Radiologic manifestations of pulmonary tuberculosis in patients of intensive care units

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ABSTRACT

Background: Tuberculosis (TB) is a serpent disease with various pulmonary manifestations, and timely diagnosis of the disease is paramount, since delayed treatment is associated with severe morbidity, particularly in intensive care units (ICU). Therefore, it is imperative that intensivists understand the typical distribution, patterns, and imaging manifestations of TB.

Aim: To describe different manifestations of pulmonary TB in patients in the ICU.

Methods: In a retrospective study, all patients with a clinical and a laboratory-confirmed diagnosis of TB who were admitted to the ICU were entered in the study. All patients had a confirmatory laboratory diagnosis of TB including positive smears. The patterns of parenchymal lesions, involved segments and presence of cavity, bronchiectasis and bronchogenic spread of the lesions with computed tomography (CT) and chest/X-ray (CXR) were recorded and analyzed.

Results: Data of 146 patients with TB were entered in the study. The most common finding in CT was acute respiratory distress syndrome (ARDS)-like radiologic manifestations (17.1%), followed by parenchymal nodular infiltration (13.6%) and cavitation (10.9%), consolidation (10.2%), interstitial involvement (9.5%), calcified parenchymal mass (8.3%), ground-glass opacities (7.5%), and pleural effusion or thickening (6.9%). Radiologic evidence of lymphadenopathy was seen in up to 43% of adults. Miliary TB was observed in 2.3% of patients, mostly in those older than 60 years of age. ARDS-like (64.5%) manifestations on CT and miliary TB (85.5%) had the highest mortality rates among other pulmonary manifestations.

Conclusion: ARDS, interstitial involvement, and Parenchymal nodular infiltration are the most common manifestations of pulmonary TB. Various features of TB in ICU patients could be misleading for intensivists.

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Introduction

Tuberculosis (TB) remains a major health problem globally [1], and there has also been an increase in the global prevalence of TB, with a rate of increase of approximately 1.1% per year [2,3]. This increase has been seen prominently in Africa and Asia. Its prevalence also has increased in Europe and North America due to HIV and immigrations [4,5]. In addition, drug-resistant strains of TB have emerged. Early diagnosis promotes effective treatment and is, therefore, essential. Patients in intensive care units (ICU) could have a significantly higher incidence of TB than the general population due to the fact that many patients with TB end up in the ICU and are also more likely to be infected with multidrug-resistant TB (MDR-TB) [6].

Pulmonary tuberculosis has been divided into active, inactive, and latent TB [7], with primary TB being considered a disease of childhood and secondary TB a disease of adulthood. However, a large number of unexposed adult populations are at risk for contracting primary TB. It can sometimes be difficult to differentiate between primary and secondary TB both clinically and radiologically, since their features can overlap. Imaging is of paramount importance in the diagnosis of TB, but there are not many reports on TB imaging in ICU patients. Chest radiography remains the first choice of initial evaluation of the patients with TB. Chest radiographs appear useful in ruling out pulmonary TB in hospitals, but their low specificity precludes ruling in TB [8].

The aim of the current study is to show various manifestations of pulmonary TB in patients in the ICU.

Methods

The present study was reviewed and approved by the University Review Board and Ethics Committee and was performed in accordance with the ethical standards laid down in an appropriate version of the 2000 Declaration of Helsinki. Information about the trial was given comprehensively, both orally and in written form, to the patients. All patients gave their written informed consents prior to their inclusion in the study.

Patient selection and study design

In a retrospective study, all patients with a clinical and laboratory confirmed diagnosis of TB admitted to the ICU were enrolled in the study. All patients had confirmatory laboratory diagnosis of TB including three positive smears.

All chest X-rays (CXR) and computed tomography (CT) of patients were collected and were recorded in a registry program. The patterns of parenchymal lesion, involved segments and presence of cavity, bronchiectasis and bronchogenic spread of the lesions with CT and CXR were recorded and analyzed.

