

Clinical and Radiographic Findings of Pulmonary Tuberculosis in Infants

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Background: Accurate diagnosis of tuberculosis in infants is important. There are a few studies around tuberculosis in infancy in the literature.

Objectives: This study defines the clinical and radiological features of tuberculosis in infants less than one year of age.

Materials and Methods: The medical records were reviewed for all infants aging 12 months or less with diagnosis of tuberculosis at TB wards of National Research Institute of Tuberculosis and Lung Disease (N.R.I.T.L.D.) in Tehran, Iran between 2006 - 2012 retrospectively.

Results: Nine infants with a median age of eight months were identified, all of whom had endo-thoracic Tuberculosis. The cause of medical evaluation was the onset of symptom in five infants and close contact with infected patients in four. Common symptoms and signs included cough in four, Night sweat in three and Crackles in two patients. Chest X-ray showed consolidation in three, nodular lesions in three, consolidation and ground glass in one, mediastinal bulging in one. Chest CT scan revealed consolidation in three, disseminated pulmonary nodules in one, tiny nodules in two, ground glass lesion in two, right Para-tracheal and subcarinal lymphadenopathies in two, pre-bronchial thickening in one and bronchiectasis in one. Culture was obtained from all of the patients and was positive in one. All infants promptly responded to the treatment. No complications and deaths occurred.

Conclusions: Pulmonary tuberculosis predominates in infants. Prompt diagnosis and treatment seem to reduce morbidity and mortality in this age group. Chest CT may be supportive in the diagnosis of infants with characteristic lymphadenopathy.

Keywords: Tuberculosis; Pulmonary; Infant; Diagnosis

1. Background

Tuberculosis (TB) remains one of the most important causes of morbidity and mortality in the world. TB incidence was estimated as 490000 cases in children and 64000 deaths per year (1). Young age is the most important risk factor for the occurrence of disseminated tuberculosis or severe disease (2). The clinical features and bacteriological findings differences of pulmonary tuberculosis between infants and older children have been understood. Studies have recognized the increased development of extra pulmonary forms of tuberculosis, particularly disseminated disease and meningitis in infancy (3-5). Primary infection of intra-thoracic TB before two years of age progresses to severe disease in the first 12 months after the infection (6). Consequently, early diagnosis and rapid treatment are so critical for infants with tuberculosis. Bacteriological confirmation of tuberculosis in children is difficult (7, 8). The tuberculin skin test

is repeatedly negative in younger infants. Consequently, a history of direct contact with patients who have had infective tuberculosis as well as chest radiographs and computed tomography (CT) has critical role in identifying infants' tuberculosis (5, 7, 9). In this retrospective study, we evaluated the clinical and radiological features of tuberculosis confirmed by culture, presenting in nine infants younger than one year old.

2. Objectives

The purpose of this study was to define specific features, effective in the early diagnosis of new patients in infancy.

3. Materials and Methods

We retrospectively evaluated nine infants who had been diagnosed with pulmonary tuberculosis, admitted to the TB wards of National Research Institute of Tuber-

Implication for health policy/practice/research/medical education:

Morbidity and mortality of tuberculosis is the highest in infancy. We retrospectively evaluated clinical and radiological findings of nine infants at the age of ≤ 12 months who were treated with anti-tuberculosis drugs. We purposed to define specific features that will be effective in the early diagnosis of the new patients in infancy.

