Assessment of the role of high resolution computed tomography in the diagnosis of suspected sputum smear negative active pulmonary TB

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Abstract  Objective: The aim of the present study is to study the utility of multi-detector CT chest in diagnosis of sputum smear negative pulmonary TB and correlation between the CT features and sputum culture results.

Patients and methods: One hundred patients suspected to have smear-negative active pulmonary TB were subjected to HRCT chest and sputum culture. At HRCT the combination of tree-in-bud, larger nodules, lobular consolidation and presence of main lesion in S1, S2 and S6 segments was ranked as rank 3 if at least three of them were present and as rank 2 if at least two of them were present. Patients with these findings mainly in the middle lobe and lingual were ranked as rank 1. The sensitivity, specificity and positive likelihood ratio for each rank was calculated.

Results: Sputum culture for AFB was positive in 60 patients. At HRCT only six out of the 28 patients ranked as I and 24 out of the 40 ranked as II and 30 out of the 32 patients ranked as III had final diagnosis of active pulmonary TB. The sensitivity, specificity and positive likelihood ratio of rank I HRCT criteria for diagnosing active pulmonary TB was 90%, 50% and 1.5%, respectively, while in rank II it was 70%, 60%, 3.2%, respectively, and in rank III it was 50%, 95%, 12.5%, respectively.

Conclusion: HRCT chest findings can help to segregate higher risk patients among those suspected of having active pulmonary TB whose smears were negative. In addition HRCT can be used to select candidate patients for further laboratory tests or bronchoscopy.

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Introduction

Despite all governmental efforts, tuberculosis (TB) remains a public health problem world-wide with almost 9 million new cases each year and almost 2 million TB related deaths world-wide [1]. Delay in diagnosis of active cases of pulmonary TB increases the burden of the disease, and this delay in diagnosis is related to many reasons: TB can present clinically and radiologically like many other diseases as pneumonia, malignancy and interstitial lung diseases, the yield of sputum smear is still low and needs few days to get the results [2]. Culture for mycobacteria TB which is the gold standard in diagnosis of TB needs up to 6 weeks for sure results, even new radiometric cultures need about 2 weeks to give results and not available in every hospital [2]. The delay in diagnosis causes delay in isolation of the patient with more chance for spread of infection and increase in severity of the disease. Because of limitations in the yield of chest X-ray in diagnosis of pulmonary TB (PTB) computed tomography (CT) scans provide more accurate information about the extent and distribution of PTB through the presence of cavities and satellite lesions that cannot be visualized on chest X-ray [3,4]. Moreover, CT can contribute to distinguish active from old infection [5,6]. There are data about the relationship between morphologic findings on high-resolution computed tomography (HRCT) and the number of AFB on sputum smears in patients with PTB. It was also shown that existence of cavities and airspace consolidation might be related to the degree of smear positivity in PTB patients [7,8]. The aim of the present study is to study the utility of multi-detector CT chest in diagnosis of sputum smear negative pulmonary TB and correlation between the CT features and sputum culture results.

 Patients and methods

Patients

One hundred patients suspected to have active pulmonary TB from the clinical features and chest X-ray findings with sputum smear negative for acid-fast bacilli (AFB) in three consecutive samples were included in this study. Patients with sputum smear positive for AFB were excluded; patients with undetermined final diagnosis were also excluded. As the centers in which the present study was done are not dealing with HIV

Fig. 1  (A) and (B) Axial HRCT showing centrilobular nodules and tree in bud appearance in the apicoposterior segment of the left upper lobe. (C) Coronal and (D) sagittal reformates showing tree in bud appearance in apicoposterior and anterior segments of left upper lobe and larger nodules in the anterior segment of the same lobe.
or immunocompromised patients these patients were not included in the study. The study was done in Chest Hospital, Ministry of Health – Kuwait and Chest Diseases Department, Faculty of medicine, Alex University – Egypt in the period from Jan. 2011 to Aug. 2012.

Methods

All patients were subjected to:

1. Detailed history taking to exclude old TB or intake of anti-tuberculous drugs, also to exclude presence of any chronic chest disease.
2. Symptom review about symptoms of pulmonary TB as: cough, hemoptysis, constitutional symptoms as loss of weight, fever, or night sweating.
3. Physical examination.
4. Tuberculin skin test (PPD).
5. Three successive samples of sputum for AFB were collected in the early morning for three successive days. If the patient was not able to give sputum spontaneously induction of sputum using hypertonic saline nebulizer in the early morning preceded by salbutamol inhalation was used to get sample for bacteriological analysis, all sputum samples were sent for direct smear examination using Ziehl–Neelsen stain and culture for mycobacterial tuberculosis using Lowenstein Jensen media and samples were incubated for 8 weeks before the final results were declared.
6. HRCT chest: all chest MDCT studies were performed with 16-MDCT scanner (Light Speed 16, GE medical systems, Milwaukee, USA). Volumetric 1.25 mm slice thickness MDCT chest acquisition was done with the patient supine in the cranial-to-caudal direction during a single breath-hold. From the volumetric CT data set a series of contiguous thin-collimation 1.25 mm axial HRCT images were reconstructed using high spatial resolution algorithm [9]. HRCT scans were assessed for the presence of centri-lobular nodules, tree in bud pattern indicative of endobronchial spread of infection, larger nodules, masses, lobular consolidations, cavities, bronchoceles, ground glass opacities and mediastinal lymph.
node enlargement. The distribution of these CT findings was also assessed for the presence of a main lesion in S1, S2 and S6 lung segments. We used the criteria designed by Nakanishi et al. [10] to predict risk for active pulmonary TB based on the combination of HRCT findings and patients were ranked from 0 to 3 (Table 1). Two radiologists record each HRCT finding and decide the rank.

