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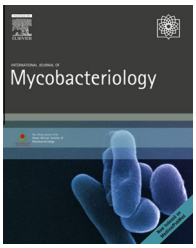

Full Length Article

Determining the lymphadenopathy characteristics of the mediastinum in lung CT scan of children with tuberculosis

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ABSTRACT

Objective/Background: Most tuberculosis cases in children are primary infection, with difficult and imprecise diagnosis mainly based on the existence of mediastinal lymphadenopathy. Here, we investigated the characteristics of mediastinal lymphadenopathy in lung computed tomography (CT) scans of children with tuberculosis. *Methods:* This cross-sectional study was performed on 75 children with tuberculosis referred to Masih Daneshvari Hospital in Tehran, Iran, from 2009 to 2013. Their medical records were investigated, and CT-scan characteristics were extracted by a radiologist. *Results:* Mean ± standard deviation age of cases was 11.2 ± 4.6 years. CT-scan results indicated 94.7% of cases had lymphadenopathy, with lower paratracheal, upper paratracheal, hilar, and subcarinal forms observed in 81.7%, 69.1%, 53.5%, and 47.9% of cases as the most involved stations in lymph nodes, respectively. In 74.6% of patients with mediastinal lymphadenopathy, perilymph node fat inflammation (matting) was observed, with 52.11% exhibiting conglomeration. Bronchial pressure was observed in 4.23% of children with tuberculosis, and bilateral-, right-, and left-parenchymal involvement was observed in 42.7%, 25.3%, and 8% of these cases, respectively. Left- and right-pleural effusion and calcification was reported in 6.7%, 12%, and 5.6% of patients, respectively. Additionally, nearly 80% of patients exhibited mediastinal lymphadenopathy and lung-parenchyma involvement simultaneously. Lung-parenchyma involvement was significantly correlated with subcarinal ($p < .001$), hilar ($p < .001$), subaortic ($p = .030$), lower paratracheal ($p = .037$), and axillary ($p = .006$) stations.

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Conclusion: Situation of mediastinal lymphadenopathy and its synchronicity with lung-parenchyma involvement can help in differential diagnosis of pulmonary tuberculosis from other lung diseases.

Introduction

Tuberculosis (TB) is one of the most common infectious diseases in the world caused by *Mycobacterium tuberculosis* [1]. About one-third of the world population is infected with latent TB infection, and a new infection is occurring every second on a global scale [2]. According to reports, lifetime risk of changing TB infection to disease is estimated at 43% in newborns, 24% in children 1–5 years, 15% in teenagers, and 5–10% in adults. In comparison with adult patients, children are infected with more severe forms of TB, such as disseminated TB [3,4]. Approximately 1 million children <15-years old were infected with TB worldwide in 2015, and 136,000 children die due to the disease annually [5]. Records show that in regions with high TB prevalence, 15–20% of all TB cases occur in children [6].

Most TB cases are caused by primary infection that is mainly transmitted to children by one of the family members. Some of the infancy and early childhood common diseases, such as human immunodeficiency virus (HIV), measles, whooping cough, and protein-energy malnutrition associated with immunodeficiency, can accelerate TB-infection activation. In most cases, lung-parenchymal lesions and lymphadenopathy are self-limiting; however, in some cases, especially in infants, they lead to mediastinal lymphadenopathy with continuing involvement. As previously reported; mediastinal lymphadenopathy with or without parenchymal disorder is a clear sign of primary TB in childhood [7–10].

TB in children is a major challenge due to the lack of a standard definition, diagnostic problems, frequency of extrapulmonary cases, and little attention to public health [10]. Many children (65–95%) have no clinical symptoms. Therefore, the diagnosis of primary pulmonary TB is very difficult and inaccurate in children and is confirmed only in 40% of cases. Major diagnostic problems often lead to neglecting TB in children [11–15].

