually caused by the surrounding paraspinal abscess.<sup>13</sup> Collapsed vertebral bodies, intervening discs and large paravertebral abscess are usually visible on plain spinal x-rays. Myelography, CT scan and now MRI can easily identify the exact level and extent of vertebral destruction, spinal cord compression or para vertebral abscess. Surgical treatment of vertebral tuberculosis is controversial. Surgery may be indicated for large abscesses, spinal stabilization, protection of vital structures and surgical decompression along with ATT and steroids are treatment of choice in patients with paraplegia.<sup>13</sup> However, in present series none of the patient under went surgical procedure even with large para vertebral abscess and in almost two third of the cases recovery was optimal. Three of the 8 patients with spinal involvement were left with paraparesis and in addition two with some degree of kyphosis. All these children had severe vertebral destruction at the time of diagnosis. Reasons for poor outcome could be that in majority of patients lesion was quite extensive and none of the paravertebral abscess was drained. However, it seemed that size of the paravertebral abscess did not affect the outcome adversely, at least in three patients who had large paravertebral abscess and recovered. In present series children with tuberculous spondylitis presented with relatively shorter duration of illness and were of younger age group. Others have reported longer duration of illness, older age group and less common residual paraplegia (16%) in children with tuberculous spondylitis.<sup>17</sup> Clinical features of spinal tuberculosis may be apparent at the time of presentation, nevertheless, CXR as well as x-ray spine should be part of initial evaluation in a child with suspected CNS tuberculosis and look for evidence of pulmonary TB and vertebral spondylitis especially in younger patients. Occasionally spinal tumors may mimic caries spine, however,

epidemiological evidence of TB and neuroimaging studies would help in differentiating other spinal pathologies. Raised ESR and Tuberculin skin reaction were positive in small number of children. We feel that these laboratory investigations were not helpful in the diagnosis of CNS TB. However, neuroimaging studies including myelography and PCR though very helpful in the diagnosis are expensive investigations.

Major limitation in our study was lack of laboratory evidence of tuberculous infection on acid-fast staining and culture. None of patient had gastric aspirates acid-fast staining or culture positive. Others have also reported low sensitivity of smears and cultures in gastric aspirate samples of children with TB.<sup>18</sup> Children with extrapulmonary tuberculosis are less likely to be smear-positive but cultures are positive in one-third of the patients.<sup>19</sup> Reasons for very low identification of mycobacteria on smear or culture are not clear. PCR is relatively new technique used for rapid diagnosis of TB. In present series PCR was a useful investigation and seven of out nine were positive for MTB. In a rather small series of intracranial tuberculomas PCR was found to be potentially useful approach for early and rapid diagnosis of cerebral tuberculosis even without meningitis.<sup>20</sup> Sensitivity of PCR is very variable and ranges from low to high.<sup>21</sup> PCR though a rapid and relatively new diagnostic technique is expensive and not readily available, therefore cannot be performed routinely. For these reasons tuberculosis is one of the infections where diagnosis often depends upon clinical judgment and more emphasis should be given to epidemiological evidence such as family history and abnormal CXR.

Very few children had been vaccinated with BCG in present study. In a meta analysis of large number of published data preventive value of BCG against all types of TB was approximately 50% and 64% in TBM.<sup>22</sup> The protective efficacy varies from 0 to 80%.<sup>23</sup> Several case control studies have shown BCG efficacy against TBM between 85 and 100%.<sup>24,25</sup> Neonatal BCG vaccination provides good protection against TBM and other disseminated forms of tuberculosis. Prevention of TB by widespread neonatal BCG immunization is a practical strategy that may be effective as well as cost effective. Every child with TB should have regular follow-up and administration of ATT in adequate doses and with good compliance. This must be explained to the parents and reinforced on every follow-up visit. Siblings and adult family members should be screened for TB.

## CONCLUSION

Cerebral tuberculomas and spinal caries though not as common as pulmonary TB or TMB, are not rare in children. Therefore, it is important that treating paediatrician should have high index of suspicion. Positive family history and CXR may provide important clues towards the diagnosis of TB. Regular follow-up and strict treatment compliance are very important.

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