

Pulmonary tuberculosis in infants under one year of age

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SUMMARY: Arıkan-Ayyıldız Z, Uzuner N, Çakmakçı H, Uysal P, Fırınıcı F, Tuncel T, Anal Ö, Karaman Ö. Pulmonary tuberculosis in infants under one year of age. Turk J Pediatr 2011; 53: 250-254.

This study describes the clinical and radiological features of tuberculosis in infants under one year of age. Medical records were reviewed for infants aged 12 months or less with proven tuberculosis. Six patients' data were evaluated. Cough and tachypnea were the major symptom and sign, respectively. Contact with an adult case of tuberculosis was present in five of the cases. Tuberculin skin test was positive in only one case. *Mycobacterium tuberculosis* was cultured from gastric aspirates of four of five infants and from cerebrospinal fluid in one case. Consolidation was the most common parenchymal lung lesion occurring in four of the patients. Mediastinal or hilar lymphadenopathies were also detected in four of the patients and calcifications were seen within the enlarged nodes in two of them. Antituberculous treatment appeared to be well tolerated without significant adverse effects. Significant radiological improvement was noted after a mean period of 4.6 months.

Key words: infant, pulmonary tuberculosis, miliary tuberculosis.

Tuberculosis is still one of the most important diseases causing mortality and morbidity in developing countries. Among all age groups, children younger than five years are at the highest risk for pulmonary tuberculosis¹. Morbidity and mortality are highest in infancy because of the frequent complications of disseminated forms of tuberculosis, such as miliary tuberculosis and tuberculous meningitis. Diagnostic delay contributes to the poor outcome because of such complications. This age group also demonstrates some differences compared to older children in addition to the mentioned complications: disease is more symptomatic in infants, and yields of diagnostic procedures also differ²⁻⁴. Radiologic findings play a major role in the diagnosis of tuberculosis in infants. Chest X-ray and computed tomography (CT) provide information that may be regarded as specific for tuberculosis.

In this study, we retrospectively analyzed the clinical and radiological features and response to therapy in infants under one year of age with proven pulmonary tuberculosis. We aimed to determine specific features that will help in the early diagnosis of new cases.

Material and Methods

We retrospectively evaluated six infants under one year of age who were diagnosed as pulmonary tuberculosis in Dokuz Eylül University Hospital, İzmir, Turkey from 2004 to 2011. The diagnosis of tuberculosis was established by positive culture of gastric aspirate or cerebrospinal fluid in five of the patients. In one of the patients, two of the following three criteria were met: 1) positive tuberculin skin test (TST); 2) Ruling out of other diseases and improvement with antituberculous medications; and 3) Discovery of a family member with contagious tuberculosis.

Presenting symptoms and duration, clinical features such as lymphadenopathy and hepatosplenomegaly, respiratory signs, neurological findings, and history of a contact with an adult case of tuberculosis were noted.

Basic laboratory examinations including complete blood count, blood chemistry and C-reactive protein results were evaluated. TST with an induration of 15 mm or greater in BCG (Bacille Calmette-Guérin)-vaccinated infants was considered as positive⁵. Microbiological

diagnosis included culture and staining for acid-fast bacilli and polymerase chain reaction (PCR) for *Mycobacterium tuberculosis*.

Chest radiography and CT findings were assessed by a pediatric radiologist. Particular attention was paid to the presence of parenchymal lesions, miliary tuberculosis and presence of hilar or mediastinal adenopathy (Figs. 1-3).

Treatment regimens and response to therapy were also extracted from the files of the patients.

Results

The study group included four girls and two boys. The mean age at presentation was 4.6 months (range: 3-6 months). Two patients were asymptomatic at presentation: one was evaluated for tuberculosis because of his parents' disease, and the other was being evaluated for persistent lung infiltration without any symptoms. The mean duration of symptoms before the diagnosis of tuberculosis was 17 days (range: 10-21 days).