Most radiological findings of TB in children involve mediastinal and hilar lymphadenopathy with central necrosis and retention of airways. Simple radiography is unreliable in determining the existence, station, and characteristics of mediastinal lymphadenopathy, while computed tomography (CT) scan is considered as the gold standard [15]. CT scans have more benefits in diagnosis of TB in children as compared with radiography and can be used in cases of complex suspected TB to provide further details of airway, parenchyma, and lymph node involvement [16]. However, a limited number of studies of CT-scan findings exclusively reported mediastinal adenopathy in children. Usually, these studies were performed on a very limited sample size. Also, these studies are performed on suspicious TB cases according to the World Health Organization diagnostic criteria [15,17].

The health of children is among the main objectives of the health system in any community. Determination of the prevalence of lymphadenopathy in children with TB is an essential point in determining the policies of those involved in the healthcare field. However, correct diagnosis assures appropriate treatment and prevents the infection of other people. Therefore, this study evaluated mediastinal lymphadenopathy characteristics of lung CT scans of children having TB in order to determine a correct and efficient diagnostic method.

Materials and methods

This cross-sectional study was performed in Masih Daneshvari Hospital in Tehran, Iran, between 2009 and 2013. The ethics committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran, approved this study. All parents provided informed written consent. In this study, a convenience-sampling method was used, and cases were selected from children <18-years old who had three of the following five points: (1) recent history of contact with an infected person with TB; (2) positive purified-protein derivative skin test ($\geqslant$10 mm in conditions of no contact and $\leqslant$5 mm in conditions involving contact with a person infected with TB); (3) radiographic signs related to TB; (4) clinical signs related to TB; and (5) pathology or bacteriology related to TB, referred to Masih Daneshvari Hospital during the aforementioned years, and having CT-scan results in their medical records. Considering type I errors (α) of 5%, bilateral hilar mediastinal lymphadenopathy ratios in children equal to 73% and accuracy of 10% around this proportion, the sample size was estimated to be 75 cases using one ratio-estimation formula [15].

Lung CT scan in the medical records of children with TB was evaluated by a radiologist, and characteristics of the CT scan were extracted and recorded in a checklist prepared by the researcher.

CT scans were evaluated for: (1) lymphadenopathy (have/have not), lymphadenopathy stations (upper paratracheal, prevascular, lower paratracheal, subaortic, paraaortic, subcarinal, paraesophageal, pulmonary ligament, hilar, and axillary), perilymph node fat inflammation (matting), conglomeration/discrete, calcification (have/have not), bronchial pressure (have/have not), lung-parenchyma involvement (right, left, bilateral, or without involvement), and pleural effusion (right, left, or without involvement).

In order to reduce interobserver bias, CT-scan results were interpreted by only an experienced radiologist. Also, to reduce

the bias due to qualitative interpretation of CT-scan results, the radiologist was blinded in terms of all factors that could interfere with interpretation of results (disease and aim of the study). To describe the data, descriptive statistics, including mean, standard deviation, frequency, and percentage were used. To examine the differences between mediastinal lymphadenopathy characteristics in both sexes, we used chi-square and Fisher's exact tests. Data analysis was performed using Stata version 11.2 software (StataCorp, College Station, TX, USA). A $p < .05$ was considered significant.

Results

In this study, 54.7% (41 patients) of a total of 75 children <18-years old and having inclusion criteria were female. Generally, the mean and standard deviation of cases was 11.2 ± 4.6 years, ranging from 1 to 17 years. In evaluating CT-scan findings in the medical records of 75 children, we found that, 94.7% (71 cases) had lymphadenopathy. Lower paratracheal, upper paratracheal, hilar, and subcarinal forms were observed in 81.7%, 69.0%, 53.5%, and 47.9% of cases and were the most involved situations in the mediastinum, respectively, that were seen in lung CT scans. Lymphadenopathy occurred only at one point of mediastinum in six children (8%). Lymph node involvement in 27 children (36%) was observed in three stations, 19 cases (25.3%) in four stations, 11 patients (14.7%) in two stations, and in 10 patients (13.3%) occurred in five stations, while only in two patients (2.7%) exhibited mediastinum involvement in six stations. Signs of perilymph node fat inflammation (matting) were observed in 74.6% of children with mediastinal lymphadenopathy (71 patients). Conglomeration was seen in 52.1% of patients with mediastinal lymphadenopathy, and discrete forms were observed in 47.9% of these. From the total number of 75 children with TB, calcification was reported in 5.6%, bronchial pressure in 4.2%, lung-parenchymal involvement for bilateral, right, and left in 45.1%, 25.4%, and 8.4%, respectively, and right and left pleural effusion in 12.7% and 7.0%, respectively (Table 1).

