

## Multiple tuberculomas and cavitating pulmonary tuberculosis in an infant

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### ABSTRACT

A five-month-old infant presented with fever and cough for 3 weeks. She was diagnosed with multiple tuberculomas and cavitating pulmonary tuberculosis. She was a household contact of an open case of tuberculosis (TB) and developed severe disease, although she had received the Bacillus Calmette-Guérin (BCG) vaccine and had no primary or secondary immunodeficiency. In infants, due to low levels of cell mediated immunity, tuberculosis can be severe and dissemination of tuberculosis to the central nervous system (CNS) can occur very early without following the usual time frame. CNS TB may not have symptoms in the early stages in infants and may require neuroimaging for diagnosis. This is the youngest child that has been reported with multiple CNS tuberculomas.

**Keywords:** Cavitory tuberculosis, CNS tuberculosis, infant, miliary tuberculomas, tuberculomas

### Introduction

Multiple tuberculomas and cavitating pulmonary tuberculosis are rarely seen in infancy. We report the youngest child with multiple tuberculomas in the brain and discuss some less-known aspects of TB in infants.

### Case History

A five-month-old infant was admitted to our hospital with fever and cough for 3 weeks. She was treated for left upper lobe pneumonia with intravenous antibiotics in a local hospital with minimal improvement.

She was the only child born to non-consanguineous parents and was exclusively breastfed. She received the BCG vaccine at birth; however, BCG vaccine scar was absent. Her paternal grandfather was on treatment for open pulmonary TB.

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Received: 30-05-2021

Revised: 10-10-2021

Accepted: 19-10-2021

Published: 18-03-2022

Upon examination, she was pale, febrile and in respiratory distress, requiring two liters of oxygen. Liver was palpable 6 cm below right costal margin and spleen 5 cm below left costal margin. Other systemic examination was unremarkable. With a provisional diagnosis of severe pneumonia, she was started on intravenous antibiotics.

Investigations revealed hemoglobin at 6.9g%, TC at 15,300 cells/cu mm (N 20%, L 62%), CRP at 62.8 mg/L, and ESR at 55 mm at 1 hour. Liver function tests and serum creatinine were normal. Chest X-ray showed left upper lobe consolidation with a cavity and bilateral miliary infiltrates. Computed tomography (CT) of the chest confirmed left upper lobe and lingular consolidation with multiple cavities in the left upper lobe and diffuse miliary tubercles [Image 1]. Ultrasound abdomen showed moderate hepatosplenomegaly. TB-PCR on the gastric aspirate was positive. Bone marrow biopsy was normal. She was diagnosed with disseminated TB.

In view of disseminated TB, magnetic resonance imaging (MRI) of the brain was done which revealed multiple small enhancing nodules in bilateral cerebral hemispheres, pons, and cerebellar

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**How to cite this article:** Peterson RR, Ramya R, Kuruvilla A, Lakshmi KS. Multiple tuberculomas and cavitating pulmonary tuberculosis in an infant. J Family Med Prim Care 2022;11:1536-8.

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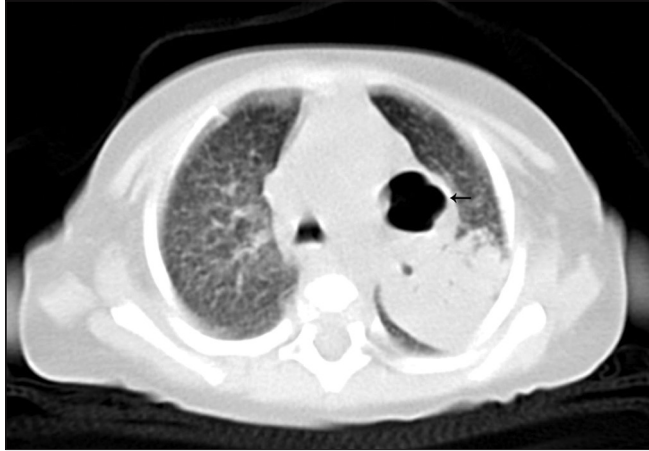


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DOI:  
10.4103/jfmpc.jfmpc\_1021\_21

hemispheres [Image 2 and 3]. Cerebrospinal fluid (CSF) examination was normal. HIV ELISA for the child and her

mother was negative. Serum immunoglobulin levels, T cell, B cell and NK cell counts, and NBT test were normal ruling out primary immunodeficiency. Parents and grandmother were negative for TB.

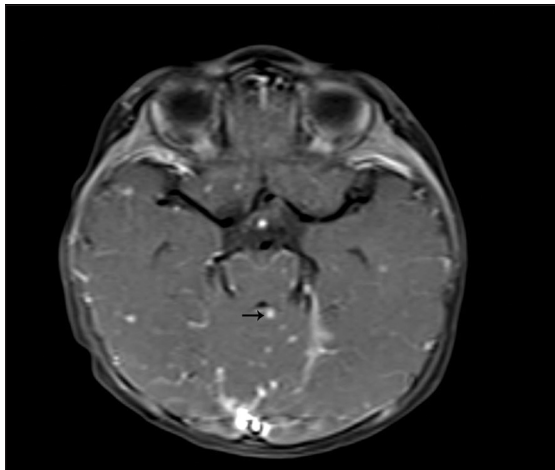


**Image 1:** CT chest axial image shows a cavity in the left upper lobe (arrow) and adjacent lingular consolidation

After initiating anti-tubercular therapy (ATT), she became afebrile and regained normal activity. Subsequently, she gained adequate weight and achieved normal development. After one year of ATT, brain MRI was normal and thorax CT showed resolution of consolidation and miliary nodules. However the cavity in the left lung persisted. She is well with normal development at two years.