Presenting features of the patients are summarized in Table I. None of the patients had underlying medical conditions documented in their medical records. All patients were vaccinated with BCG, and physical examination of the BCG site and the peripheral lymph nodes revealed no abnormalities.

Screening of family members revealed an undiagnosed adult tuberculosis case in four

Table I. Presenting Features of the Cases

History and symptoms	n
Contact with adult pulmonary tuberculosis	5
Cough	3
Fever	1
No symptoms	2
Lethargy	1
Signs	
Tachypnea	3
Crackles	3
Malnutrition	-
Positive neurological findings	1
Lymphadenopathy	-
Hepatosplenomegaly	3

n: Number of the cases.

of the patients, and one patient already had parents with tuberculosis.

Tuberculin skin test (TST) was done and read in all infants and was significant in only one patient. It resulted in an induration of <15 mm in two infants, and it was anergic in the remaining three. Complete blood count revealed physiological anemia in two of the patients, and blood chemistry was normal in all. C-reactive protein was high in four of the five patients.

Positive culture for *M. tuberculosis* was obtained in five of the patients. *M. tuberculosis* was cultured from gastric aspirates of four of five infants. Cerebrospinal fluid was the source in only one case. Examination of gastric aspirate for acid-fast bacilli was negative in all patients, but PCR was found to be positive in two cases who already had culture positivity.

Consolidation was the most common parenchymal lung lesion occurring in four of the patients. One of the patients had cavitory lesion within parenchymal lesions. Disseminated nodular lesions were detected in two of the cases. Mediastinal or hilar lymphadenopathies were also detected in four of the patients and calcifications were seen within the enlarged nodes in two of them.



Fig 1. CT scan shows nodular infiltration of lungs in a three-month-old girl with pulmonary tuberculosis.

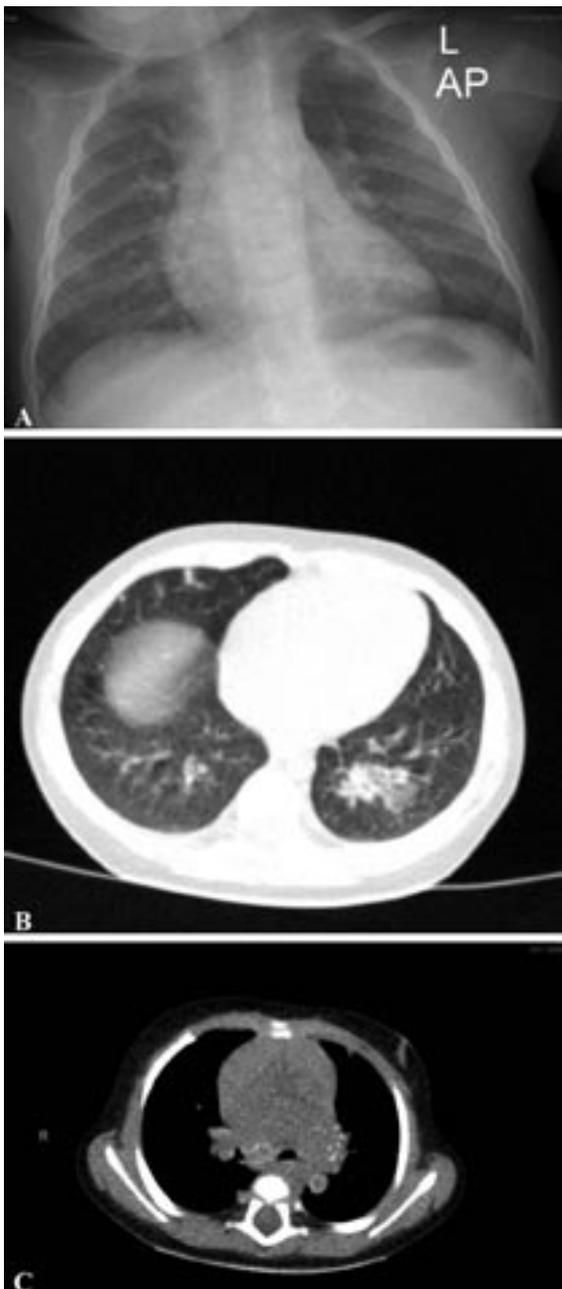


Fig. 2. A five-month-old boy with pulmonary tuberculosis. **A.** Chest radiograph shows alveolar densities on both sides of the lungs. **B.** CT scan shows consolidation in left lower lobe. **C.** Calcifications within mediastinal and hilar lymphadenopathies are shown in CT scan of the same patient.