Tuberculosis diagnosis

Active TB was defined if: (1) patient specimens showed positive acid-fast staining, or Mycobacterium tuberculosis (MTB) was cultured; or (2) patient data met the definition of a clinical case of TB according to the World Health Organization (WHO). For clinical cases of TB, radiographic lesions compatible with active TB on CT scans were mandatory. Active pulmonary TB was defined as the presence of cavities, branching linear opacity, or multiple non-calciﬁed nodules on CT scan. However, lesions that appeared mainly as calcifed nodules or ﬁbrotic bands were excluded from the diagnosis of active TB. MDR-TB is deﬁned as resistance to at least isoniazid and rifampin.

Acid-fast smear and mycobacterial culture of sputum

Samples were obtained from sputum or tracheal aspiration by bronchoalveolar lavage (BAL) and sent to the pathology lab for acid fast bacillus (AFB) (3 times). For negative results, BAL was performed for better results.

Chest radiology

For CXR, posteroanterior views of the chest in full inspiration were obtained using a digital imaging system and the results were interpreted by a radiologist. For patients admitted to the ICU under mechanical ventilation, portable anterior-posterior CXRs were obtained.

All lung CT scans were performed with thin-section CT scans with 1-mm collimation at 10-mm intervals without contrast through the thorax at end inspiration. The scans were reconstructed with bone algorithm without targeting. The scans were photographed with both mediastinal (window width [WW], 400 Hounsﬁeld units; window length [WL], 30 Hounsﬁeld units) and lung (WW, 1500; WL, −700) windows.

CT scans were assessed prospectively by two different radiologists. The observer radiologists were blinded to clinical history and chest radiographic findings except for the age and sex of the patients. The observers were also unaware that the patients were being assessed for suspicion of pulmonary TB. Radiologists recorded predominant pattern and distribution of parenchymal lesions, the presence or absence of bronchogenic spread of pulmonary abnormalities, and findings of sequelae of previous TB. Patterns of abnormalities were subclassiﬁed as being areas of acute respiratory distress syndrome (ARDS) like bilateral inﬁltration, micro-nodules (<10 mm in diameter), nodules (1–2 cm in diameter), masses (>2 cm in diameter), cavitation formation, alveolar or collapse consolidation, atelectasis, emphysematous bulla, calciﬁed parenchymal masses, interstitial involvement, ground-glass attenuation, Parenchymal nodular inﬁltration, pleural effusion and thickening, pericardial effusion, prominent pulmonary artery, adenopathies and any other abnormal ﬁndings. Distribution of abnormalities was recorded to be present in each segment. Micro-nodules were further subclassiﬁed as centrilobular (including any abnormality of the branching linear structure), acinar, miliary, or random in distribution.

Statistical analysis

Statistical calculations were conducted using SPSS 18 (Chicago, IL, USA). The parametric variables were presented...
as mean ± SD and were analyzed by student t-test or ANOVA and Pearson correlation test as appropriate. Statistical analysis was performed using Chi-Square or Mann–Whitney U-test and Spearman correlation coefficients for non-parametric samples. \( p < 0.05 \) was considered as statistically significant. Sample size was estimated using sample size calculator software with 95% confidence interval and \( p < 0.05 \). The mortality rate was estimated based on the total number of deaths in the period of patient admission to the ICU.

**Results**

**Demographic characteristics**

A total of 146 patients were enrolled in the present study, and radiologic manifestations of pulmonary TB were studied. The mean age of the patients was 34.5 ± 21.32 years. Sixty-five (44.5%) patients were female and 81 (55.5%) were male. Ninety-nine (68%) patients were current smokers. All participants were negative for HIV. One hundred and two (69.5%) of the participants had a previous history of TB. Out of 146 patients, 27 patients (18.4%) were misdiagnosed and treated as atypical pneumonia rather than as active TB.