### Statistical analysis

The data were collected and tabulated. Statistical analysis was done using Statistical Package for Social Sciences (SPSS/ version 17) software, statistical significance is calculated when $p < 0.05$. HRCT findings significantly associated with increased risk of pulmonary TB were selected by multiple logistic regression. The combination of HRCT findings that were significantly associated with increased risk of pulmonary TB were determined using stepwise regression. Inter-observer variation for each finding was analyzed using the $k$ statistics and inter-observer variation in the ranking of each patient was examined using a weighted $k$ statistics.

### Results

The mean age of the patients were $34.1 \pm 8.5$ years with the main affection in the age group between 30 and 40 years, there was predominance of male gender (70% of the patients were males), constitutional symptoms as fever, loss of weight, night sweating were present in 95% of patients while specific chest symptoms as cough, expectoration, chest pain, dyspnea and haemoptysis were present in 90% of patients. PPD skin test was positive (more than 10 mm) in 85% of patients, sputum smear for AFB was negative in all patients. In the present study final diagnosis of pulmonary TB was dependent on AFB culture result which is the gold standard for diagnosis of pulmonary tuberculosis, culture was positive in 60% of patients (Table 2).

According to the rank obtained by CT features patients were divided into three groups:

- At HRCT only six out of the 28 patients ranked as I had final diagnosis of active pulmonary TB while in the remaining patients six had non-tuberculous mycobacterium infection (NTM), 12 had bronchopneumonia, two had cryptogenic organizing pneumonia (COP) and two had allergic broncho-pulmonary aspirgillosis (ABPA).
- The 40 rank II patients had final diagnosis of active pulmonary TB in 24 patients, NTM in two patients, bronchopneumonia in six patients, COP in six patients and ABPA in two patients.
- Thirty out of the 32 patients ranked as III had final diagnosis of active pulmonary TB while in the remaining two patients one had final diagnosis of bronchopneumonia and one had final diagnosis of COP (Table 3).

- The sensitivity, specificity and positive likelihood ratio of rank I HRCT criteria for diagnosing active pulmonary TB was 90%, 50% and 1.5%, respectively, while in rank II it was 70%, 60%, 3.2%, respectively, and in rank III it was 50%, 95%, 12.5%, respectively (Table 4). Figs. 1–3 demonstrates some of the CT features in our patients.

### Table 1  Ranking of patients according to HRCT features.

<table>
<thead>
<tr>
<th>Rank number</th>
<th>HRCT findings required for diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 (Highly suspect pulmonary TB)</td>
<td>Presence of at least three of the following findings: Main lesion in S1, S2 or S6 segments Tree in bud appearance Lobular consolidations Larger nodules</td>
</tr>
<tr>
<td>2 (Probable pulmonary TB)</td>
<td>Presence of at least two of the following findings: Main lesion in S1, S2 or S6 segments Tree in bud appearance Lobular consolidations Larger nodules</td>
</tr>
<tr>
<td>1 (Non-specific or difficult to differentiate from other disease)</td>
<td>Lesions located mainly in the middle lobe or lingular segment Findings indicative of other specific disease</td>
</tr>
<tr>
<td>0 (Other suspected disease)</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2  Demographic and clinical criteria of the patients.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>34.1 ± 8.5</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>70/30</td>
</tr>
<tr>
<td>Constitutional symptoms</td>
<td>95/100</td>
</tr>
<tr>
<td>Chest symptoms</td>
<td>90/100</td>
</tr>
<tr>
<td>+ve PPD skin test</td>
<td>85/100</td>
</tr>
<tr>
<td>−ve sputum smear for AFB</td>
<td>100/100</td>
</tr>
<tr>
<td>+ve sputum culture for AFB</td>
<td>60/100</td>
</tr>
</tbody>
</table>

### Table 3  Final diagnosis of the patients.

<table>
<thead>
<tr>
<th>Final diagnosis</th>
<th>HRCT criteria</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary TB</td>
<td>Rank I 6</td>
<td>Rank II 24</td>
</tr>
<tr>
<td>NTM</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Bronchopneumonia</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>COP</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>ABPA</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>40</td>
</tr>
</tbody>
</table>
Discussion