Three patients were treated with isoniazid, rifampicin and pyrazinamide, and the other three patients with miliary tuberculosis, tuberculous meningitis and cavitary lesions received four antituberculous drugs (isoniazid, rifampicin, pyrazinamide and streptomycin)

for the first two months. Patients received isoniazid and rifampicin for an additional seven months except the latter three patients whose therapy lasted a year. Steroid treatment was also a part of the treatment in two patients: one with tuberculous meningitis and the other with paratracheal lymph nodes compressing the bronchus. No major side effects of the drugs were observed during the treatment period. Significant resolution of radiological findings occurred after a mean period of 4.6 months (range: 3-6 months). All of the patients were cured eventually.

Discussion

The mortality, morbidity and clinical picture of tuberculosis vary between different age groups^{6,7}. Diagnosis of tuberculosis is more important during infancy when the results of missed or delayed diagnosis are likely to be more serious than at a later age. The

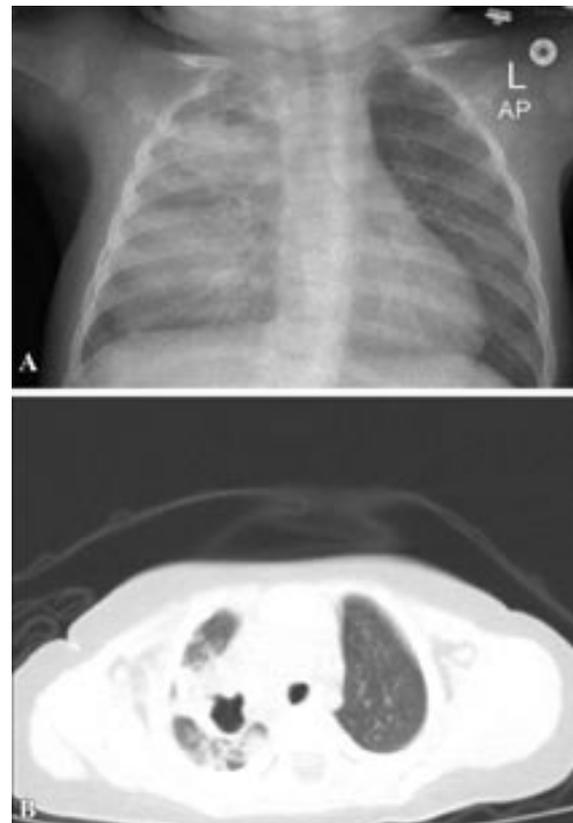


Fig. 3. A six-month-old girl with pulmonary tuberculosis. **A.** Chest radiograph shows cavity within consolidation in the right lobe. **B.** CT scan also shows large cavity within consolidation in the right upper lobe.

nonspecific nature of the symptoms and signs of tuberculosis in early infancy may lead to delayed diagnosis. Classically, a combination of persistent, unremitting cough for >3 weeks, fever for >2 weeks and documented weight loss when other causes have been excluded are important indicators of the possibility of childhood tuberculosis⁸. However, these symptoms have lower sensitivity under three years, and a symptom-based approach to diagnosis also lacks specificity in this age group⁹. In several studies, it was reported that the duration of symptoms before diagnosis could be less than one week in some of the infants^{10,11}. This shows that presentation of tuberculosis can be acute in infants besides its classical features. Our study is also in agreement with the literature, as the mean duration of symptoms before the diagnosis of tuberculosis ranged between 10 and 21 days. Symptoms are usually similar to any case of lower respiratory infection, and do not help in the differentiation. Lymphadenopathy and hepatosplenomegaly are accepted to be indicators of generalized disease, but these are not commonly found in infants as expected^{11,12}. We found hepatosplenomegaly in three of our cases, but lymphadenopathy was not present in any of them. Nevertheless, presentation with neurologic symptoms in any case should raise the suspicion of tuberculosis. Asymptomatic cases were also present in our study group, indicating that the fact of more symptomatic disease in infants was not valid in each case.

