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Pulmonary Changes of Pleural TB
Up-to-Date CT Imaging

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BACKGROUND: The objective of this study was to evaluate pulmonary abnormalities of pleural TB by CT scanning and to determine CT scan findings for the development of the paradoxical response (PR).

METHODS: CT scans were performed for 349 patients with pleural TB (between 2008 and 2013). We excluded 34 patients with coexisting pulmonary disease (n = 13) or a totally collapsed lung (n = 21). We analyzed CT scans focusing on pulmonary abnormalities such as the presence of consolidation, cavitation, interlobular septal thickening, and micronodules and their distribution. In addition, we recorded the development of PR during follow-up and statistically analyzed differences in clinical and CT scan findings between patients with and without PR.

RESULTS: A total of 270 of 315 patients (86%) had pulmonary abnormalities. Common CT scan findings were micronodules (n = 209 [77%]), interlobular septal thickening (n = 202 [75%]), and consolidation (n = 120 [44%]). Cavitation was seen in 49 patients (18%). Among 209 with micronodules, the nodules were in the subpleural region (n = 146 [70%]), peribronchovascular interstitium (n = 113 [54%]), and centrilobular region (n = 64 [31%]). PR occurred in 81 patients (26%), and patients with PR tended to be young, male, and without underlying disease ($P < .05$ by t test, Pearson χ^2 test). Subpleural micronodules were more common in patients with PR than in those without PR (Pearson χ^2, $P = .025$).

CONCLUSIONS: Pulmonary abnormalities are very common in pleural TB. The most common CT scan findings were micronodules in the subpleural and peribronchovascular interstitium and interlobular septal thickening, suggesting the lymphatic spread of TB. In addition, PR is not rare in patients with pleural TB, especially in young, previously healthy, male patients who show subpleural nodules on initial CT scans. CHEST 2014; 146(6):1604-1611

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ABBREVIATIONS: ADA = adenosine deaminase; AFB = acid-fast bacilli; LAP = lymphadenopathy; MDCT = multidetector CT; PCR = polymerase chain reaction; PR = paradoxical response

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Pleural TB develops from pulmonary lesions that form a small subpleural TB focus. Breakdown of these foci release their contents into the pleural space, which is followed by acute inflammation and exudation caused by a delayed hypersensitivity reaction. Operative specimens reveal that subpleural TB lesions are observed frequently in patients with pleural TB.[1-3] However, the subpleural TB focus is seldom visualized on imaging, even though it plays a major role in the development of pleural TB. Most previous studies on CT scan findings of pulmonary changes of pleural TB have focused on bronchocentric lesions such as centrilobular nodules, a tree-in-bud appearance, and consolidation, because these are the most characteristic findings of active pulmonary TB.[4,5] However, there are no reports describing subpleural nodules on CT scans as active TB lesions in pleural TB. Moreover, the subpleural nodules have additional clinical significance because they are thought to be responsible for the development of paradoxical response (PR).

Pleural TB can manifest as a primary disease from recent infection or as a reactivated disease from remote infection. TB pleurisy due to reactivation is more likely to be associated with radiographic parenchymal infiltrations. However, it is difficult to determine with absolute certainty whether individual patients have TB caused by recent or remote infection, because definitive evidence of the exact time of TB infection is usually not available.[5] In addition, classification of pleural TB into primary and reactivation forms has no clinical implication.[6] Therefore, we analyzed all the parenchymal changes of pleural TB with recent CT scanners regardless of the form, after discarding preconceptions about CT scan findings of active pulmonary TB. In addition, combined pulmonary changes on CT scan can be helpful in the differentiation of pleural TB from other pleural disease. We also examined the prevalence of PR and compared the characteristic clinical and CT scan findings of patients who showed PR during follow-up with those of patients who did not develop PR.

Materials and Methods

Patients

We selected patients with pleural TB who underwent CT scans at the time of diagnosis between May 2008 and September 2013. We excluded patients with other coexisting pulmonary disease or a large amount of pleural effusion resulting in total collapse of the lung. We retrospectively reviewed clinical features and pleural effusion parameters, including differential cell count and levels of lactate dehydrogenase and adenosine deaminase (ADA). We analyzed the CT scan findings of all patients and checked for the development of PR during follow-up. Patients were divided into two groups according to the development of PR, and clinical and CT scan findings were compared between the PR and non-PR groups.

Diagnosis of Pleural TB and PR

The diagnosis of pleural TB was based on a lymphocyte-prominent ($>50\%$) effusion that met Light's criteria for exudative effusions, with demonstration of an elevated ADA level of >40 IU/L, positive results for acid-fast bacilli (AFB) staining, growth of *Mycobacterium tuberculosis* from pleural fluid or sputum, positive results for TB in a polymerase chain reaction (PCR) assay, the presence of classic caseating granulomatous inflammation in the pleural tissue, or a successful response to anti-TB therapy.[5,7]

We defined PR as a radiographic worsening of pleural TB in patients who initially improved with anti-TB treatment; in these patients, the onset of PR must have occurred after the initiation of treatment, without evidence of positive AFB results in a sputum study. We determined that radiographic findings were worsened if pleural effusions increased or new pulmonary lesions developed. The time to development of PR was defined as the interval between the initiation of anti-TB treatment and the onset of PR, as defined previously. Patients who developed PR within 14 days after initiation of anti-TB treatment were excluded from the PR group.[7,8]

CT Scanning

CT scans were obtained with two CT scanners, LightSpeed VCT (General Electric Medical Systems) and Somatom Definition Flash (Siemens Heathcare), with or without IV administration of contrast medium (100 mL at rate of 2.0-2.5 mL/s). Attending physicians requested a CT scan with contrast enhancement if chest radiographs led them to suspect a malignancy or TB lymphadenitis. Scanning parameters included a 130-mA tube current, 120-kV tube voltage, 128×0.6-mm collimation, and pitch of 1.2. All images were reconstructed into axial images with a 5-mm slice thickness at 5-mm intervals and coronal images with a 3-mm slice thickness.

CT Scan Analysis

All CT scans and medical records were reviewed retrospectively by two chest radiologists (J. M. K. and H. J. P.) with 4 and 11 years of experience, respectively. Interpretation was based on a consensus between the two radiologists. CT scans obtained to assess pleural effusion were analyzed with specific attention to pulmonary findings, such as micronodules, consolidation, and cavitation. A micronodule was defined as a small rounded opacity with a diameter <7 mm and was classified by distribution as centrilobular, perilymphatic (subpleural or peribronchovascular), or random.[9] The presence of interlobular septal thickening and clustered or coalescent micronodules showing a cluster or galaxy sign was included in our analysis.[10] We checked for the presence of lymphadenopathy (LAP) and extrathoracic TB involvement. Findings of old scar lesions such as bronchiectasis, fibrotic linear opacities, and ciccatricial emphysema were excluded from our CT scan analysis.

Statistical Analysis

We compared clinical and CT scan findings between the PR group and the non-PR group. All tests of significance were two-sided. Univariate comparisons between the PR and the non-PR group were performed using the Pearson χ^2 test or Fisher exact test for categorical variables and the Student t test for continuous variables. A P value $<.05$ was considered statistically significant.