Case Report

Congenital Tuberculosis: A Diagnosis Delayed in a Child with Atrial Septal Defect

Pallavi Sinha, Lavleen Singh[1], Dhulika Dhingra[2]

Department of Pathology, Maulana Azad Medical College, Departments of [1]Pathology and [2]Paediatrics, Chacha Nehru Bal Chikitsalaya, Delhi, India

Abstract

Congenital tuberculosis (CTB) is a rare disease presenting in infants with very few cases reported despite a high burden of tuberculosis. The fewer reported cases reflect in part the difficulty in making a definitive clinical diagnosis as signs and symptoms are non- specific along with difficult laboratory confirmation due to several reasons. We report a case of 4-month-old male child presenting with fever and cough for 3 months and respiratory distress and feeding difficulties for 5 days with no response to antibiotics. Systemic examination revealed bilateral crepitations, pansystolic murmur, and hepatosplenomegaly. Echocardiography revealed an 8 mm atrial septal defect. The patient did not respond to decongestive therapy. Ultrasonography revealed an enlarged liver with a 12 cm liver span. Liver biopsy showed necrotizing epithelioid cell granuloma. Based on the Cantwell's criteria, the diagnosis of CTB was proffered.

Keywords: Congenital, hepatomegaly, infection, postnatal, tuberculosis

Received on: 03-12-19 **Review completed on:** 25-12-19 **Accepted on:** 16-02-20 **Published on:** 08-08-20

Introduction

Congenital tuberculosis (CTB) presents in infants due to infection with *Mycobacterium tuberculosis* in the intrauterine period or during passage through the birth canal. Global tuberculosis (TB) report 2017 estimated 10.4 million TB cases in 2016, with a case-fatality ratio being 16%.[1] Out of this 6.9%, new and relapse cases were reported in <15 years children.[1] Despite such a high burden of TB, <300 and 10 cases of CTB are reported worldwide and India, respectively.[2] This may be due to a lack of clinical suspicion and challenges in the laboratory diagnosis in infants. The symptoms of mycobacterial infection acquired in an intrauterine or intrapartum period are severe though nonspecific with high mortality and morbidity.

Case Report

A 4-month-old male child presented with fever and cough for 3 months and respiratory distress and feeding difficulties for 5 days with no response to antibiotics. On examination, the patient was febrile with mild pallor. His weight was 5.1 kg, head circumference: 40 cm, heart rate: 134 beats/min, and respiratory rate 64 breaths/min with lower chest retractions. There was an absence of icterus and lymphadenopathy. There were bilateral crepitations, pansystolic murmur, and hepatosplenomegaly on systemic examination. Clinically differentials considered were congestive heart failure and infective endocarditis and intrauterine infections namely cytomegalovirus, rubella, and CTB.

Complete blood count revealed hemoglobin of 9.4 g/dl and a total leukocyte count of 24700/mm^3. Echocardiography revealed an 8 mm atrial septal defect. The patient did not respond to decongestive therapy. Blood culture was sterile, ruling out the possibility of infective endocarditis. Tests for toxoplasmosis, rubella, cytomegalovirus, and herpes simplex were insignificant. HIV was nonreactive. Ultrasonography revealed an enlarged liver with 12 cm liver span and increased parenchymal echogenicity with no space-occupying lesion. Chest X-ray showed elevation of the right diaphragm with

Access this article online

Quick Response Code:

Website: www.atpjournal.org

DOI: 10.4103/atp.atp_42_19

Address for correspondence: Dr. Lavleen Singh, Department of Pathology, Chacha Nehru Bal Chikitsalaya, Geeta Colony, Delhi - 110 031, India.
E-mail: singhlavleen04@gmail.com

How to cite this article: Sinha P, Singh L, Dhingra D. Congenital tuberculosis: A diagnosis delayed in a child with atrial septal defect. Ann Trop Pathol 2020;11:79-81.

