Perinatal Tuberculosis in a 73-Day-Old Infant

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A 73-day-old female infant presented with cough and fever. A chest roentgenogram showed a pneumonic patch, but empirical antibiotic treatment failed. The pathology of an excisional biopsy specimen confirmed pulmonary tuberculosis. We emphasize that tuberculosis should be considered for neonates or infants with unresponsive pneumonia because delayed diagnosis is associated with a fatal outcome.

CASE REPORT

A 73-day-old female infant presented with a 2-day history of cough, poor feeding, and fever in Taiwan. The baby was the first child of a 22-year-old mother and was born vaginally at 38 weeks of gestation, weighing 2,520 g, with Apagar scores of 8 and 9 at 1 and 5 min, respectively. The routine prenatal screening and obstetric ultrasonography during her pregnancy were all normal, and the baby had an uneventful postdelivery course. Bacillus Calmette-Guérin vaccination was administered on the second day of life. Upon admission, physical examination revealed fine rales and decreased breath sounds over the right lung field. There was no hepatic or splenic enlargement. A chest roentgenogram showed an ill-defined hyperdense patchy lesion over the right lower lung field (Fig. 1A). She was evaluated for possible infection with culture of blood and urine and treated with amoxicillin (amoxicillin)-clavulanate and erythromycin. Her white blood cell count was 14,580 cells/mm³, and her C-reactive protein level was 4.0 mg/dl. On the second day of treatment, her cough improved and fever subsided. Erythromycin was discontinued after a 5-day course. The bacterial cultures were negative, but the chest roentgenogram revealed progression of the patchy lesion on the 7th day of treatment.

She was therefore transferred to a medical center because of treatment failure, and antibiotic treatment was shifted to ampicillin-sulbactam. Further evaluation revealed a negative bacterial culture of blood and negative sputum antigen detection of Chlamydia, respiratory syncytial virus, and parainfluenza virus types 1 and 3. The hyperdense patchy lesion did not improve much, as shown by chest roentgenogram 2 days later, and a chest echogram disclosed a mass-like lesion over her right perihilar area. Chest computed tomography was thus performed and revealed enlarged lymph nodes at the paratracheal and subcarinal regions and a low-density mass-like shadow at the right hilum (Fig. 1B). There were also numerous small nodules in her right lung. An abdominal echogram showed a negative finding, except for mild hepatomegaly with normal liver parenchyma. Three serial samples of both gastric aspirates and sputum were taken and sent for mycobacterial culture and acid-fast staining, but all the acid-fast stains were negative. In consideration of malignant disease or atypical infection, video-assisted thoracoscopy was performed. There was a 0.5-cm by 0.5-cm whitish tumor located in lung parenchyma of the right upper lobe, near the superior vena cava, and excisional biopsy was done smoothly. The pathology revealed granulomatous inflammation with positive acid-fast bacilli. Sputum PCR of the Mycobacterium tuberculosis complex was also positive (Cobas AmpliCor Mycobacterium tuberculosis complex PCR; Roche). The antibiotic treatment was changed to isoniazid (13.6 mg/kg/day), rifampin (rifampicin) (13.6 mg/kg/day), and pyrazinamide (29 mg/kg/day) orally. A tuberculin skin test showed 7 mm and 7 mm at 48 h and 72 h, respectively. Previous mycobacterial culture of gastric aspirates and sputum finally turned out to be M. tuberculosis, and the organism was sensitive to all three antituberculosis medications we used.

