

Congenital tuberculosis with possible placental transmission and paradoxical reaction to anti-tuberculosis treatment

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Abstract

Congenital tuberculosis (CTB) is a rare disease with a high mortality rate, requiring high index of suspicion to diagnose because of non-specific presentation. This report describes a case of 6 month male child with congenital tuberculosis with possible placental transmission. Infant had fever, fast breathing and cough since 20 days of life. Ultrasonography (USG) abdomen showed granulomatous lesions in liver. Although mother was diagnosed to be having tuberculosis during 3rd week after delivery and started on anti-tuberculosis treatment (ATT), child remained undiagnosed for 6 months and didn't get appropriate treatment. Fever, respiratory distress and cough initially improved after starting ATT but patient worsened after 2 weeks of ATT which could not be attributed to cause other than tuberculosis paradoxical reaction (TB-PR). Patient was given steroid following which he gradually improved. This case highlights the importance of keeping high index of suspicion for congenital TB in infants, especially in developing nations, and need for early diagnosis and treatment for the survival of these infants. PR should be considered even in infancy if patient shows worsening of symptoms after initial improvement that couldn't be explained otherwise.

Introduction

Congenital tuberculosis is extremely rare condition with less than 400 cases reported in the literature [1] having a high mortality. Reported incidence is gradually declining significantly with only 18 cases been reported from 2001 to December 2005 [2]. Paradoxical reaction to ATT in case of congenital tuberculosis has been described only once in literature [3]. The importance of early diagnosis and treatment of CTB is crucial considering nonspecific nature of presentation and high mortality associated with it. Paradoxical reaction (PR) to ATT should be thought of if there is worsening of clinical or radiological findings following the initiation of appropriate antituberculosis treatment as early institution of steroid could be life saving in these children.

We report a case of congenital tuberculosis remaining undiagnosed for 6 months, till it presented to our institute, who when started on ATT after initial improvement, worsened and then responded favourably to steroid. A written consent was sought from the legal guardians of the index child to publish the findings, however ethical clearance was waived for this being a retrospective anonymous case report.

Case

A 6 month male child presented with history of fast breathing, cough, fever since 20 days of life. He was normal vaginal delivered at term, weighing 1.5 kg. Child had received multiple antibiotics prior to presentation in our institute. During third week after delivery mother developed productive cough, fever and was diagnosed to be having tuberculosis (TB) and was started on ATT.

On examination he was sick looking, malnourished, weighing 3.24kg (z score < -3.0) with length of 60 cm (z score < -3.0) and head circumference of 37cm (z score < -3.0). He was afebrile, pale, dyspnoeic and had subcostal, intercostal and suprasternal retractions with heart

rate 110/min and capillary filling time <2 sec. Respiratory rate was 66/min. with bilateral wheeze. Abdomen was distended with liver being 3 cm palpable below right costal margin with span of 6.5 cm. Other systems were normal.

Investigations revealed: haemoglobin of 11.6 g/dl, total leukocyte count 12,200/mm³, with 39% polymorphs and 51% lymphocytes. Review of serial previous X-rays showed prominent pulmonary vascularity. Mantoux test was negative. USG abdomen showed small target/granulomatous lesions in liver. USG of cranium and Echocardiography was normal. Blood culture showed no growth. Liver biopsy and high-resolution computed tomography thorax and abdomen couldn't be done due to non availability of these facilities at that time.

Child was initially treated for pneumonia with injection ceftriaxone and gentamycin without any improvement. In view of mother's chest X-Ray being suggestive of pulmonary tuberculosis, child's symptomatology beginning from 3rd week of life, target lesions in liver on USG with failure to thrive possibility of congenital tuberculosis was considered & patient was started on 4 drug Anti-tuberculosis treatment (ATT) viz. isoniazide, rifampicin, ethambutol and pyrazinamide (HREZ). Following this child condition initially improved with progressive weight gain, improved appetite and activity.