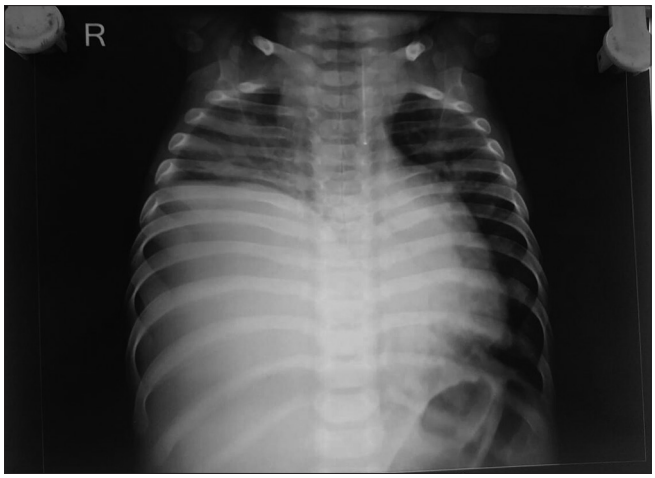

Figure 1: Chest X-ray showing elevation of the right diaphragm with compressive atelectasis of right lung

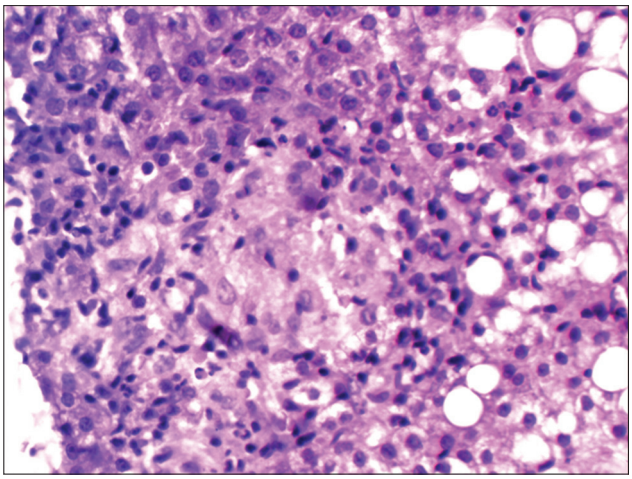

Figure 2: Section of the liver showing macrovesicular steatosis and necrotizing epithelioid cell granuloma (H and E, ×400)

compressive atelectasis of the right lung [Figure 1]. Liver enzymes were elevated. Tuberculin test was positive and gastric aspirate microscopy for acid-fast bacillus (AFB) was negative. GeneXpert of gastric aspirate was positive for mycobacterial TB and sensitive to rifampicin. A provisional diagnosis of CTB was made and liver biopsy was planned.

Liver biopsy showed marked macrovesicular steatosis and mixed lobular infiltrate. A necrotizing lobular epithelioid cell granuloma was identified in one of the slides [Figure 2]. Stain for AFB was noncontributory. Based on the Cantwell criteria for CTB, the case was diagnosed as CTB. The case improved after treatment with antituberculous drugs.

Discussion

The transmission of *mycobacterium* can occur through the amniotic fluid by ingestion or aspiration of infected fluid or by umbilical vein leading to a primary complex formation in the liver, lung, and intestine.[3] The prevalence of vertical transmission of TB can be as high as 16%.[4]

The manifestation of *M. tuberculosis* infection depends on the host defense mechanism. Both innate and cell-mediated immunities are necessary to prevent the disease. However, in infants, the cell-mediated immunity is not well developed. They depend on maternal antibodies and innate immunity. Innate immunity in infants also has reduced function. This leads to reduced defense against *M. tuberculosis*.[5] Associated malnutrition in TB further reduces the immune response.

Signs and symptoms of CTB are very nonspecific in infants. The age of presentation is variable, with the average age being 24 days (1–89 days).[6] The presentation is similar to infants born with other congenital infections such as the TORCH group of infections. The child usually presents with nonspecific symptoms such as fever, cough, respiratory distress, feeding difficulties, and failure to thrive which make the diagnosis challenging. The associated signs are hepatomegaly, splenomegaly, lymphadenopathy, and ascites.[7] The uncommon presentations reported in the literature are meningitis, otitis media, mastoiditis, parotitis, osteomyelitis, obstructive jaundice, paravertebral abscess, and disseminated intravascular coagulation.[6]

Criteria for the diagnosis of CTB were first given by Beitzke and later modified by Cantwell *et al*.[7,8] The diagnosis of CTB in resource-limited countries is often not established. Patel and De Santes proposed certain clinical and diagnostic clues for suspecting CTB in the newborn in resource-limited setting.[9] The authors proposed that CTB should be considered in a newborn with worsening pneumonia unresponsive to routine antibiotics, especially in an area with high TB burden, nonspecific symptoms among infants whose mother is diagnosed with TB, and infants with lymphocytic pleocytosis without identifiable organism or fever with hepatosplenomegaly.