**Pulmonary manifestation in CT**

Pulmonary manifestations of TB diagnosed and confirmed by CT in the total number of patients (146) are classified in Table 2. The most common finding in CT of these patients was ARDS-like radiologic manifestations (17.1%), followed by parenchymal nodular infiltration (13.6%) and cavitation (10.9%), consolidation (10.2%), interstitial involvement (9.5%), calcified parenchymal mass (8.3%), ground-glass opacities (7.5%), and pleural effusion or thickening (6.9%). Radiographic evidence of lymphadenopathy was seen in up to 43% of adults. Miliary TB was observed in 2.3% of patients, mostly in those older than 60 years of age. In 73% of cases of parenchymal infiltration, more than one pulmonary segment was involved (see Table 1).

**Chest-X-ray and high-resolution computed tomography scan of chest**

From 146 patients enrolled in the study, only 34 (23.5%) participants had abnormal lesions on CXR suggestive of TB. The remaining 112 (76.5%) patients had non-diagnostic CXR and only had an abnormality in CT patients. In patients with diagnostic abnormalities on CXR lesions, consolidations (26%) was the most frequently seen feature, while in patients with non-diagnostic CXR, ARDS (16.9%) and parenchymal nodular infiltration (16.1%) were the most frequently observed features. However, all 146 patients had abnormal CT suggestive of TB. The interpretation of the CT scan results showed almost perfect agreement between the two separate radiologists for the presence of abnormal TB lesions.

From the 146 patients, 102 (69.5%) patients had a TB diagnosis before admission to the ICU. The remaining 44 (30.5%) patients were diagnosed with TB after admission to the ICU. In patients whose diagnosis was delayed until admission to the ICU (44 cases), the most common findings were ARDS (31.5%), parenchymal nodular infiltration (17.5%), calcified parenchymal mass (15.5%), and interstitial involvement (12.5%) (Fig. 1). ARDS-like radiologic manifestations were significantly higher in radiologic imaging of ICU-diagnosed patients than pre-ICU diagnosed (31.5% vs. 21.5%) \( (p = 0.017) \); while cavitations were more often seen in radiologic imaging of pre-ICU diagnosed compared with ICU diagnosed patients (23% vs. 4.5%) \( (p = 0.025) \).

**Mortality outcome**

Mortality outcome was determined in patients based on type of radiologic pulmonary manifestations. Apparently, ARDS (64.5%) and miliary TB (85.5%) had the highest mortality rate among other pulmonary manifestations. Interestingly, patients with pleural effusion or thickening had the lowest mortality rate (14.9%) among others. In regression analysis, only delayed ICU diagnosis of TB were risk factors for increased mortality rate compared with the ones who were diagnosed with TB prior to admission to the ICU (RR 1.65, 95% CI 1.05–2.55).

**Table 1 – Frequency of pulmonary manifestations in computed tomography (CT); duration of ICU stay; and mortality of 146 patients admitted to the intensive care unit (ICU).**

<table>
<thead>
<tr>
<th>CT findings</th>
<th>Patients</th>
<th>Duration ICU stay</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARDS</td>
<td>25 (17.1%)</td>
<td>14.2 ± 4.7</td>
<td>64.5</td>
</tr>
<tr>
<td>Parenchymal nodular infiltration</td>
<td>20 (13.6%)</td>
<td>7.8 ± 4.3</td>
<td>25.6</td>
</tr>
<tr>
<td>Cavitation</td>
<td>16 (10.9%)</td>
<td>8.7 ± 5.4</td>
<td>24.6</td>
</tr>
<tr>
<td>Consolidation</td>
<td>15 (10.2%)</td>
<td>12.3 ± 6.3</td>
<td>35.2</td>
</tr>
<tr>
<td>Interstitial involvement</td>
<td>14 (9.5%)</td>
<td>9.7 ± 6.3</td>
<td>30.5</td>
</tr>
<tr>
<td>Calcified parenchymal mass</td>
<td>12 (8.3%)</td>
<td>11.5 ± 7.7</td>
<td>26.7</td>
</tr>
<tr>
<td>Ground-glass opacities</td>
<td>11 (7.5%)</td>
<td>11.8 ± 4.8</td>
<td>33.9</td>
</tr>
<tr>
<td>Pleural effusion or thickening</td>
<td>10 (6.9%)</td>
<td>15.3 ± 5.5</td>
<td>14.9</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>8 (5.5%)</td>
<td>23.6 ± 11.5</td>
<td>36.7</td>
</tr>
<tr>
<td>Emphysematous bulla</td>
<td>6 (4.2%)</td>
<td>8.9 ± 6.1</td>
<td>18.8</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>4 (2.7%)</td>
<td>14.4 ± 7.2</td>
<td>24.3</td>
</tr>
<tr>
<td>Miliary TB</td>
<td>3 (2.1%)</td>
<td>22.5 ± 8.2</td>
<td>85.5</td>
</tr>
<tr>
<td>Others</td>
<td>2 (1.4%)</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>
95% CI: 1.28–3.27, \( p = 0.028 \)). In addition, miliary TB was also a risk factor for increased mortality rates compared with the non-miliary TB patients in the ICU (RR 1.95, 95% CI: 1.12–4.35, \( p = 0.015 \)).