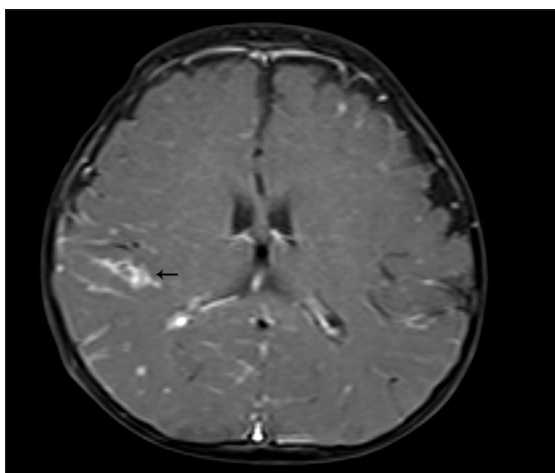
## Discussion

Tuberculosis is a common health problem in developing countries. In infants, TB can pose diagnostic difficulties as the manifestations may not follow the classical pattern as described for adults and older children. Our experience with this infant throws some light on some features of TB in infancy.



**Image 2:** Post contrast T1- weighted axial image shows multiple small enhancing nodules (arrow) in the cerebellum

Central nervous system (CNS) TB in the form of tuberculomas or TB meningitis is seen in less than 4% of children infected under five years of age and extremely rare in infancy.<sup>[1]</sup> An infant with primary pulmonary tuberculosis may develop tuberculomas due to hematogenous dissemination secondary to severe bacteremia.<sup>[2]</sup> In infants, signs of meningeal irritation are difficult to elicit and signs of raised intracranial tension may not be prominent in the early stages of CNS TB due to the presence of the anterior fontanelle. Infants also may not be able to vocalize symptoms like headache, and mild irritability or lethargy may be missed or attributed to other factors. Multiple tuberculomas were picked up in the baby upon neuroimaging, although she had no clinical features suggestive of CNS TB. Hence brain MRI and CSF examination are warranted to rule out CNS involvement in infants and young children with disseminated TB.



**Image 3:** Post contrast T1- weighted axial image shows diffuse meningeal enhancement with focal nodular enhancement in the right parietal region (arrow)

Usually, CNS TB takes a year or two to manifest after primary TB infection. However, it can be seen within the first year of life in infants with primary pulmonary tuberculosis. This is due to weak cell mediated immunity due to immature monocytes, macrophages, impaired innate signaling pathways, diminished cytokine responses, and priming of Th1 and CD8T cell responses when compared to adults. Additionally, poor tissue repair and low secretion of bioactive molecules facilitate rapid multiplication and dissemination of bacteria. This accelerates disease progression with multi-organ involvement in infants.<sup>[2-4]</sup>

In infants, cavitory lesions due to TB are rare. Poor containment of primary infection, inadequate host immune response, HIV infection, or malnutrition make them vulnerable to primary cavitating tuberculosis and disseminated TB.<sup>[2]</sup>

In a systematic review, the efficacy of BCG vaccination for pulmonary TB varied from 44% to 99% with one study showing no protection at all.<sup>[5,6]</sup> A metaanalysis showed that vaccination helps decrease the incidence of TB meningitis by 73%.<sup>[5,7]</sup> Various

studies indicate that BCG vaccine has high efficacy in decreasing severe TB by 85% and further up to 90% when given in the neonatal period.<sup>[8]</sup>

BCG vaccine has scar failure rate of up to 10%. This does not indicate a lack of immunogenicity and BCG revaccination in such subjects has not been found to provide additional protection.<sup>[9,10]</sup>

According to the WHO in 2016, 1.3 million children aged less than 5 years, who were treated for TB, were household contacts of bacteriologically confirmed pulmonary TB.<sup>[11]</sup> The primary physician treating an adult with open TB should meticulously enquire regarding contacts of index case, especially children less than six years of age. They should advise against further contact, institute isoniazid prophylaxis, and monitor for evolution of TB disease in these children. This can significantly lower the burden of pediatric TB. Close contact between the infant and grandfather could not be avoided in our patient due to social reasons and failure of the primary physician to inquire and counsel regarding the dire consequences.

Early dissemination is a feature of TB in infants. BCG vaccination does not provide complete protection from severe disease; hence a high index of suspicion is needed even in vaccinated infants. CNS TB can be asymptomatic in the early stages, and should be ruled out in infants and young children with disseminated TB. The primary physician should be responsible for tracing and follow-up of young children in contact with adult TB. National health programs too should implement the same.

### Key messages

- TB in infants can be severe with early dissemination.
- CNS TB should be ruled out via neuroimaging even in neurologically asymptomatic infants with disseminated TB.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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