Clinical suspicion is the key to the diagnosis of CTB. Once the diagnosis of CTB is suspected, chest X-ray, tuberculin skin test (TST), culture of *M. tuberculosis*, and polymerase chain reaction should be done. The use of TST in neonates is limited owing to their low immunity. Liver biopsy is important in CTB, as the primary complex is often hepatic. Liver biopsy shows giant cell granulomas in the hepatic lobule with or without caseous necrosis. AFB stain may be required to confirm the diagnosis, but the negative stain does not exclude the diagnosis. Fatty changes in liver biopsy may be an associated finding that may be attributed to associated malnutrition.[10] Other investigations include complete blood count, erythrocyte sedimentation rate, and C-reactive protein.

History of the mother should be taken regarding the symptoms of TB, especially pulmonary, miliary TB, or meningeal disease during pregnancy. A history of irregular menstruation/recurrent abortions signifies endometrial involvement. Histological examination of the placenta, endometrial aspirate, and curettage must be done.

The major diagnostic challenge is nonspecific signs and symptoms in infants which masquerade common neonatal

diseases. Samples required to diagnose CTB involve invasive procedures and are difficult to obtain from infants. Moreover, cell-mediated immunity is less developed in infants which leads to poor granulomatous response on organ biopsy. The closest differential of CTB is early postnatally acquired TB. Differentiation between these two is difficult due to similar presenting complaints. The importance of detailed history cannot be overstated as maternal TB and history of contacts are important clues to differentiate the former from the latter.

Conclusion

The diagnosis of CTB should be suspected in a child with pneumonia and hepatosplenomegaly unresponsive to antibiotic therapy. Other causes of hepatomegaly such as congestive heart failure may delay the diagnosis. The granulomatous response may be absent or poor owing to the weak immune system of neonates. Thus, in any suspected cases of CTB, a diligent search of granuloma should be done on cytological/histological material.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. World Health Organization. Global Tuberculosis Report 2017. Geneva: World Health Organization; 2017.
2. Ray M, Dixit A, Vaipei K, Singhi PD. Congenital tuberculosis. Indian Pediatr 2002;39:1167-8.
3. Khilnani GC. Tuberculosis and pregnancy. Indian J Chest Dis Allied Sci 2004;46:105-11.
4. Pillay T, Sturm AW, Khan M, Adhikari M, Moodley J, Connolly C, *et al*. Vertical transmission of *Mycobacterium tuberculosis* in KwaZulu Natal: Impact of HIV-1 co-infection. Int J Tuberc Lung Dis 2004;8:59-69.
5. Basu Roy R, Whittaker E, Kampmann B. Current understanding of the immune response to tuberculosis in children. Curr Opin Infect Dis 2012;25:250-7.
6. Obringer E, Heald-Sargent T, Hageman JR. Neonatal tuberculosis. Pediatric Annals 2015;44:e126-30.
7. Hassan G, Qureshi W, Kadri SM. Congenital tuberculosis. Mini Rev JK Sci 2006;8:193-4.
8. Cantwell MF, Shehab ZM, Costello AM, Sands L, Green WF, Ewing EP Jr., *et al*. Brief report: Congenital tuberculosis. N Engl J Med 1994;330:1051-4.
9. Patel S, DeSantis ER. Treatment of congenital tuberculosis. Am J Health Syst Pharm 2008;65:2027-31.
10. van Zutphen T, Ciapaite J, Bloks VW, Ackereley C, Gerding A, Jurdzinski A, *et al*. Malnutrition-associated liver steatosis and ATP depletion is caused by peroxisomal and mitochondrial dysfunction. J Hepatol 2016;65:1198-208.