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culosis and Lung Disease (NRITLD) in Masih Daneshvari Medical Center, Tehran, Iran from 2006 to 2012. The demographic characteristics, History of close contact with TB cases, symptoms and physical examination findings of the infants were recorded in forms. The diagnosis of TB was confirmed by clinical and radiological findings, contact with TB patients, PPD test > 5 mm (because all of the infants had close contact with TB patients) and a positive culture for acid-fast bacilli on gastric aspiration and response to anti-tuberculosis medications. Presenting symptoms and signs such as cough, lymphadenopathy, respiratory signs, and history of a contact with an adult patient of tuberculosis were noted. The laboratory tests included erythrocyte sedimentation rate (ESR), complete blood count, C-reactive protein and TST results. Chest radiography (CXR) was taken on the first request for the patients. Microbiological diagnosis included culture and staining for acid-fast bacilli and polymerase chain reaction (PCR) for *Mycobacterium tuberculosis*. Chest radiography and CT findings were evaluated by a radiologist. Treatment-planning and response to therapy were also extracted from the files of the infants.

4. Results

In this retrospective study, nine infants (one girl and eight boys) who were hospitalized with initial impression of tuberculosis were enrolled. The mean age of the patients was eight months (1.5 - 12 months). Their characteristics are listed in Table 1. Seven patients were Iranian and two were Afghan. One patient was immunodeficient for IgA but other infants had no underlying disease. HIV testing was not done on our patients. Vaccination was complete in eight cases.

Table 1. Characteristics of Nine Infants With Tuberculosis

Characteristic	Patients, No. (%)
Sex	
Male	8 (89)
Female	1 (11)
Immigrants	2 (22)
Routine vaccination status	
Completed according to patient's age	8 (89)
No vaccine received	1 (11)
Previous BCG vaccination	9 (100)

All infants were vaccinated with BCG, and evaluated for scar of BCG. Four patients were asymptomatic at presentation: three were evaluated for tuberculosis because of their parents' disease, and the other one was tested due to contact with his grandfather who was diagnosed with TB. Endothoracic tuberculosis was the most common primary diagnosis, detected in nine infants. Meningitis or miliary tuberculosis was not identified in any of the patients. Signs and symptoms at the time of admittance are

presented in Table 2. The source of infection included a parent in five (mother with TB in three infants and father with TB in two infants) and other members of family in four. One infant had multiple contacts. Five patients were symptomatic. The most frequent symptoms were cough in 4 (44%), night sweating in 3 (33%) and fever in 2 (22%) of the infants. Four patients didn't have any symptoms.

Table 2. Presenting Features of the Patients

Findings	Patients, No. (%)
Contact with adult pulmonary tuberculosis	9 (100)
Cough	4 (44)
productive cough	1 (11)
Fever	2 (22)
Night sweat	3 (33)
Dyspnea	2 (22)
Poor feeding	1 (11)
Weight loss	1 (11)
Tachypnea	0
Crackles	2 (22)
Lymphadenopathy	0

Tuberculin skin test (TST) was done in all of the patients and the median induration was 11 mm (range of 8 - 16). Negative TST resulted with an induration of < 5 mm in three infants. Complete blood count showed leukocytosis in one of the patients, and blood chemistry was normal in all. The mean value of ESR was 11 mm/hour. ESR and C-reactive protein (CRP) were high in three and one infants, respectively. The sputum smears was done in one patient and was negative. Gastric aspirates were cultured for *M. tuberculosis* in all of infants. Analysis of gastric aspirate for acid-fast bacilli was negative in all cases, but PCR was identified to be positive in one case, even though his culture was negative. *M. tuberculosis* culture of Gastric aspirates was positive in one of the patients. The progression of symptoms, TST induration or chest X-ray findings were not different between patients who had caught tuberculosis microbiologically compared to those whose organism was not isolated. Surgical intervention for therapeutic or diagnostic aims was not necessary in any of the nine infants. The diagnosis of tuberculosis was documented by positive culture of gastric aspirates *M. tuberculosis* in one patient and in the remaining nine patients, more than two of the following three criteria were seen: TST positivity (six cases); detection of at least one family member with tuberculosis (nine cases) and response to therapy as the improvement of clinical or radiological abnormalities (nine cases) (10).

