Is HRCT Reliable In Determining Disease Activity In Pulmonary Tuberculosis?

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Abstract

AIMS AND OBJECTIVES

The purpose of our study is to (1) determine the activity of disease based on the HRCT findings (2) to define indications for the use of HRCT in evaluation of Pulmonary TB and (3) to determine whether additional information provided by HRCT alters clinical management of the disease.

MATERIALS AND METHODS

The present study was carried out at Shree Sayajirao General Hospital (SSGH), Baroda, Gujarat, India from January 2002 to December 2002. Twenty five patients with sputum positive post-primary pulmonary TB were studied prospectively with chest radiographs and HRCT. The diagnosis of active TB was based on detection of acid-fast bacilli in sputum. None of the patients in our study population was HIV positive. All patients underwent x-ray chest and HRCT chest (Philips Tomoscan, Best, Netherlands). The pattern, extent and severity of HRCT findings were recorded and compared with the plain x-ray findings. The gathered information and investigations were subjected to statistical analysis.

RESULTS

Our study population consisted of sputum positive (AFB positive) 25 patients, 22 of them were newly diagnosed/suspected post-primary tuberculosis (GROUP 1) and 3 of them had taken six months of AKT (GROUP 2). Our study included 22 males and 3 females with average age of 38 years (range, 14-65 years.) In total chest radiographic signs of active tuberculosis were seen in twelve (48%) patients. HRCT showed evidences of active tuberculosis in all 22 patients of newly diagnosed tuberculosis; and in 2 out of 3 patients with prior history of AKT. Thus, total of 24 (96%) patients had evidence of active pulmonary TB on HRCT. One patient with prior history of AKT showed evidence of pulmonary Koch’s sequel.

CONCLUSION

Although chest radiography remains the foremost imaging technique in the evaluation of pulmonary TB, HRCT can be useful in certain circumstances and can provide important information in the diagnosis and management of the disease. HRCT is helpful in the distinction of active form inactive TB. HRCT is better than plain chest radiograph in identification of extent of pulmonary TB, especially subtle areas of consolidation, cavitation, bronchogenic and miliary spread. HRCT is recommended when the radiographic findings are normal or inconclusive and tuberculosis is suspected clinically for the confirmation of diagnosis and determination of activity.

Ind J Radiol Imag 2006 16:2:221-228

Key words : - Computed Tomography (CT), High-resolution Lung CT, Tuberculosis pulmonary,

INTRODUCTION

Tuberculosis remains an important cause of morbidity and mortality worldwide. Although the prevalence of TB has declined since the advent of modern chemotherapy, pulmonary TB remains an important cause of disease.

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Received 12 November 2005; Accepted 10 April 2006
worldwide and has experienced resurgence in the western world since the pandemic of AIDS. Chest radiography remains the first imaging technique in the evaluation of thoracic tuberculosis. Conventional CT and HRCT may be needed for further evaluation of known or suspected tuberculosis in the thorax. The purpose of our study is (1) to determine the activity of disease based on the HRCT findings (2) to define indications for the use of HRCT in evaluation of Pulmonary TB and (3) to determine whether additional information provided by HRCT alters clinical management of the disease.

MATERIALS AND METHODS

The present study was carried out at Shree Sayajirao General Hospital (SSGH), Baroda, Gujarat, India from January 2002 to December 2002. Twenty five patients with sputum positive post-primary pulmonary TB were studied prospectively with chest radiographs and HRCT. The diagnosis of active TB was based on detection of acid-fast bacilli in sputum. None of the patients in our study population was HIV positive. All patients underwent x-ray chest and HRCT chest (Philips Tomoscan, Best, Netherlands) examination using the following protocol. Serial slices 2 mm in width and 10 mm apart were taken from the apex of the lung to base in supine position and reconstructed on a High-resolution bone algorithm. Scanning time was 2 s. All images were obtained at window levels appropriate for lung parenchyma settings (window width 1300 HU; window level -600 HU). HRCT scans were interpreted by two consultant radiologists. The pattern, extent and severity of HRCT findings were recorded and compared with the plain x-ray findings. The gathered information and investigations were subjected to statistical analysis.

Out of 25 patients, 22 cases were newly diagnosed (GROUP 1), and 3 patients had already completed 6 months of AKT (GROUP 2). HRCT was done in Group 2 patients for evaluation of lesions of post-tuberculous sequel and possibility of reactivation of tuberculosis in appropriate clinical settings.