Her serum alanine amino transferase level was elevated by more than six times on the 11th day of antituberculosis treatment, so pyrazinamide was discontinued. The follow-up liver enzyme level became normal gradually. Further immunological evaluations, including lymphocyte subset testing, mitogen stimulation testing, and quantification of serum immunoglobulin G (IgG), IgA, and IgM, were all normal. Her mother was evaluated with a chest roentgenogram, pelvic echogram, and mycobacterial culture of a cervicovaginal swab for a contagious source survey. Family members also underwent chest roentgenograms, tuberculin skin tests, and history surveys of chronic cough. There was no suspected contagious source to be identified. On the 18th day of antituberculosis treatment and respiratory isolation, the infant appeared to be clinically stable and was discharged to her home. Isoniazid and rifampin were administered for a 9-month course. The outpatient course was smooth, and the patchy lesion resolved gradually, as shown by serial chest roentgenograms.

Perinatal tuberculosis presents with a variety of signs and symptoms (5, 8). Unlike older children, infants with pulmonary tuberculosis have a higher incidence of respiratory symptoms and a high yield (75%) of M. tuberculosis from gastric aspirates (7). However, early diagnosis is difficult because those nonspecific symptoms mimic bacterial or other congenital infections (1). Tuberculosis infection should be suspected and tuberculous investigation should be performed for any infant with unresponsive, worsening pneumonia or unexplained cervical adenitis, particularly for those from areas of disease endemic-
Tuberculosis should be evaluated when present with nonspecific symptoms. A contact investigation of the household should be initiated immediately when an infant is suspected of having tuberculosis, as this helps to establish the diagnosis and guide therapy in infants (8). However, an inability to identify a contagious source cannot exclude a diagnosis of tuberculosis. Infants develop tuberculosis disease from infection more rapidly, and this makes contact investigation more difficult (6). For more than 60% of cases of perinatal tuberculosis, maternal tuberculosis disease was diagnosed after it was found in children (3).

There are many routes of transmission for perinatal tuberculosis. It can be truly congenital by hematogenous spread from placenta or by ingestion or inhalation of infected amniotic fluid. It can also be neonatally acquired early in life by airborne transmission from the mother or others (6). The only criteria for distinguishing congenital tuberculosis from postnatally acquired tuberculosis were first proposed by Beitzke in 1935 and revised by Cantwell et al. in 1994 (2). According to the revised criteria, the infant must have proven tuberculosis lesions and at least one of the following: (i) lesions present in the first week of life; (ii) a primary hepatic complex or caseating hepatic granulomas; (iii) tuberculosis infection of the placenta or the maternal genital tract; or (iv) exclusion of the possibility of postnatal transmission by a thorough investigation of contact. Besides, the median age of presentation of congenital tuberculosis is 24 days (range, 1 to 84 days), and the median age of diagnosis of tuberculosis in infants is 8 months (range, 3.5 to 12 months) (2, 8). Hepatomegaly (76%), respiratory distress (72%), fever (48%), and lymphadenopathy (38%) are the most common symptoms and signs of congenital tuberculosis (2). In our case, postnatally acquired tuberculosis was less favored due to early presentation of tuberculosis symptoms, but none of the four criteria of Cantwell et al. was achieved. No other lesion identified, except pulmonary tuberculosis, suggests infection via aspiration of contaminated amniotic fluid or postpartum airborne transmission rather than hematogenous acquisition (4), so we considered that our case might have acquired tuberculosis infection from contaminated amniotic fluid during the intrapartum period or from postpartum airborne transmission in the very early stage of her life.

Differentiation of congenital tuberculosis from early postnatally acquired tuberculosis is only of epidemiological importance and helps to identify the latent contagious source. Prenatal identification and treatment of maternal active disease or latent infection can prevent perinatal tuberculosis or allow for early diagnosis. Since early therapy is very important for preventing mortality and morbidity, treatment should be initiated as early as possible to improve the chance of survival.

In conclusion, perinatal tuberculosis is a rare disease, and its nonspecific presentations mimic bacterial infection. However, delayed therapy is associated with a poor outcome (3). The diagnosis of tuberculosis should be considered in neonates with unresponsive pneumonia. Differentiation of congenital tuberculosis infection from postnatally acquired tuberculosis infection is difficult but helps to identify the contagious source and has epidemiological importance.

REFERENCES