Pulmonary manifestation in MDR-TB

Thirty-two patients were diagnosed with MDR TB among the patients in the ICU. Pulmonary manifestation of MDR-TB patients in the ICU is depicted in Fig. 2. Overall, ARDS-like pulmonary involvement was significantly higher in MDR-TB than non-MDR patients (39.5% vs. 21%) (\( p = 0.01 \)). However, consolidations (\( p = 0.033 \)), cavitary (\( p = 0.012 \)) and calcified (\( p = 0.024 \)) lesions were significantly higher in non-MDR compared with MDR patients (Fig. 2). Interstitial and ground-glass involvements were higher in MDR patients compared with non-MDR patients (\( p > 0.05 \)) (Chi-square test).

Discussion

Radiologic work-ups could be helpful in the diagnosis of pulmonary TB in most cases. This article reviews the CT features of pulmonary TB in critically ill patients admitted to the ICU. CT forms the mainstay of cross-sectional imaging in pulmonary TB. On the basis of CT findings, distinction of TB from other disguising features can be made in most cases.

Critically ill patients in the ICU require rapid diagnostic procedures for TB that is both sensitive and specific so that appropriate management decisions can be made promptly [9]. The study of TB pulmonary manifestations showed that CT scanning could substantially increase diagnosing ability of active TB if considered early. Only 23.5% of participants had abnormal lesions on CXR suggestive of TB. The remaining 112 (76.5%) patients had non-diagnostic CXR; however, all 112 patients had abnormal CT suggestive of TB lesions that were suggestive of active pulmonary TB on CT scan. Many of these patients had been misdiagnosed or treated as atypical pneumonia rather than as active TB. LTBI is usually defined as a positive tuberculin test result with normal plain radiography findings [10]; therefore, the results of the present investigation showed that none of these patients admitted to the ICU had LTBI. In fact, patients with non-diagnostic CXR were active TB, but only with abnormal CT findings. In Fig. 1 data is presented on a number of patients that had diagnostic

Table 2 – Pulmonary manifestations on CT when CXR had diagnostic abnormalities versus non-diagnostic findings.

<table>
<thead>
<tr>
<th>Pulmonary manifestation</th>
<th>Diagnostic CXR (34)</th>
<th>Non-diagnostic CXR (112)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consolidation</td>
<td>9 (26%)</td>
<td>14 (11.5%)</td>
</tr>
<tr>
<td>ARDS</td>
<td>3 (8.8%)</td>
<td>19 (16.9%)</td>
</tr>
<tr>
<td>Parenchymal nodular infiltration</td>
<td>2 (5.8%)</td>
<td>18 (16.1%)</td>
</tr>
<tr>
<td>Cavitation</td>
<td>8 (23%)</td>
<td>15 (13.3%)</td>
</tr>
<tr>
<td>Interstitial involvement</td>
<td>5 (15%)</td>
<td>13 (11.7%)</td>
</tr>
<tr>
<td>Calcified parenchymal mass</td>
<td>3 (8.8%)</td>
<td>15 (13.4%)</td>
</tr>
<tr>
<td>Ground-glass opacities</td>
<td>3 (8.8%)</td>
<td>13 (11.6%)</td>
</tr>
<tr>
<td>Others</td>
<td>1 (3%)</td>
<td>5 (4.5%)</td>
</tr>
</tbody>
</table>

Fig. 1 – Pulmonary manifestations of TB patients in CT scans when diagnosed before (pre-ICU diagnosed) and after admission to the ICU (ICU diagnosed). ARDS: acute respiratory distress syndrome; parenchymal nodule: parenchymal nodular infiltration; calcified: calcified parenchymal mass; interstitial: interstitial involvement.