Chest X-rays were performed in all nine patients which was normal in three. Among other patients, consolidation was shown in three (33%). Nodular lesions were found in three (33%), and among them, consolidation and ground

glass were seen only in one (11%). Mediastinal bulging, suggesting hilar lymphadenopathy was also found in one (11%). Thorax CT scan was performed in eight and one obtained normal result. On chest CT scans, consolidation was seen in three patients (37.5%). Disseminated pulmonary nodules were shown in one patient (12.5%) and tiny nodules were seen in two (%25%). Ground glass lesion was observed in two patients (25%). On enhanced CT, right para-tracheal and subcarinal lymphadenopathies were shown in two patients (%25%). Pre-bronchial thickening was observed in one patient (12.5%) and Bronchiectasis

in another (12.5%). Two patients with normal chest X-ray showed abnormal CT scan among whom massive consolidation and Pre-bronchial thickening was seen in one and Tiny nodular infiltration in another. The distribution of lesions in pulmonary section was Right upper lobe (five patients), Left upper lobe (four patients), Right middle lobe (two patients), Right lower lobe (one patient) and Left lower lobe (one patient). Multiple radiographic findings were noticed in patients by thorax CT. Radiological findings of the cases are shown in Table 3.

Table 3. Radiological Findings of the Tuberculosis Patient

Case	Chest Radiography	Thorax Computerized Tomography
1	normal	normal
2	nodular infiltration	nodular infiltration, para-tracheal and subcarinal lymphadenopathy
3	normal	Tiny nodular infiltration
4	normal	massive consolidation, prebronchial wall thickening
5	reticulonodular opacity, ground glass area, air trapping consolidation (Ranke complex)	patchy consolidation, mediastinal lymphadenopathy, ground glass area, air trapping, consolidation (Ranke complex)
6	hilar bulging	bronchiectasis, thickening of prehilum
7	alveolar consolidation	-
8	tiny nodular infiltration	sub-pleural consolidation, parenchymal nodular infiltration
9	consolidation	ground glass area, tiny nodular infiltration

A median of three days (ranging 1 - 8 days) interfered from admission to start of the treatment. Treatment in all infants was done with the standard Isoniazid (INH) and Rifampin (RP) program for six months. During the first two months, Pyrazinamide (PA) and Ethambutol (EB) were also prescribed in all patients, including nine pulmonary tuberculosis cases. Treatment in six patients was completed during six months and these patients were finally cured. Three infants were absent for follow-up. No main drug side effects were detected during the treatment period.

5. Discussion

Annually, at least one million children develop tuberculosis (11). Clinical manifestations are very different among various age groups of children. Identification of tuberculosis is essential in infants because diagnosis delay leads to more serious complications in this age group compared to the elder children (12). Infants are at the highest risk; 50% of them progress to TB after infection in the lack of preventive procedures and up to 30% progress to advanced pulmonary or disseminated TB (6). The common symptoms in children with TB are;

A) A persistent cough (> 2 - 3 weeks), not improving after antibiotics therapy B) Fever of unknown origin, C) Weight loss or failure to gain weight (13). Cough, fever, night sweating and crackles were the most frequent symptoms and sign in the patients of the present study. Fascinatingly, four of the infants didn't have any symp-

toms or signs. History of contact was the cause of their medical assessment and clue to the diagnosis was TST positivity in these four cases and abnormal CT in three of them. Nearly two-thirds of our patients were symptomatic at the time of admission. Similar findings were seen in another study (14) which were significantly higher than for the reports on elder children with intrathoracic tuberculosis who often had silent clinical manifestation in the early stages of disease (12, 15). Children develop symptom when enlarged lymph nodes result in airway compression especially in small-sized airway and a terminal bronchus collapses consequently, which is demonstrated as collapse-consolidation pattern in Thoracic-CT in the younger children (12). Local anatomic parameters may partly describe the clinical differentiations among the infants with other age groups (3). A variety of non-specific symptoms and signs was identified in our patients. It is recommended that for infants with an unusual picture even in the lack of respiratory symptoms suggestive of an infectious process, a high index of suspicion is essential and tuberculosis must be considered as a differential diagnosis.

