Short Communication

Congenital Tuberculosis because of Misdiagnosed Maternal Pulmonary Tuberculosis during Pregnancy

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SUMMARY: We report the death of an infant due to severe sepsis caused by congenital tuberculosis following treatment with antituberculous drugs and antibiotics, who was born to a mother with misdiagnosed symptomatic pulmonary tuberculosis during pregnancy. Therefore, pregnant women with chronic cough and constitutional symptoms must be examined for pulmonary tuberculosis, particularly in tuberculosis endemic areas.

Congenital tuberculosis is considered to result from vertical transmission of infection from maternal circulation to fetal circulation, forming a primary hepatic complex, or from ingestion and aspiration of amniotic fluid or maternal blood by the fetus during delivery, leading to pulmonary or gastrointestinal tuberculosis (1,2). Congenital tuberculosis is a rare disease associated with a high mortality rate of up to 44% (3); less than 300 cases of congenital tuberculosis were reported worldwide before 1984, and over 80 additional cases have been reported thereafter (3,4). The clinical manifestations of congenital tuberculosis are difficult to distinguish from those of bacterial sepsis or viral infection due to nonspecific symptoms (5). Mothers who gave birth to an infant with congenital tuberculosis usually lacked clinical manifestations, and half of them were not diagnosed with tuberculosis until their infants had been diagnosed (5,6). Here, we report an infant with congenital tuberculosis who was born to a mother with misdiagnosed with maternally active pulmonary tuberculosis during pregnancy. The diagnostic criteria and early symptoms of suspected congenital tuberculosis are also reviewed.

A 37-year-old, gravida 1, para 0, Thai woman delivered a female infant (1,740 g) by Caesarean section at gestational week 34 due to premature rupture of membrane. The Apgar scores at 1 and 5 min were 9 and 9, respectively. On postnatal day 18, the infant presented with a 1-day history of lethargy and poor feeding. A physical examination of the infant revealed lethargy and hepatomegaly. A chest X-ray revealed prominent generalized interstitial infiltration in both lungs (Fig. 1A). Late onset neonatal sepsis from pneumonia was suspected in the differential diagnosis. A complete blood count showed a hematocrit of 42%, platelet count of 388,000 cells/mm³, and a white blood cell (WBC) count of 13,050 cells/mm³, comprising 83% polymorphonuclear cells, 15% lymphocytes, and 2% monocytes. Cerebrospinal fluid (CSF) sample contained a WBC count of 3 cells/mm³ and a red blood cell count of 4 cells/mm³. Gram staining of the CSF was negative for microorganisms. Ampicillin and gentamicin therapy was initiated, although the CSF and blood cultures revealed no bacterial growth. On post-admission day 5, she developed frequent apnea; therefore, an endotracheal tube was placed and ventilatory support was initiated. Gram stain of tracheal suction sputum sample was negative for microorganisms or fungi. However, a sputum smear showed numerous of acid-fast bacilli (AFB), and sputum cultures, 24 h incubation in blood agar media and disk diffusion susceptibility test in Mueller-Hinton agar media, revealed Klebsiella pneumoniae (an extended-spectrum beta-lactamase-producing strain). Congenital tuberculosis with hospital-acquired pneumonia was then suspected. We immediately changed the antibiotic to meropenem due to the susceptibility test results and continued for 14 days. Isoniazid, rifampin, pyrazinamide, and streptomycin were also initiated along with meropenem on post-admission day 5. A sputum culture from 30 days of a fully automated, nonradiometric, mycobacteria culturing system (BACTEC™ MGIT™ 960, Becton Dickinson Co., Franklin Lakes, N.J., USA), revealed Mycobacterium tuberculosis. Positively stained AFB from the mother’s endocervical biopsy later confirmed the diagnosis of congenital tuberculosis. Pathological analysis of the endocervical biopsy revealed endocervicitis due to tuberculosis (Fig. 2). Placenta was discarded. Ultrasonography of the entire abdomen revealed mild hepatomegaly without a focal hepatic lesion or splenomegaly.

On post-admission day 7, a follow-up chest X-ray showed an increased small reticulonodular and patchy interstitial infiltration in both lungs with a ground-glass appearance, which was a suspected cause of respiratory distress syndrome (RDS) and respiratory failure in the infant (Fig. 1B). On post-admission day 15, a follow-up chest X-ray showed persistent small reticulonodular infiltration and new atelectasis in the upper lobe of the right lung (Fig. 1C). Septic shock with disseminated intravascular coagulation and upper gastrointestinal bleeding later developed. Dopamine, ranitidine, and fresh frozen plasma were then administered. On post-admission day 17, the infant developed 40% pneum-
Fig. 1. A chest radiograph of the infant upon admission. (A) Prominent generalized interstitial infiltration in both lungs. (B) Increased small reticulonodular and patchy interstitial infiltration in both lungs with a ground-glass appearance, which was a suspected cause of respiratory distress syndrome. (C) Persistent small reticulonodular infiltration and atelectasis in the upper lobe of the right lung. (D) 40% pneumothorax of the right lung.

mopthorax (Fig. 1D); therefore a chest-tube was placed. However, the infant continued to develop frequent desaturation. The infant eventually died on post-admission day 27, and no autopsy was performed.