Pulmonary TB can mimic a lot of diseases in clinical and laboratory findings, reliability on sputum smear has many limitations as sputum may be false negative if the disease is mild, decreased load of bacilli in the sputum sample, patient is giving saliva instead of sputum. The culture which is the gold standard for diagnosis of TB can take several weeks. Patients with suspected pulmonary TB whose sputum smears are negative for AFB cause an important medical problem in daily medical practice that is difficult to analyze. Clinicians have some difficulties about whether antituberculous therapy should be initiated for these patients. Prompt initiation of antituberculous therapy for pulmonary TB is an important issue both because of its benefits for the patient and for control of the disease. Since smear-negative patients have smaller mycobacterium burden and I have different clinical and radiological findings, it may not be appropriate to use criteria for smear-positive disease to predict risk in the patients with smear negative pulmonary TB.[5]

The value of CT chest in diagnosing pulmonary TB was studied by many authors: Lee KS and colleagues in 1996[11] studied the utility of CT in the evaluation of TB among patients without AIDS, they succeeded to predict presence of TB in 133 out of 146 patients proved to have TB and to exclude TB in 32 out of 42 patients proved to have other diseases, they concluded that CT can be helpful in the diagnosis of pulmonary tuberculosis in most cases. On the basis of CT findings, distinction of active from inactive disease can be made in most cases. Lee SW and colleagues in 2010[12] studied the use of CT in investigation of TB out break and with the use of CT they could diagnose active TB in nine patients who had normal chest X-ray and they concluded that adding CT to routine investigation of TB outbreak may be helpful in differentiating active TB from Latent TB infection.

HRCT findings in patients with active pulmonary TB include: micronodules, tree in bud appearance, nodules, airspace consolidation, ground glass opacities and cavities[13]. Matsuoka et al. [7] investigate the relationship between computed tomography (CT) findings in patients with active pulmonary tuberculosis (PTB) and number of the acid-fast-bacilli (AFB) on sputum smears and they found that the frequency of micronodules and nodules did not significantly differ among the smear positive and smear negative groups. In contrast, the frequency of consolidation and cavitation increased with the number of AFB. In another study by Kosaka and his colleagues in 2005[8] they found that air space consolidation, cavitation and ground glass opacities occurred significantly more frequently in the smear positive than in the smear negative active PTB patients while the frequency of centrilobular nodules (micronodules) did not differ between the two groups.

Tozkoparan et al. [5] found that HRCT had good diagnostic value in detecting activity of smear negative pulmonary tuberculosis. In their series the sensitivity, specificity, positive predictive value and accuracy of HRCT in detecting disease activity were 88%, 88%, 92% and 88%, respectively. On the other hand in the study of Lee et al. [14] the sensitivity, specificity, positive predictive value and positive likelihood ratio of HRCT in the diagnosis of smear negative pulmonary tuberculosis were 80%, 70%, 71% and 2.71%. They concluded that HRCT alone had relatively good sensitivity but the low positive predictive value hampered the decision of starting anti-TB medication. However in the previous two studies, the HRCT diagnosis of active pulmonary TB was by consensus.

Nakanishi and his colleagues in 2010[10] investigated whether or not HRCT can predict risk for sputum smear-negative pulmonary TB. They ranked the patients from 1 to 3 according to a combination of HRCT findings that were significantly associated with increased risk of pulmonary TB that include: large nodules, tree in bud appearance, lobular consolidation and presence of main lesion in S1, S2 and S6 segments. They found that this ranking was reliable enough to predict the risk of pulmonary TB with good reproducibility. In their series rank 2 had sensitivity, specificity and positive likelihood ratio of 85%, 74% and 3.27% while rank 3 had sensitivity, specificity and positive likelihood ratio of 40%, 97% and 13.3%. These results are confirmed by the results of our study. In the present study the sensitivity, specificity and positive likelihood ratio of rank 2 were 81%, 70% and 3.1% while sensitivity, specificity and positive likelihood ratio of rank 3 were 48%, 91% and 12.5%.

The main role of HRCT for diagnosing pulmonary TB is the selection of probable or highly suspected pulmonary TB with pulmonary infiltrates of unknown origin and with negative sputum smears[10]. In the present study 24 out of the 40 ranked at HRCT as rank II and 30 out of the 32 rank III patients had final diagnosis of active pulmonary TB.

In conclusion in HRCT chest findings can help to segregate higher risk patients among those suspected of having active pulmonary TB whose smears were negative. In addition HRCT can be used to select candidate patients for further laboratory tests or bronchoscopy.

References


Table 4 Sensitivity, specificity and positive likelihood ratio of different HRCT ranks.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive likelihood ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>90</td>
<td>50</td>
<td>1.5</td>
</tr>
<tr>
<td>II</td>
<td>79</td>
<td>70</td>
<td>3.1</td>
</tr>
<tr>
<td>III</td>
<td>48</td>
<td>91</td>
<td>12.5</td>
</tr>
</tbody>
</table>