Results of data analysis showed that involvement of mediastinal lymphadenopathy in subcarinal ($p < .001$), hilar ($p < .001$), subaortic ($p = .030$), lower paratracheal ($p = .037$), and axillary ($p = .006$) was significantly associated with involvement of the lung parenchyma. Simultaneously, mediastinum involvement accompanied bilateral involvement of lung parenchyma with a frequency of 64.7%, 52.6%, 50.0%, 48.3%, and 29.6% of these stations, respectively, and was greater than rest of lung-parenchymal involvement. Simultaneous right-parenchyma involvement with mediastinal lymphadenopathy was placed in the next row with a lower percentage, and less involvement was observed in the left parenchyma. Lung-parenchyma involvement showed no significant correlation with other stations of mediastinal lymphadenopathy involvement. Also, no significant correlation was seen between lung-parenchymal involvement and conglomeration, perilymph node fat inflammation (matting), bronchial pressure, pleural effusion, or calcification (Table 2). Our findings also showed no significant correlation between pleural effusions with different mediastinal lymphadenopathy station involvement. Conglomeration, perilymph node fat inflammation (matting), bronchial pressure, and calcification also showed no significant correlation with pleural effusion (Table 3).

Discussion

In this study, we investigated the prevalence and characteristics of mediastinal lymphadenopathy in lung CT scans of children with TB. We found that approximately 95% of patients (71 patients) had lymphadenopathy, and that 92% exhibited involvement in more than one situation of mediastinal lymph node station, with the most involved lymph node stations being lower paratracheal, upper paratracheal, hilar, and subcarinal, respectively.

Lymphadenopathy with or without simultaneous parenchymal disorder is a radiologic sign of primary TB in childhood. Although in almost all children with pulmonary TB enlarged lymph nodes or lung-parenchymal malformations exist, it is potentially difficult to detect this, even with use of high-quality chest radiological tools [17–19]. In our study, 75 children <18-years old and exhibiting inclusion criteria were investigated, of which 32 (42.7%) cases were <10-years old and 43 (57.3%) of cases were between 11- and 17-years old. Our results showed that CT scans were able to detect 94.7% (71/75) of patients having TB with lymphadenopathy. Khalilzadeh et al. [20], showed that CT scan detected 46% of patients with TB in a study where 124 cases had close contact with infected people. In a retrospective study by Kim et al. [17] which examined 41 children diagnosed with TB using bacteriological and radiological procedures, it was shown that 83% of the patients were diagnosed with mediastinal or hilar lymphadenopathy [17]. The study by Andronikou et al. [15] on 54 boys and 46 girls suspected to have TB with an average age of 21.5 months (2 to 142 months), showed that lymph nodes have been observed in 92% of patients, regardless of their size and characteristics [15]. In the studies mentioned, different people with probable or definite TB diagnosis and also children in contact with TB patients were examined. However, although the precision of the instrument used and conditions evaluating the results of the CT scan were different, it seems that mediastinal lymphadenopathy is clearly present in a significant number of children with TB, and that CT scan is an appropriate and effective approach to confirm lymphadenopathy in children with TB.