Descriptive terms used to interpret HRCT were defined as follows. (a) Centrilobular nodule: well defined lesions 2-4 mm in size, separated by more than 2 mm from the pleural surface or interlobular septa; (b) Tree in bud: a branching, linear structure with more than one contiguous branching site (c) Poorly defined nodule: 5-8 mm in diameter and poorly defined, and (4) Consolidation- as an area of increase opacity with obscuration of underlying bronchovascular markings.

Chest radiographic findings in active tuberculosis were defined as following- (1) poorly defined nodular opacities, consistent with bronchogenic spread of Tuberculosis. (2) Cavitory lesions (3) infiltrate (areas of bronchopneumonic consolidation) and (4) miliary opacities. HRCT findings consistent with presence of active tuberculosis were defined as presence of poorly defined nodules, tree in bud appearance, randomly distributed (miliary) nodules, cavitation, consolidation, bronchogenic spread and pleural effusion. Findings consistent with bronchogenic spread were presence of centrilobular nodule with branching linear structure, a tree-in-bud appearance, and poorly defined 4-8mm size nodule.

RESULTS

Our study population consisted of sputum positive (AFB positive) 25 patients, 22 of them were newly diagnosed/ suspected postprimary tuberculosis (GROUP 1) and 3 of them had taken six months of AKT (GROUP 2). Our study included 22 males and 3 females with average age of 38 years (range, 14-65 years.) Chest radiographic findings in active tuberculosis were- poorly defined nodular opacities in ten (40%) of twenty five patients [FIG 1] - consistent with bronchogenic spread of tuberculosis and cavitory lesions were seen in three patients (12%), while infiltrates (areas of bronchopneumonic consolidation) were seen in ten patients (40%), lobar consolidation was seen in one patient and miliary opacities in one patient [FIG 2]. In total radiographic signs of active tuberculosis were seen in twelve (48%) patients.

HRCT showed evidences of active tuberculosis in all 22 patients of newly diagnosed tuberculosis; and in 2 out of 3 patients with prior history of AKT. Thus, total of 24 (96%) patients had evidence of active pulmonary TB on HRCT. One patient with prior history of AKT showed evidence of pulmonary Koch's sequel. In our study, out of 25 patients with sputum positive tuberculosis, 23(92%) had HRCT findings of bronchogenic spread of the disease and one (4%) had miliary tuberculosis. Findings consistent with bronchogenic spread on HRCT were a centrilobular nodule with branching linear structure - "tree-in-bud appearance"
(n=20[80%]), poorly defined 4-8 mm size nodule (n=10[40%]). Other findings of active tuberculosis were presence of cavitary nodules or consolidation (n=16[64%]). Whenever a cavity developed within a consolidated lobule, it occurred centrally within the lobule. In eight patients centrilobular nodule and or tree-in-bud was seen without any evidence of cavitation on HRCT.

Cavities were seen in 16(64%) patients, 12 patients had a single cavity and four had multiple. Out of 16, 11 patients had thin walled cavities, three patients had thick walled cavities and two patients had both thick and thin walled cavities. Thick walled cavities are seen frequently in patients with early active tuberculosis and represents early stage of necrotizing consolidation in the early stage of cavity formation. The most common site for the cavity formation includes upper lobe in 14 patients and lower lobes in two patients- in superior segment of lower lobe-the site consistent with the preferential areas of consolidation in patients with active tuberculosis.

Consolidation was seen in 13 (52%) patients and in 8 patients it was unilateral and predominantly in the upper lobe- apicoposterior segment of upper lobe. Three patients had bilateral upper lobe consolidation and two patients had multifocal consolidation. In patients with consolidation of lower lobe- it was limited to the superior segment of lower lobes.

Three patients in our study had taken AKT for the period of six months and presented with symptoms consistent with reactivation of pulmonary tuberculosis. Chest
Radiographs were equivocal in determining the activity of tuberculosis. HRCT was done in these patients as they were sputum positive for Mycobacterium Tuberculosis. Out of three, two patients with previously treated tuberculosis had active tuberculosis and consisted of bronchogenic spread. All three patients showed HRCT evidences of Koch's sequel.

**Fig 6** HRCT chest shows random distribution of small nodules with subtle intralobular and interlobular septal thickening- miliary tuberculosis.

