Congenital Tuberculosis

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**MINI REVIEW**

**Introduction** : Congenital tuberculosis is a very rare condition (1-6). Only 300 cases were reported in the literature till 1989 (3); subsequently, 58 cases were reviewed by Abughali N et al (7) in 1994, and from 2001 to December 2005, 18 more cases have been reported (5,8-13). Even though, tuberculosis (TB) among pregnant women is not uncommon, documented cases of congenital TB are conspicuous by their rarity. It is because placenta forms a protective barrier against the invasion of the fetus by the tuberculous organisms. It is assumed that the infection has been acquired in utero, because of: (i) the age of the infant, (ii) absence of any known contact with an open case of TB, and (iii) generalized dissemination of the disease.

The risk of TB in pregnancy has increased owing to recent changes in the epidemiology of the disease, which has led to an increased risk of congenital TB (5,6) although a rare disease, congenital TB should be distinguished from the more frequent acquired neonatal TB, in which the infant is infected after birth by an adult suffering from the disease. Congenital TB may occur as a result of maternal TB when it involves the genital tract or placenta. The signs and symptoms are non-specific; the atypical clinical manifestations of congenital TB and the devastating consequences in absence of early therapy signify the importance of early diagnosis and treatment during the neonatal period (1,2,5,6)

**Mode of Infection** : Three possible modes of infection of the fetus have been proposed. Hematogenous infection via the umbilical vein, fetal aspiration of infected amniotic fluid and fetal ingestion of infected amniotic fluid (2,3,5).

**Diagnostic Criteria** : Diagnostic criteria for the diagnosis of congenital tuberculosis were laid down by Beitzki in 1935 and subsequently were revised by Cantwell in 1994 (14). These are summarized in Table I.

**Clinical Manifestation** : The affected infant is frequently born premature, but signs of disease usually do not appear for several days or weeks. The most common presentation is with respiratory distress, lethargy, poor feeding, fever, irritability, abdominal distension and failure to thrive. Hepatosplenomegaly and lymphadenopathy are common. Meningitis is uncommon, as is the jaundice. In a small percentage of cases otitis media with or without mastoiditis, is the first sign of congenital TB. Obstructive jaundice due to glands in the porta hepatitis may occur and popular or pustular skin lesions may be found in few cases (2,3,5,6,9) some may have progressive liver dysfunction in absence of respiratory symptoms (10) finally, the course is often fulminant, characterized in many cases by dissemination of the infection (5).

**Investigations** : Congenital TB is particularly difficult to diagnose. The mothers are often apparently healthy. In one review, 24 of 32 mothers were asymptomatic (7), because the signs and symptoms of tuberculosis in neonates are non-specific; they are initially attributed to other causes like prematurity, congenital viral infections or sepsis (15,16), so the diagnostic testing for tuberculosis is necessary.

1. Mantoux test is frequently negative (2,3,5,6) in the classical study of Hageman et al (17) only 2 of the 14 infants with congenital TB had positive tuberculin tests. Similarly in another study of 9 infants with congenital TB, only 2 showed the positive reactions (> 10mm) (9).

2. Chest radiography and computed tomography show the presence of scattered infiltrates, bronchopneumonia, consolidation or periportal hypodensity (5,6,13).

3. Positive smear and / or culture results can often be obtained from gastric washings, open liver biopsy, lymph node biopsy, spinal fluid, ear discharge, endotracheal aspirate or bone marrow (2,3,5).

4. Newer modalities like polymerase chain reaction (PCR) are highly beneficial in the diagnosis of congenital TB (1,5).

5. Recently phage typing has been used to establish the identity of mycobacteria isolated from mother and the infant (2,3).

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Table I. Diagnostic criteria for congenital tuberculosis

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<th>A. Beitzki criteria (2,6)</th>
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<td>i. Isolation of M. tuberculosis from the infant,</td>
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<td>ii. Demonstration of the primary complex in the liver, and</td>
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<td>iii. In the absence of primary complex in the liver : -</td>
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<tr>
<td>a) Evidence of tuberculosis within days after birth.</td>
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<td>b) Absence of contact with a case of tuberculosis after birth.</td>
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<th>B. Revised criteria by Cantwell (14)</th>
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<td>Proven tuberculosis lesions in the infant plus one of the following:</td>
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<td>i. Lesions occurring in the first week of life,</td>
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<td>ii. A primary hepatic complex,</td>
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<td>iii. Maternal genital tract or placental tuberculosis, and</td>
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<td>iv. Exclusion of postnatal transmission by thorough investigation of contacts</td>
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Vol. 8 No. 4, October-December 2006 193
Treatment: Congenital TB is a rare entity, even in human immunodeficiency virus (HIV) endemic populations, and is uniformly fatal if untreated (5,8). 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 (2,3,6).

Since congenital TB is rare, no therapeutic trials have determined the optimal treatment, however, several regimens have been evaluated and established (4,18). Treatment regimens should contain at least 2 and preferably 3 drugs to which the organisms are likely to be susceptible (2,12). Complete recovery has been obtained by combination of isoniazid, rifampin and pyrazinamide for 18 months with intravenous amikacin for initial 2 months. A 6 month course of isoniazid (H), rifampin (R), pyrazinamide (Z) and streptomycin (S) for 2 months and biweekly (R and H) for 4 months has shown good results with a relapse of only 1%, and no deaths from the disease. There are also case reports of successful treatment with HZS, HS and HRZ (18-20). Streptomycin (20-30 mg / kg / day) can be used in infants but is contraindicated in pregnant women (4). Currently the accepted mode of treatment is isoniazid (10-15 mg / kg / day), rifampin (10-20 mg / kg / day) and pyrazinamide (15-30 mg / kg / day) and either streptomycin or ethambutol (15-25 mg / kg / day) for first 2 months followed by isoniazid and rifampin for 4 to 10 months (4,14). Supportive therapy such as oxygen may be required. Corticosteroids may be given empirically if the baby is very ill (2,3).

Prognosis: The prognosis is poor. In the pre-chemotherapy era the reported survival rate was very low (around 50%), but since the advent of chemotherapy, the chances of successful treatment have improved the overall survival. Delay in the diagnosis contributes to the increased mortality (2-4,18).

Prevention: Prevention should be possible through early detection of disease during pregnancy and institution of appropriate therapy (2,5).

Recommendations: In view of the increasing burden of tuberculosis, chances of congenital TB are also likely to increase. As most of the women are asymptomatic for the disease during pregnancy, we recommend that screening of all possible pregnant women for tuberculosis should be made a necessary protocol.

References