We investigated details of lymphadenopathy stations in the lungs of children with TB. Our results showed that lower paratracheal, upper paratracheal, hilar, and subcarinal were the most involved stations observed in lung CT scans. In 92% of children with mediastinal lymphadenopathy, involvement occurred in more than one situation, and the mediastinal lymph node stations were mostly involved in three positions. In a study conducted by Andronikou et al. [15] on 100 children, the mediastinal lymph node stations were mostly involved in subcarinal (90 patients), hilar (85 left, 72 right, and 61 bilateral), axillary (79 cases), precarinal (64 cases), and right paratracheal (63 cases). A total of 88 patients exhibited more than one station of involvement, four

Table 1 – Mediastinal lymphadenopathy in pulmonary tuberculosis in children admitted to Masih Daneshvari Hospital between 2009 and 2013 based on CT scan.

Variables	Have lymphadenopathy		The frequency of situations of lymph node involvement					
	No.	%	1	2	3	4	5	6
Gender								
Female	38	53.52	4	6	13	11	5	2
Male	33	46.48	2	5	14	8	5	0
The station of lymphadenopathy								
Upper paratracheal	49	69.01	2	7	14	19	7	0
Prevascular	14	19.72	2	3	3	3	2	1
Lower paratracheal	58	81.69	2	10	16	23	7	0
Subaortic	4	5.63	0	2	1	1	0	0
Paraaortic	13	18.31	0	2	4	7	0	0
Subcarinal	34	47.89	2	9	13	8	2	0
Paraesophageal	6	8.45	1	4	1	0	0	0
Pulmonary ligament	4	5.63	0	1	2	0	1	0
Hilar	38	53.52	2	7	14	11	3	1
Axillary	23	32.39	1	5	8	9	0	4
Bronchial pressure								
No	68	95.77	1	10	19	25	11	2
Yes	3	4.23	0	0	2	0	0	1
Conglomeration/discrete								
Conglomerate	37	52.11	0	1	5	16	10	2
Discrete	34	47.89	2	9	14	11	1	0
Fade the signs of fat around lymph nodes								
No	18	25.35	0	0	3	8	6	1
Yes	53	74.65	2	10	16	19	5	1
Pulmonary parenchyma								
No	18	24.00	0	1	2	7	4	4
Left	6	8.00	0	0	1	3	1	1
Right	19	25.33	0	4	5	7	2	1
Double-sides	32	42.67	2	5	11	10	4	
Calcification								
No	67	94.37	5	11	22	18	9	2
Yes	4	5.63	0	0	3	1	0	0
Pleural effusion								
No	61	81.33	2	8	13	22	10	6
Left	5	6.67	0	0	1	3	1	0
Right	9	12.00	0	2	5	2	0	0

patients exhibited subcarinal lymphadenopathy, and 35 patients exhibited lymphadenopathy in all above-mentioned positions simultaneously. Other studies did not report lymphadenopathy station details. Identifying stations involved in mediastinal lymphadenopathy can be effective in differentiating TB from other lung diseases. According to our findings and the study mentioned above, three hilar, subcarinal, and paratracheal positions were special situations of the lymph nodes that exhibited the highest involvement in children with TB. Therefore, the interpretation of the CT-scan results of these patients should be performed more carefully.

We found calcification in 5.6% of all patients (4/75). Moon et al. [21] studied 49 patients diagnosed with mediastinal lymphadenopathy over a period of 8 years (1988–1996). In that study, patients were divided into active and passive groups, and the number of lymph nodes and calcification were examined in each. The results showed that in 37 patients with active disease, a total of 151 nodes with different sizes between 1.5 cm and 6.7 cm and calcifications were observed in 19% of patients ($n = 7$), while in 12 patients with inactive disease, a total of 34 nodes with sizes between 1.0 cm and 4.7 cm were observed, with calcification seen in 83% of inactive patients ($n = 13$). The size of the node in inactive patients was smaller, but accompanied by increased calcification. Calcification was also reported in only 9% of patients [15]. In another study, calcification was seen in only 15 –21% of patients having primary pulmonary TB [17]. Although calcification was not observed in all cases in these studies, it can be a key indicator in diagnosing lymphadenopathy in children.