**DISCUSSION**

Tuberculosis is a chronic granulomatous infection characterized by caseation necrosis and great propensity for fibrosis and calcification. Tuberculous lesion may develop in the lung in a variety of ways: local progression, bronchogenic dissemination, or hematogenous dissemination [1, 21]. Tuberculosis is caused by Mycobacterium tuberculosis- a strictly aerobic, acid fast rod shaped bacillus.

Traditionally, TB infection has been considered in two stages: primary infection and reactivation or post primary disease. Primary pulmonary TB is acquired by the inhalation of airborne organisms and occurs in patients not previously exposed to M. Tuberculosis. The initial site of lung infection is variable, but often, the middle and lower lung zones are first involved. A focal area of consolidation typically well defined, homogeneous, segmental or lobar consolidation results, with subsequent hilar and mediastinal lymphadenopathy. In majority of subjects (90-95%), primary tuberculosis remains clinically silent and development of immunity results in healing of the lesions within 1-3 weeks [2]. However, in 5% to 10% of patients who have primary TB, the infection is progressive and dissemination occurs; this is termed as progressive primary TB, findings of which are identical to that of post primary TB.

Post-primary TB occurs in patients previously sensitized to M. tuberculosis and results either from re-infection or from reactivation of dormant bacilli in primary infection (90% of cases) and occurs predominantly in adolescents and adults [4, 5]. Post-primary or reactivated pulmonary tuberculosis begins with an acute necrotizing consolidation followed by Transbronchial spread [6]. Reactivation of dormant bacilli occurs during periods of immunsuppression, malnutrition, and debilitation or as a result of aging [21]. CAVITATION is the hallmark of Post primary TB and the cavity can rupture into the pleural space, resulting in empyema and bronchopleural fistula. Tubercle erosion into a pulmonary artery leads to pseudoaneurysm formation and potentially fatal hemoptysis. Erosion into smaller, systemic vessels or pulmonary veins results in symptomatic hematogenous dissemination and miliary TB. Healing of Postprimary TB typically occurs with fibrosis and calcification. Bronchial strictures, lobar or segmental collapse, and bronchiectasis can result from endobronchial disease. Tuberculomas also can result from postprimary disease [21, 30].

Radiographically, post-primary TB is characterized by its predilection for the upper lobes, absence of lymphadenopathy, and a propensity for cavitation. Radiographic findings include patchy consolidation, streaky opacities or both (100%), primarily in the apical and posterior segments of the upper lobes (91%), cavitation (40% to 87%), bronchogenic spread of disease with ill-defined nodules (19% to 58%), evidence of fibrosis (29%), pleural effusion (18%) [2]. The CT and HRCT findings seen in post-primary TB are numerous, varied and reflect the protean manifestation of this disease. Findings include (1) airspace consolidation of varying degrees; (2) cavitation; (3) centrilobular nodules and branching linear opacities "tree-in-bud appearance" - that reflect endobronchial spread of infection; (4) small, well-defined, randomly distributed nodules that indicate miliary or hematogenous spread of infection (5) pleural effusion; (6) lymph node enlargement with central necrosis and (7) changes of pulmonary fibrosis [7, 8]. A combination of these findings is most helpful in making a diagnosis of TB. HRCT findings in patients with TB sequel include distortion of bronchovascular structures, bronchiectasis, emphysema, and fibrotic bands indicative of prior infection with scarring [7, 8].

Determination of diagnosis and activity in patients with pulmonary tuberculosis usually depends on the detection of acid-fast bacilli in sputum smear or culture [9]. However, the sensitivity of sputum smear for AFB is 46 to 74%, and that of the sputum culture is 2 to 95% with active pulmonary disease. The alternative diagnostic modality to determine the activity of pulmonary tuberculosis has gained importance [29]. Specificity of both is more than 98% [29]. This high diagnostic value of sputum culture is comparable to or even better than the HRCT. The real value of HRCT lies in the degree of confidence that it
provides to the radiologist and the clinician in differentiating the other diseases that produce similar appearances without using invasive methods to obtain material for bacteriological examination. Moreover, the delay in obtaining result from sputum culture (6 to 8 weeks) poses a clinical problem. In this situation, HRCT can provide presumptive diagnosis of tuberculosis and empirical therapy may be started. [29].