Fig. 2 – Pulmonary manifestation in multi-drug resistant (MDR) and non-MDR Tuberculosis (* \( p < 0.05 \), Chi-square test). ARDS: acute respiratory distress syndrome; parenchymal nodule: parenchymal nodular infiltration; calcified: calcified parenchymal mass; interstitial: interstitial involvement.
lesions in CXR or CT. Although pulmonary TB is associated with CXR abnormalities [11], the lesions are not specific, and their interpretation depends on factors related to the clinicians. Furthermore, there is a report of negative plain radiograph and positive bacteriology of mycobacterium. Therefore, the usefulness of chest radiography was questioned in the early detection of active TB in the ICU. In addition, the low sensitivity of CXR to detect TB lesions has been suggested previously [12]. CXRs are also associated with concerns inherent to their use (sensitivity and specificity of 72% and 57%) [13] and several limitations in the diagnosis of TB as described in the present study [14]. On the other hand, CXRs are still the first imaging tool in the ICU due to low cost and availability [15]. Therefore, it is more satisfactory if intensivist's request a CT scan (depending on patients' conditions) if clinical suspect is high despite CXR non-diagnostic findings.

Various TB pulmonary manifestations should be a matter of concern in the ICU. The present study showed that, surprisingly, ARDS, parenchymal nodular infiltration and consolidations are most commonly found in TB patients in the ICU. Previous reports have shown that tree-in-bud patterns were the most characteristic CT findings to predict active disease in patients with pulmonary TB [16]. When patients were categorized based on diagnosis time (pre- and post-ICU), then an ARDS-like pattern was the most likely feature that intensivists may encounter in first-time diagnosed TB in the ICU. It is highly unlikely that cavitary lesions remain undiagnosed until admitted to the ICU. It is prudent to request TB diagnostic exams for any patient with an ARDS-like pattern in the ICU if clinical suspicion of infectious agents is high.

The most common finding in CT of these patients was ARDS-like bilateral diffuse infiltration. A similar study by Balkema et al. [17] showed that the primary reason for ICU admission was acute respiratory failure in two thirds of patients. TB was the sole cause of acute respiratory failure in 74% of patients, most of them due to massive hemoptysis. However, the most common radiologic finding in their study was diffuse bronchopneumonia. This difference is a reflection of the differences in the study design. The present study was a retrospective study on TB patients admitted to the ICU which was a prospective observational in their study, and the difference in admission criteria could cause this variability. In the Balkema study, mortality rates of acute respiratory failure secondary to TB are much higher than those of patients with respiratory failure due to non-tuberculous pneumonia. The present study showed similar results that ARDS (64.5%) and miliary TB (85.5%) had the highest mortality rates.

In conclusion, the clinical and radiologic features of TB may mimic those of many other diseases. A high degree of suspicion is required, especially in high-risk populations. Although in many cases biopsy or culture specimens are still needed to yield the definitive diagnosis, it is important for radiologists and clinicians alike to understand the spectrum of imaging features of TB to aid in making an early diagnosis. Despite these limitations, there were a number of important strengths. Considering that the Chronic Respiratory Disease Research Center (CRDRC) is one of the largest centers for TB patients, contributed radiology information on a large number of individual patients admitted to the ICU allowed the present study to comprise a detailed and comprehensive analysis.

This study provides a thorough review of possible radiologic scenarios of TB-involved patients in the ICU and will enable clinicians to predict TB involvement and start targeted management earlier.

Conflict of interest
None.

REFERENCES