Nearly all TB cases in children are accompanied by pulmonary parenchymal disorders [4]. Our findings indicated that CT was able to detect 76% of patients with parenchymal involvement, and that most stations of involvement were allocated to bilateral, right, and left sides. Our results also showed that nearly 80% of patients exhibited mediastinal lymphadenopathy and lung-parenchymal involvement

Table 2 – The relationship between different features of mediastinal lymphadenopathy with parenchymal lung involvement in children with pulmonary tuberculosis admitted to Masih Daneshvari Hospital between 2009 and 2013 based on CT scan.

Variables	Pulmonary parenchyma				
	No	Left	Right	Double-sided	*p*
The station of lymphadenopathy					
Upper paratracheal	11 (22.45)	3 (6.12)	14 (28.57)	21 (42.86)	0.702
Prevascular	5 (35.71)	0 (00.00)	3 (21.43)	6 (42.86)	0.578
Lower paratracheal	13 (22.41)	2 (3.45)	15 (25.86)	28 (48.28)	0.037
Subaortic	0 (00.00)	2 (50.00)	0 (00.00)	2 (50.00)	0.030
Paraaortic	1 (7.69)	1 (7.69)	5 (38.46)	6 (46.15)	0.377
Subcarinal	1 (2.94)	1 (2.94)	10 (29.41)	22 (64.71)	<.001
Paraesophageal	1 (16.67)	1 (16.67)	0 (00.00)	4 (66.67)	0.266
Pulmonary ligament	0 (00.00)	0 (00.00)	2 (50.00)	2 (50.00)	0.552
Hilar	2 (5.26)	6 (15.79)	10 (26.32)	20 (52.63)	<.001
Axillary	12 (44.44)	0 (00.00)	7 (25.93)	8 (29.63)	0.006
Bronchial pressure					0.844
No	14 (20.59)	6 (8.82)	17 (25.00)	31 (45.59)	
Yes	1 (33.33)	0 (00.00)	1 (33.33)	1 (33.33)	
Conglomeration/discrete					0.154
Conglomerate	4 (10.81)	4 (10.81)	11 (29.73)	18 (48.65)	
Discrete	11 (32.35)	2 (5.88)	7 (20.59)	14 (41.18)	
Fade the signs of fat around lymph nodes					0.385
No	5 (27.78)	2 (11.11)	2 (11.11)	9 (50.00)	
Yes	10 (18.87)	4 (7.55)	16 (30.19)	23 (43.40)	
Calcification					0.351
No	16 (23.88)	3 (4.48)	17 (25.37)	31 (46.27)	
Yes	1 (25.00)	1 (25.00)	1 (25.00)	1 (25.00)	
Pleural effusion					0.585
No	16 (26.23)	6 (9.84)	16 (26.23)	23 (37.70)	
Left	0 (00.00)	0 (00.00)	3 (40.00)	3 (60.00)	
Right	2 (22.22)	0 (00.00)	1 (11.11)	6 (66.67)	

simultaneously. Khatami et al. [3] showed that 89.5% of children <36 months had mediastinal lymphadenopathy and parenchymal-lung involvement simultaneously. Also, our results indicated that lung-parenchymal involvement was significantly related to mediastinal lymphadenopathy positions, such as subcarinal, hilar, subaortic, lower paratracheal, and axillary. These findings suggested that lung-parenchymal involvement occurred along with most involved mediastinal lymphadenopathy stations simultaneously. Therefore, it appears that simultaneous evaluation of lymphadenopathy and parenchymal symptoms could be effective in differentiating mediastinal lymphadenopathy from other lung lymphadenopathies.

Finding pleural effusion is an opportunity for the physician to use it for detection of TB versus non-TB diseases. TB is among the leading causes of pleural effusion, and 31% of patients with TB also exhibit pleural effusion. In people with TB and positive for HIV, pleural effusion is more common and increases with age from 5 to 45 years. Pleural involvement with TB can be primary or secondary to pulmonary TB [13–15]. In our findings, right and left pleural effusion were reported in 12% and 6.7% of patients, respectively. Our results showed no significant relationship between pleural effusion and different situations of mediastinal involvement or its other features, such as fading fat surrounding nodes and conglomeration/discrete. Also, bronchial pressure and calcification were not significantly related to pleural effusion involvement.

