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Congenital Tuberculosis in a Neonate Born from a HIV Negative Mother, in a HIV Endemic Country: A Case Report

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Abstract

Introduction

Congenital tuberculosis (TB) which is acquired during the intrauterine period or during the normal birth process is rare, with 490 cases reported up to date. Congenital Tuberculosis poses a diagnostic challenge because its clinical presentation and radiographic findings are nonspecific.

Case Presentation

We present an African neonate born prematurely at gestation age of 32 weeks, weighing 1250 grams at Muhimbili National Hospital. The mother was admitted at the Intensive Care Unit (ICU) before delivery due to empyema thoracis and later on died. She was HIV negative, later on diagnosed with TB and initiated on anti –Tb medications 3 days before her demise which was two weeks post-delivery. The baby who was never breastfed, presented with a history of poor weight gain, persistent fever, cough and difficulty in breathing during the neonatal period. On physical examination she had reduced breath sounds on the right side of the chest and hepatosplenomegaly. Gastric aspirate for Gene Xpert confirmed the presence of *Mycobacterium tuberculosis*. The patient was initiated on anti –Tb medication and responded well with adequate weight gain and improvement of the clinical symptoms.

Conclusion

A high index of suspicion is required to diagnose congenital TB, in light of poor response to antibiotics in TB endemic areas, especially when the mother is presenting with respiratory symptoms.

Key Words: *Congenital Tuberculosis, Neonate, Case Report.*

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Introduction

Few cases of congenital Tuberculosis have been reported globally with 468 cases reported up to 2009, additional 21 cases were reported between 2011–2018 and only 3 cases were reported in 2001 from the same newborn unit in Dar es Salaam Tanzania (1–3). Tuberculosis (TB) is among the top 10 causes of morbidity and mortality among children worldwide .(4). Tanzania is among the 30 high TB burden countries. In high burden countries, the prevalence of Tuberculosis among pregnant women ranges between 0.07% to 0.5% among HIV negative women and between 0.7% to 11% among HIV positive women.(5). Congenital tuberculosis is a rare entity, but fatal if left untreated.(6).It results from vertical transmission of *Mycobacterium tuberculosis* to an infant in utero or during the birth process. Fetal contamination by mycobacteria may occur hematogenously or by pulmonary aspiration of contaminated amniotic fluid(7).

The most common clinical presentations are poor feeding, fever, irritability, failure to thrive, hepatosplenomegaly, lymphadenopathy, abdominal distension, respiratory distress and cough(8).These nonspecific symptoms and signs are often mistaken for other common infections of early infancy such as sepsis or other congenital intrauterine infections. Chest X-ray, sputum and Mantoux test are negative in majority of cases and mothers of the infants are seldomly symptomatic.

Nevertheless early diagnosis and treatment is crucial because mortality can be as high as over half of the cases, Thus a high index of suspicion is warranted in light of poor response to adequate antibiotics and maternal respiratory illness (6). We report a case of neonatal TB in an infant born to a HIV negative mother.

Case Presentation

A female baby was delivered via spontaneous vaginal delivery at our facility at 32 weeks' gestational age, she weighed 1250 grams at birth and had an Apgar score of 5 and 7 at the 1st and 5th minutes respectively. Mother was 39 years old, para 5 with three living children. She was initially admitted at 24 weeks of gestation when she presented with cough and difficulty in breathing. Her clinical condition deteriorated with severe respiratory distress necessitating obstetric ICU admission till the time of delivery at 32 weeks of Gestational Age. Baseline evaluation which included chest x-ray and computed tomography (CT) scan

showed lung abscess and empyema thoracis. Both sputum and pleural fluid samples were negative for Gene Xpert and acid-fast bacillus (AFB)

During the course of stay in the ICU she was treated with broad-spectrum antibiotics, but no significant improvement was noted. Repeat chest CT scan revealed a pattern consistent with miliary TB, thus she was started on anti TB three days before her demise which was two weeks post-delivery.

According to intergrowth charts, baby's weight was just above the 10th centile corresponding to weight appropriate for gestational age (AGA) and she had a normal newborn examination. She was admitted to neonatal unit due to very low birth weight- AGA, with possible early onset neonatal sepsis following a history of preterm premature rupture of membranes (PPROM). The baseline complete blood count on the first day of life indicated a raised total white blood cell count (30450/uL) with predominant (81%) neutrophils, 14% lymphocytes, 2.59% monocytes and C- reactive protein was 79.5mg/L. Mother's milk was not available thus she was fed on formula milk prepared and fed by nurses in the unit. She was initially started on intravenous Ampicillin and Gentamycin which was then switched to ciprofloxacin after 3 days. The patient developed jaundice on 3rd day of life corresponding to Kramer 2, serum bilirubin was 160 µmol/L with direct bilirubin of 8.8 µmol/L thus phototherapy was initiated. The rest of the examination was otherwise normal

The patient developed new onset fever and persistent cough almost two weeks after completion of antibiotics with a rise of C-reactive protein (CRP) levels to 243mg/L with low hemoglobin level and negative blood culture. Third line antibiotic meropenem was initiated with no improvement of the clinical symptoms. Physical examination findings showed hepatosplenomegaly, and reduced breath sounds on the right lung. Despite receiving adequate amount of formula milk, there was no net weight gain whereas by one month of age she weighed only 1150 grams, a 100 grams less than birth weight. In view of the mother's history with unresponsiveness to conventional antibiotics and failure to gain weight, Neonatal tuberculosis was suspected. Chest X-ray showed a consolidation on the right upper lobe and a lung cavity. Results of HIV 1& 2 antibodies were negative. Erythrocyte sedimentation rate (ESR), C-reactive protein and adenosine deaminase were 5mm/hr, 200/µL, and 292U/L respectively. Gastric aspirate for Gene Xpert detected mycobacterium tuberculosis, which confirmed a diagnosis of neonatal TB.