Activity of post-primary disease cannot be accurately assessed by chest radiography. A normal chest radiograph has a high negative predictive value for the presence of active TB. However, the frequency of false-negative examinations is approximately 1% in the adult immunocompetent population and increases to 7%-15% in HIV-seropositive individuals [21, 22, 23]. Radiographic differentiation between active and inactive disease can only be reliably made on the basis of temporal evolution. Lack of radiographic change over a 4- to 6-month interval generally indicates inactive disease. However, because even long-term stability of radiographic findings may occasionally be associated with culture-positive disease, Miller and MacGregor emphasize that such findings should be described as "radiographically stable" rather than "inactive" [21,24]. HRCT may identify indicators of active disease not seen on chest radiograph [3, 7, 19].

X-ray chest signs of active TB include focal consolidation, generally apical or, less commonly, in the superior segments of the lower lobes, cavitation, miliary disease, pleural effusion, empyema and low density hilar/mediastinal lymph nodes [7]. HRCT findings in active tuberculosis include patchy unilateral or bilateral airspace consolidation, frequently peribronchial in distribution, cavitation-thick or thin walled, scattered airspace nodules, centrilobular branching structures and tree-in-bud appearance, miliary disease, pleural effusion, empyema and bronchopleural fistula, and low density hilar/mediastinal lymph nodes[7,9]. Lesions in and around the small airways appear to be the most characteristic CT feature of early active tuberculosis and may be a reliable criterion for disease activity [9].

Large areas of consolidation manifest as areas of increase attenuation with loss of underlying bronchovascular markings on HRCT scans. Consolidation is seen most commonly in the apical and posterior segments of upper lobes and superior segments of lower lobes [21].

Cavitation is the hallmark of post-primary Tuberculosis [10]. Cavities result when areas of caseation necrosis erode into the bronchial tree, expelling liquefied debris. Cavity always develops centrally within a consolidated segment [FIG 3]. Cavities were seen in 16(64%) patients of whom 12 patients had single cavity while four patients had multiple cavities. Out of all, 11 patients had thin walled cavities (less than 8mm) and three patients had thick walled cavities (more than 16mm thickness), while two patients had both thick and thin walled cavities. Thus it is interpreted that thick walled cavities are seen frequently in patients with early active tuberculosis and represents early stage of necrotizing consolidation in the early stage of cavity formation. The most common site for the cavity formation includes upper lobe in 14 patients and lower lobes in two patients-in superior segment of lower lobe-the site consistent with the preferential areas of consolidation in patients with active tuberculosis. One of the most important roles of CT is demonstrating the presence of cavitation in a patient with suspected tuberculosis. HRCT is more sensitive than plain radiography in the detection of small cavities, particularly ones in the apices, lung bases, and paramediastinal and retrocardiac locations [7]. In the complicated case in which extensive fibrosis and distortion make interpretation on radiograph difficult, the cross-sectional format of HRCT allows more definitive evaluation of superimposed cavitation [FIG 4] [17, 18]. On HRCT, cavities due to TB can be thick or thin walled and smooth or irregular. Disease activity cannot be determined on the basis of CT appearance of the cavity alone, and diagnosis must be made from results of sputum cultures. Air-fluid levels in tuberculous cavities have been reported but are regarded by many as somewhat unusual and as a strong indication of superimposed bacterial or fungal infection.

Endobronchial spread of infection also indicates activity and may occur in the absence of radiographically demonstrable cavitation. Bronchogenic spread of tuberculosis occurs from breakdown of a lobar infection or a pulmonary cavitory lesion or from rupture of an infected lymph node into the bronchus. On chest x-ray, endobronchial spread is associated with poorly defined pulmonary nodules varying between 5 and 10 mm in size [3, 7]. Of greatest importance in making an accurate HRCT diagnosis of active Tuberculosis are findings of endobronchial spread of infection. On HRCT, endobronchial spread of TB appears as poorly defined centrilobular nodules, or rosettes of nodules, 2 to 10mm in diameter, branching centrilobular opacities, appropriately described as "tree-in-bud"[FIG 5] [21]. With more extensive disease, coalescence of the centrilobular opacities occurs, resulting in focal areas of bronchopneumonia. Findings of bronchogenic spread of TB can be seen even in the absence of cavitation. Finding centrilobular nodules and a tree-in-bud appearance in HRCT is more sensitive than the chest radiograph in detection of early endobronchial disease [8].