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However after 2 weeks of ATT child showed sudden clinical worsening in form of fever, lethargy, decreased appetite and increased respiratory distress. For possibility of hospital acquired infection antibiotic was upgraded to injection piperacillin and tazobactam. However no supportive laboratory evidences for the same could be found. When no improvement was noticed, possibility of tuberculous paradoxical reactions (PR) was considered and steroid was started. Following this child responded in form of resolution of fever, decreased respiratory distress and persistent weight gain. Patient is in our regular follow-up and is thriving well and repeat USG abdomen after 2 months of ATT showed clearance of these granulomatous hepatic lesions. Steroid was tapered off after 6 weeks and ATT was continued for 1 yr (2HREZ + 10HR).

Discussion

Tuberculous bacilleamia during pregnancy may result in infection of the placenta or the maternal genital tract [4,5]. Congenital tuberculosis is defined when tubercular infection is transmitted to the foetus either haematologically via the umbilical vein or by infected amniotic fluid, which is ingested or aspirated in utero, or during delivery [6]. It should be distinguished from acquired neonatal tuberculosis, where the infant is infected after birth by a contagious adult. Our patient had granulomatous lesions in liver which could not be explained by acquired neonatal tuberculosis.

Diagnostic criteria for congenital tuberculosis were laid down by Beitzki in 1935 and subsequently were revised by Cantwell in 1994 [7]. Singh et al. [8] in 2007 suggested laboratory and clinical findings that may suggest congenital TB, which include a newborn from a TB endemic area with unresponsive worsening pneumonia, a mother with TB and a baby with nonspecific symptoms and the presence of hepatosplenomegaly and fever. Our case, from a TB endemic region, having an unresponsive worsening pneumonia associated with hepatomegaly, with a history of TB in mother, meets the above criteria. Signs and symptoms in congenital TB appears after the first 3 weeks of life at a median age of 28 days (range: 1 to 84 days) [7], index case became symptomatic during 3rd week of life.

Congenital tuberculosis is particularly difficult to diagnose since the non-specific presenting signs and symptoms such as respiratory distress, hepatosplenomegaly, jaundice, fever, lymphadenopathy, lethargy and failure to thrive are also seen in other non tubercular infections.

After 2 weeks of ATT patient showed sudden deterioration and it was difficult to rule out hospital acquired infection (HAI) as patient was still in PICU. He was treated for HAI however; laboratory evidences for HAI were negative. When no improvement was noticed possibility of TB-PR was considered.

Occurrence of PR in HIV-negative patients with pulmonary TB is reported to be 2.4 % [9], where as in patients of extrapulmonary TB it is much higher ranging from 16 to 50 % [10]. Paradoxical response is defined as the clinical or radiological worsening of pre-

existing tuberculous lesions or the development of new lesions not attributable to the normal course of disease in a patient who initially improves with antituberculosis therapy and in whom the onset of paradoxical response is at least 2 weeks after the initiation of treatment [9]. When ATT is started an immune rebound may occur, probably due to the release of *M. tuberculosis* antigens during the destruction of infected macrophages, which may explain the worsening of clinical symptoms. This clinical entity can be misdiagnosed as superimposed infections, treatment failure, or TB relapse. Our patient having initial improvement with ATT had clinical worsening after 2 weeks with no evidence of secondary infection or treatment failure fulfils these criteria for tuberculosis PR. This is only the 2nd case to be reported of TB-PR in congenital tuberculosis.

Congenital TB is a rare entity and is uniformly fatal if untreated. Treatment of the infant should begin as soon as the diagnosis is suspected without waiting for laboratory confirmation, while appropriate specimens should be obtained fast for bacteriological and histological examination [2]. Our case highlights the importance of keeping high index of suspicion for congenital TB especially in tuberculosis endemic area even in absence of bacteriological isolation and timely institution of ATT.

In case of unexplained clinical or radiological worsening after initial improvement with ATT with no evidence of secondary infection, poor drug compliance or treatment failure, TB-PR should be suspected and steroid considered as this could be life saving for these patients.

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