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The neonate was treated with anti-tuberculosis for six months, ½ a tablet fixed dose combination of RHZ (Rifampicin, Isoniazid, Pyrazinamide) (75/50/150mg) and ½ a tablet of Ethambutol (E) 100mg. After initiating anti-TB treatment, the neonate showed dramatic improvement with adequate weight gain of 22grams/day after two weeks of treatment. She completed six months course of ant TB, currently she is symptoms free, with normal growth and developmental milestones.

Discussion

Congenital TB has a vertical mode of transmission, whereby maternal bacillemia on the placenta or amniotic fluid infect the infant's liver forming the primary complex before disseminating to the lungs by hematogenous spread. Otherwise the acquisition may be via aspiration or ingestion of infected amniotic fluid in utero or through direct contact with infected birth passage (9)(10). Congenital TB is estimated at 2% in high endemic countries like Tanzania(3). A study done in northern Tanzania by Sherrif et al established the prevalence of latent TB among pregnant women to be high, in the range between 26.2% and 37.4% (11).

Signs and symptoms are usually non-specific and often confused with other common illness in early infancy(6).The patient presented in this case report was born prematurely and had risk factors for sepsis and presented with signs of early onset sepsis. This was also supported by initial laboratory results including high neutrophil count and raised CRP. Since there was some initial response to antibiotics, there are possibilities of a coexistence of both of septicemia and congenital Tb. Furthermore, because antibiotics such as Gentamicin and Ciprofloxacin which the patient was using has some anti-tb activities could have masked signs of congenital TB. This case opens our eyes especially in a high endemic area to have high index of suspicion, which should prompt TB consideration. (12).

The diagnostic criteria for the diagnosis of congenital TB was first proposed by Beitzke in 1935 and revised by Cantwell in 1994.(13). It requires presence of proven tuberculosis disease with at least 1 of the following: (1) Lesions in the newborn baby during the 1st week of life, (2) Primary hepatic complex or caseating hepatic granuloma, (3) Tuberculous infection of the placenta or maternal genital tract or (4) Exclusion of possibility of postnatal transmission by investigating all possible TB contacts. Although we did not examine the placenta, the case we present here is consistent with congenital TB as we had a diagnosis based on positive Gene X-pert from the gastric aspirate. Gene X-pert, which was used in this

case has appreciable diagnostic test sensitivity and specificity in diagnosis of TB(14). Furthermore, we could not establish the contact, which would support the possibility of postnatal infection, especially since the baby never came into contact with the mother after delivery, thus congenital tuberculosis is more likely. The mantoux test was not done in this patient due to the fact that it has low utility in neonates (15).

Treatment without delay with anti TB chemotherapy is indicated in patients with established congenital TB. (16). Congenital tuberculosis is fatal with mortality as high as 50% with no treatment and with treatment is up to 15.5% (6)(1).The patient in this case report was started on Isoniazid, Rifampicin, Pyrazinamide and Ethambutol (RHZE) for six months in accordance with Tanzania TB national guideline.(17). Despite the delayed treatment, the patient showed significant improvement with adequate weight gain (22g/day) and had a good outcome after 4 weeks of treatment.

This infant was immunized with Bacillus Calmette-Guérin (BCG) as part of the Immunization and Vaccine Development schedule of Tanzania before the diagnosis of congenital TB was sought. It has been established, BCG has no added benefit in congenital TB (15). In most case scenarios HIV/TB coinfection is expected especially in a region where HIV and TB are both endemic. The first three cases in Tanzania were reported by Manji et al in 2001, these were neonates born from HIV infected women with suspected Tuberculosis.(2). However, in our case, the patient's mother tested negative for HIV and Tuberculosis was not detected during the initial evaluation. Nevertheless, not all mothers are diagnosed with tuberculosis before delivery. In our case this contributed to the delay in diagnosis for both the mother and her newborn, possibly contributing to the death of the mother.
The case presented, highlights the importance of proper maternal history and evaluation in Tb endemic areas, which will facilitate early diagnosis of congenital or neonatal TB so as to ensure appropriate and prompt treatment.

Conclusion

Due to the non-specificity of the presenting symptoms, a high index of suspicion is required to diagnose congenital TB. When there is poor response to antibiotics and other supportive therapy in a neonate, congenital TB should be suspected.

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Ethics Declaration

Ethics approval and consent to participate

Consent for participation was given by the aunt who is the current legal guardian of the child.

Consent for Publication

Written informed consent was obtained from the patient's legal guardian (Aunt) for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing Interest

The authors declare that they have no competing interests.

Author's Contribution

MK, HS, admitted the patient and were attending physicians of the baby daily in the Neonatal Ward. HN provided expert opinion in the management of this patient. MK, HS and OU prepared the manuscript. All authors read and approved the manuscript.

Abbreviations

AFB	Acid Fast Bacillus
AGA	Appropriate for Gestational Age
CRP	C Reactive Protein
CT	Computerized Tomography
E	Ethambutol
HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
PPROM	Preterm Premature Rupture of Membranes
RHZ	Fixed dose combination with rifampicin (R) isoniazid (H), pyrazinamide (Z)
TB	Tuberculosis

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