Miliary TB results when the host's defense system is overwhelmed by massive, hematogenous dissemination of organisms Miliary TB results in diffuse small discrete nodules of 1-3mm in diameter and may be inconspicuous on plain radiographs and may take up to 6 weeks to become apparent [2,12]. CT can demonstrate miliary disease before it becomes radiographically apparent [21,
HRCT scans show poorly or well-defined 1 to 3 mm diameter nodules, random distribution and involving all the segments diffusely and associated with diffuse reticulation- intra and interlobular septal thickening [FIG 6].

This table shows that our study revealed findings similar to the other two studies. It shows that the bronchial wall thickening and tree in bud sign have the maximum sensitivity for diagnosis of active Tuberculosis. Presence of cavity is also a good sensitive indicator of active Tuberculosis, with sensitivity of 64%. Miliary nodules have poor sensitivity of active Tuberculosis, although they have high specificity.

Although "tree in bud" sign has high sensitivity for diagnosis of active Tuberculosis [13, 14], its specificity is low. Originally reported in cases of endobronchial spread of Mycobacterium tuberculosis, this pattern is now recognized as a CT manifestation of many diverse entities [15]. These entities include peripheral airway diseases such as infection (bacterial, fungal, viral, or parasitic), congenital disorders, idiopathic disorders (obliterative bronchiolitis, panbronchiolitis), aspiration or inhalation of foreign substances, immunologic disorders, and connective tissue disorders and peripheral pulmonary vascular diseases such as neoplastic pulmonary emboli [15, 21]. On CT scans, endobronchial TB typically manifests as irregular or smooth circumferential bronchial narrowing associated with mural thickening [21,25,26], although causes of this pattern are frequently radiologically indistinguishable, the presence of additional radiologic findings, along with the history and clinical presentation, can often be useful in suggesting the appropriate diagnosis[15].

The HRCT signs of active Tuberculosis are patchy unilateral or bilateral airspace consolidation, cavitition, scattered airspace nodules, tree-in-bud appearance, miliary disease, pleural effusion, empyema and bronchopleural fistula, and low density hilar/mediastinal lymph nodes [7, 9, 17].Lesions in and around the small airways appear to be the most characteristic CT feature of early active tuberculosis and may be a reliable criterion for disease activity. The most accurate HRCT features of active Tuberculosis are combination of centrilobular nodules and tree in bud appearance [8, 16].

**LIMITATIONS OF STUDY**

(1) Mediastinal lymphadenopathy which is an important indicator of the activity of the disease is not mentioned as primary aim of our study was to characterize the pulmonary parenchymal abnormalities on HRCT and to determine the activity of pulmonary TB based on HRCT findings.

**CONCLUSIONS**

Although chest radiography remains the foremost imaging technique in the evaluation of pulmonary TB, HRCT can be useful in certain circumstances and can provide important information in the diagnosis and management of the disease. HRCT is helpful in the distinction of active from inactive TB. "Tree in bud" appearance- suggestive of endobronchial spread and hence active disease was the most common and characteristic findings on HRCT scan obtained in patients in our study population. These lesions are not seen frequently on chest radiographs, and HRCT is particularly sensitive in picking up this finding. Inspite of the poor specificity of these findings, in countries with high prevalence of tuberculosis- presence of this finding along with centrilobular nodules favors the possibility of endobronchial spread of tuberculosis. HRCT is efficacious in detecting small foci of parenchymal cavitition, both in areas of confluent consolidation and in areas of dense fibrocalcitic disease associated with distortion of the underlying lung parenchyma. HRCT is better than plain chest radiograph in identification of extent of pulmonary TB, especially subtle areas of consolidation, cavitition, bronchogenic and miliary spread. HRCT is recommended when the radiographic findings are normal or inconclusive and tuberculosis is suspected clinically for the confirmation of diagnosis and determination of activity.

| Table: Comparison of HRCT findings of active Tuberculosis with previous studies |
|-----------------------------|-------------------|-------------------|-------------------|
| HRCT FINDING               | STEVEN et al (n=45) | LEE et al 16 (n=41) | OUR STUDY (n=25) |
| Centrilobular branching nodule (Tree in bud) | 32(71%) | 39(95%) | 20(80%) |
| Poorly defined 4-8 mm nodules | 5(11%) | 25(61%) | 10(40%) |
| Random distribution nodules | ---- | 1(2.5%) | 1(4%) |
| Cavity                      | 16(36%) | 24(58%) | 16(64%) |
| Consolidation               | 23(51%) | 17(41%) | 13(52%) |
| Pleural effusion            | ---- | 4(10%) | 3(12%) |
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