Compared with chest radiography, CT scans offer advantages in defining the severity of TB and its complications in bronchus, pleura, the pericardium, and its use to diagnose chest TB was approved [6,11,16]. However, due to the high cost, need for anesthesia, and risks associated with dye injection, routine use of this method is not recommended for diagnosis. CT scans can be helpful in diagnosing TB only in certain complex circumstances and in situations where other low-risk methods cannot detect the disease.

This study had several limitations: (1) CT scans were evaluated only by a single radiologist; therefore, bias could occur due to qualitative interpretation and using personal experience to interpret results (intraobserver bias); however, due to the skill of the radiologist, this is largely negligible; (2) given cases are referred to a large referral hospital, the severity of lesions and the level of disease progression occurred more often than normal, and referral bias was common in this study. In interpreting the results of this study, it should be noted that due to referral nature of our hospital and expected higher severity of the disease in these cases, prevalence and severance of the findings are lower in population of children with TB. Also, this study investigated station details and other

Table 3 – The Relationship Between Different Features of Mediastinal Lymphadenopathy With Pleural Effusion in Children With Pulmonary Tuberculosis Admitted to Masih Daneshvari Hospital Between 2009 and 2013 Based on CT Scan.

Variables	Pleural effusion			
	No	Left	Right	*p*
The station of lymphadenopathy				
Upper paratracheal	38 (77.55)	3 (6.12)	8 (16.33)	0.300
Prevascular	10 (71.43)	1 (71.14)	3 (21.43)	0.509
Lower paratracheal	46 (79.31)	4 (6.90)	8 (13.779)	0.863
Subaortic	0 (00.00)	0 (00.00)	4 (100.00)	1.000
Paraaortic	8 (61.54)	2 (15.38)	3 (23.08)	0.096
Subcarinal	26 (76.47)	3 (8.82)	5 (14.71)	0.608
Paraesophageal	4 (66.67)	0 (00.00)	2 (33.33)	0.194
Pulmonary ligament	4 (100.00)	0 (00.00)	0 (00.00)	1.000
Hilar	33 (86.84)	1 (2.63)	4 (10.53)	0.333
Axillary	23 (85.19)	1 (3.70)	3 (11.11)	0.899
Bronchial pressure				0.237
No	55 (80.88)	4 (5.88)	9 (13.24)	
Yes	2 (66.67)	1 (33.33)	0 (00.00)	
Conglomeration/discrete				0.190
Conglomerate	27 (72.97)	3 (8.11)	7 (18.92)	
Discrete	30 (88.24)	2 (5.88)	2 (5.88)	
Fade the signs of fat around lymph nodes				0.248
No	14 (77.78)	0 (00.00)	4 (22.22)	
Yes	43 (81.13)	5 (9.43)	5 (9.43)	
Calcification				0.593
No	54 (80.60)	5 (7.46)	8 (11.94)	
Yes	3 (75.00)	0 (0.00)	1 (25.00)	

features of mediastinal lymphadenopathy that may be effective in differential diagnosis of TB from other lymphadenopathies, while this was not considered extensively in previous studies.

Conclusion

CT scans can detect a high percentage (95%) of children having TB with mediastinal lymphadenopathy. According to our results and previous studies, paratracheal, hilar, and, subaortic positions were the most common positions of lymph node stations. Also, simultaneous involvement of mediastinal lymphadenopathy and pulmonary parenchyma was observed in a significant number of patients. However, lung-parenchyma involvement was significantly related to the most common situations involved in mediastinal lymphadenopathy. Therefore, it appeared that CT scans could be an efficient method for diagnosis of mediastinal lymphadenopathy in children having TB. Also, focusing on station details associated with mediastinal lymphadenopathy, especially involving the aforementioned stations, and checking their synchronicity with lung-parenchyma involvement can be effective in the differential diagnosis of pulmonary TB from other lung diseases.

Conflict of Interests

All authors declare no conflicts of interest.

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