The mother’s medical history was then retrospectively reviewed. One month before her pregnancy, she presented at the hospital with a 3-month history of chronic non-productive cough and low-grade fever. A chest X-ray was performed and sputum sample was collected for 3 consecutive days and stained for AFB. The sputum smear showed no AFB, whereas the chest X-ray revealed patchy infiltration in the middle and lower right lung. Atelectasis of the upper lobe of the right lung was noted, and she was diagnosed and treated for community-acquired pneumonia but was lost to follow-up in the out-patient unit. During antenatal care, she experienced poor weight-gain and cachexia. Ultrasound screening at gestational week 20 was normal; however, a Mantoux tuberculin skin test or chest X-ray was not performed. The postpartum chest X-ray revealed generalized reticulonodular infiltration in both lungs (miliary pattern) and persistent right upper lung atelectasis, and a sputum smear showed AFB infiltration. Although the patient denied a history of tuberculosis exposure, she was diagnosed with active tuberculosis and immediately treated. Her family members also underwent tuberculosis screening by chest X-rays and sputum smears, but all were negative.

While tuberculosis remains a significant public health concern worldwide, it can also contribute to the risk of maternal mortality because tuberculosis is one of the three leading causes of death among women aged 15–44 years (7). However, no exact incidence of tuberculosis in pregnancy has been reported. In Thailand, 10 cases of congenital tuberculosis have been reported to date: 9 in 2003 (8) and 1 in 2004 (9), with an overall mortality rate of 30.0%, and no sequelae were found in surviving neonates after treatment completion.

Beitzke initially established a diagnostic criteria for congenital tuberculosis in 1935 (10), and Cantwell et al. proposed the revised criteria in 1994 (11), which recommend that the infant must have proven tuberculosis lesions and at least one of the following: (i) a lesion in the first week of life, (ii) a primary hepatic complex or caseating hepatic granuloma, (iii) tuberculosis infection of the placenta or maternal genital tract, and (iv) exclusion of postnatal transmission by a thorough contact investigation.

Congenital tuberculosis is typically present by the age of 2–3 weeks, but its characteristically non-specific clinical manifestations lead to difficulty in early diagnosis. In our case, consistent with previous reports (11,12), the infant presented at the age of 18 days with hepatomegaly, lethargy, and poor feeding, which are 3 of 5 common clinical manifestations from recent reviews (65.6%, 39.7%, and 39.1%, respectively), whereas the other two common presentations are fever and respiratory distress (64.4% and 63.8% respectively). Moreover, in our case, the clinical manifestations were not improved after antibiotic administration, and, in general, preterm infants have a significantly higher mortality rate compared with term infants (5). Therefore, due to the difficulty of early diagnosis, congenital tuberculosis should be considered when the infants present with following symptoms: (i) respiratory distress, hepatosplenomegaly, and fever within 3 months after birth; (ii) clinical manifestations
cannot be improved after multiple antibiotic treatments, and a congenital virus infection is ruled out; (iii) miliary tuberculosis is indicated in chest imaging by postnatal week 4; (iv) multiple focal lesions in the liver and spleen are shown in abdominal imaging; and (v) the mothers have active tuberculosis during pregnancy (5).

Moreover, pneumothorax developed in our patient after RDS and positive-pressure mechanical ventilation. Normally, frequent underlying causes of secondary pneumothorax after mechanical ventilation in neonates include RDS, meconium aspiration syndrome, transient tachypnea, pneumonia, pulmonary hypoplasia, and persistent pulmonary hypertension (13,14). Pneumothorax is suspected as a life-threatening condition in the newborn because of its high mortality (15) and morbidity (16) rates. We speculated that the pneumothorax in our case was a result of RDS.

To minimize the risk of death, all neonates diagnosed with congenital tuberculosis should be treated immediately with oral isoniazid, rifampin, pyrazinamide, and intramuscular streptomycin for 2 months and isoniazid and rifampin for an additional 6 months. However, a 12-month regimen is necessary for infants with extrapulmonary tuberculosis (e.g., tuberculosis meningitis) (17,18). Ethambutol is not recommended because of potential adverse treatment effects, such as optic neuritis and red-green color blindness (3).

In our case report, tuberculosis during pregnancy was misdiagnosed, which consequently resulted in an improper treatment. Previous case reports have found that adverse events and prognosis of tuberculosis during pregnancy are influenced by disease severity, time of diagnosis, the presence of extrapulmonary dissemination, human immunodeficiency virus infection, and treatment regimen, and poor treatment compliance (19,20). Moreover, spontaneous abortion, small-for-date uterus, and suboptimal weight gain in pregnancy have also been reported in pregnant tuberculosis patients (21,22). Tuberculosis during pregnancy increases the occurrence of preterm labor, low birth weight, and neonatal mortality (20). Late diagnosis of tuberculosis in pregnancy may increase the risk of obstetric morbidity by 4-fold and that of preterm labor by up to 9-fold (23,24).

Tuberculosis screening should be incorporated in prenatal and antenatal care, particularly in endemic areas, for early diagnosis and prompt treatment of pregnant tuberculosis (3).

Pregnant woman with suspected tuberculosis should be treated as soon as possible with a daily regimen of isoniazid, rifampin, and ethambutol for 2 months, followed by isoniazid and rifampin for an additional 7 months. Streptomycin is contraindicated because it is classified by the United States Food and Drug Administration as a pregnancy category D drug, and pyrazinamide is also not recommended in pregnancy because of unknown teratogenic effects (17).

In conclusion, congenital tuberculosis is a rare condition, and distinguishing it from other infection is difficult. However, congenital tuberculosis should be considered in infants presenting with respiratory distress, hepatosplenomegaly with multiple focal lesions, failure of antibiotic treatments with exclusion of congenital viral infection, miliary pattern in chest imaging, or maternally active tuberculosis during pregnancy. Pneumothorax and air-leaked syndrome should be considered in cases complicated by RDS necessitating positive-pressure mechanical ventilation.

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Conflict of interest None to declare.

REFERENCES