Evaluation of close contacts with TB patients is important in the diagnosis of infants with possible pulmonary tuberculosis. Most of the studies of infants suffering from pulmonary tuberculosis reported that at least 25% of the cases were exposed to adult sources (5, 7, 16). In the current study, all of the patients were also exposed to household members with active pulmonary tuberculosis. A positive TST is frequently a characteristic of primary

infection with *Mycobacterium Tuberculosis*. Nevertheless, TST is unhelpful in the diagnosis of infants. Schaaf et al. in their series of 38 infants, reported nearly 74% of infants having tuberculosis, without reaction (5). Vallejo et al. in their series of 47 infants, reported no reaction to TST among 22% of infants with tuberculosis (3). This finding was not supported by our study which revealed a negative TST reaction in 33% of the patients. Lack of TST reaction is a common finding at the time of primary diagnosis of tuberculosis. In non-HIV-infected patients, tuberculin skin anergy seems to be associated with decreased activity of circulating T cells and in these patients tuberculin skin anergy does not indicate an immune deficiency in the host (17).

In various studies, *M. tuberculosis* was achieved in up to 70% of infants whose gastric aspirate cultures were attempted (3, 15). The bacteriologic yield in younger children with advanced tuberculosis is significantly higher than uncomplicated disease (77% vs. 35%) (18). Another diagnostic technique for identifying *M. tuberculosis* is PCR but its sensitivity is 30 - 40% compared to standard cultures (8). In this study, we could find one *M. tuberculosis* positive culture in gastric aspirate samples and PCR was positive in one of the culture-negative cases.

Radiological findings of intrathoracic tuberculosis usually include lymphadenopathy (mediastinal or hilar) and lung parenchymal lesions. The common radiological features of pulmonary tuberculosis in infants are also hilar or mediastinal lymphadenopathy with central necrosis and air-space consolidations (7, 16). The less-common findings such as disseminated nodules, airway complications, bronchial wall thickening and bronchiectasis are also seen in this age group (7). We detected consolidation, disseminated pulmonary nodules, para-tracheal and sub-carinal lymphadenopathy, bronchial wall thickening and bronchiectasis on CT scan. It is well-established that CT scan is more useful than chest radiography for detecting parenchymal lesions and tuberculosis lymphadenopathy (7). However, it should be performed in suspicious patients for the diagnosis or when the lesions are not seen on chest radiography.

The diagnosis of Tuberculosis in infancy may be difficult due to non-specific symptoms or asymptomatic presentation before progression of disease in this age group. TB in infants is mostly diagnosed by a high index of suspicion, a history of contact with a tuberculosis patient, chronic signs and symptoms, a positive TST and suggestive chest radiographic findings (19). First-line anti-TB treatment seems to be well-tolerated and effective in infants with pulmonary tuberculosis. Our patients also had no side effects during the therapy. Infants are commonly infected by household contact with an adult TB patient, particularly the mother or primary caregiver. Early detection and treatment of tuberculosis in pregnancy will improve the recovery of both infant and mother (19). Presentation of tuberculosis in the infants may be different and thus,

diagnosis is difficult. The very young children are subjected to increasing rates of infection leading to the disease due to the fact that immunity may be compromised. Initial treatment is important to prevent severe morbidity and mortality in infants. Finally, pediatricians should be aware of clinical forms of TB in infants to help the early diagnosis and treatment.

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Authors' Contribution

Mohammad Reza Bolursaz: designed research, Soheila Khalilzadeh conducted the research, Noshin Baghaie conducted the research, Payam Mehrian analyzed the research, Hosseinali Ghafaripoor analyzed the research, Farahnaz Aghahosseini prepared the data, Ferial Lotfian wrote the paper, Aliakbar Velayati analyzed the research.

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