Evaluation of close contacts for possible pulmonary tuberculosis is essential in the diagnosis of infants. Most of the studies of young children with tuberculosis yielded adult sources in at least 25% of the cases¹⁰⁻¹². In this study, five of the patients were also exposed to household members with active tuberculosis. Although the source case for young children with tuberculosis is usually a household member, in one study, a source could not be identified in 32% of the cases⁴.

Diagnostic difficulties pose the greatest challenge in childhood tuberculosis management. A positive TST is usually a hallmark of primary infection with *M. tuberculosis*. However, TST is not helpful in the diagnosis of infants. Most infants immunized with BCG at birth have a negative TST by 1-2 years^{13,14}. Approximately

one- to two-thirds of the patients with tuberculosis are anergic (4,15). It is postulated that a TST usually becomes positive in 5 to 10 weeks following infection; however, infants might not be able to react to TST despite having widespread infection^{12,16}.

Diagnosis of tuberculosis relies on bacteriological confirmation. Microscopic evaluation of clinical samples for acid-fast bacilli using Ziehl-Neelsen (ZN) stain and mycobacterial culture are the most commonly used diagnostic methods. Unfortunately, less than 20% of the children with proven tuberculosis will have a sputum or gastric acid sample that is positive on ZN stain compared with 75% in adults¹⁷. Three consecutive morning gastric aspirates yield *M. tuberculosis* in 30% of cases and may be as high as 70% in infants⁴. PCR is another diagnostic method for identifying *M. tuberculosis*; however, it has a sensitivity of 30-40% compared with standard cultures³. In this study, we could not find any positivity of ZN staining from samples, but PCR was positive in two of the culture-positive cases. Negativity of ZN staining and PCR from samples would not rule out tuberculosis in any way. History of close contacts positive for tuberculosis and radiological findings may be the only objective criteria on hand for cases unresponsive to nonspecific antibacterial treatment while awaiting the results of cultures.

Radiological evidence of pulmonary tuberculosis usually includes lymphadenopathy (hilar or mediastinal) and lung parenchymal changes. Frequent radiological findings of pulmonary tuberculosis in infants are also mediastinal or hilar lymphadenopathy with central necrosis and air space consolidations^{12,18}. Disseminated nodules including miliary lesions and airway complications are also detected in this age group¹². CT is more useful than chest radiography and gives diagnostic clues for tuberculosis, as it can better show parenchymal lesions and tuberculous lymphadenopathy. However, it should be used in cases in which the lesions are not detected on chest radiography or when suspicion exists in the diagnosis. Cavitory lesions within consolidations are usually regarded as findings of adult cases, but it should be emphasized that the finding is not that uncommon in children and infants^{12,19-21}.

Tuberculosis in infants can be diagnosed after response to the treatment in some cases during clinical practice. In these instances, waiting for the resolution of radiological findings can be a confusing issue because radiological improvement occurs late in the course of the disease. First-line antituberculous drugs appear to be well-tolerated and effective for the treatment of pulmonary tuberculosis in infants. Our patients also had no side effects during therapy, and significant radiological improvement occurred after a mean period of 4.5 months.

In summary, diagnosing tuberculosis in infants requires suspicion at first and then screening of close contacts. Tuberculosis should always be kept in mind even in mild clinical presentation in infants. TST might not be helpful in this age group, so gastric aspirates should be investigated for *M. tuberculosis* in suspected cases. It is essential to start therapy early if radiologic findings also support clinical findings.

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