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Clinical/Pathologic Correlations in 553 Patients With Primary Centrilobular Findings on High-Resolution CT Scan of the Thorax*

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Background: **Clinical/pathologic correlations in patients with high-resolution CT (HRCT) scan findings presenting with two patterns of centrilobular opacity remain unclear.**
Methods: **Chest HRCT scans in 553 patients with predominant centrilobular opacities or preferential centrilobular disease were retrospectively evaluated. In 141 patients who underwent biopsy, CT scan images were compared with actual specimens.**
Results: **Centrilobular nodules with a tree-in-bud appearance and bronchial wall thickening were observed in most patients who were carriers of human T-lymphotropic virus type 1 (88 patients and 57 of 99 patients, respectively), *Mycoplasma pneumoniae* pneumonia (44 patients and 45 of 52 patients, respectively), *Mycobacterium tuberculosis* (38 patients and 37 of 52 patients, respectively), *Mycobacterium avium-intracellulare complex* (22 patients and 27 of 37 patients, respectively), *Mycobacterium kansasii* (27 patients and 19 of 33 patients, respectively), allergic bronchopulmonary aspergillosis (6 patients and 7 of 9 patients, respectively), diffuse panbronchiolitis (12 patients and 10 of 12 patients, respectively), and diffuse aspiration bronchiolitis (12 patients and 12 of 13 patients, respectively). On the other hand, ill-defined centrilobular nodules of ground-glass attenuation were frequently seen in patients with subacute hypersensitivity pneumonitis (all 15 patients), metastatic calcification (all 4 patients), Churg-Strauss syndrome (4 of 12 patients), microscopic polyangiitis (27 of 48 patients), systemic lupus erythematosus (7 of 8 patients), and respiratory bronchiolitis-associated interstitial lung disease (all 8 patients). Pathologically, the tree-in-bud appearance correlated well with the plugging of small airways with mucous, pus, or fluid; dilated bronchioles; and bronchiolar wall thickening. Ill-defined centrilobular nodules represented peribronchiolar inflammation or the deposition of hemorrhagic materials.**
Conclusions: **Knowledge of the two centrilobular patterns is of proven worth for generating differential diagnoses and is of particular value in suggesting a likely infectious etiology in cases with tree-in-bud appearance.** ***(CHEST 2007; 132:1939–1948)***

Key words: airway infection; bronchiolitis; CT scan

Abbreviations: ABPA = allergic bronchopulmonary aspergillosis; ATLL = adult T-cell leukemia/lymphoma; CSS = Churg-Strauss syndrome; DAB = diffuse aspiration bronchiolitis; DPB = diffuse panbronchiolitis; FB = follicular bronchiolitis; GGA = ground-glass attenuation; HP = subacute hypersensitivity pneumonitis; HRCT = high-resolution CT; HTLV-1 = human T-lymphotropic virus type 1; HU = Hounsfield units; MAIC = *Mycobacterium avium-intracellulare complex*; MDP = methylene diphosphonate; MPA = microscopic polyangiitis; MTB = *Mycobacterium tuberculosis*; RB-ILD = respiratory bronchiolitis-associated interstitial lung disease; SLE = systemic lupus erythematosus; TBLB = transbronchial lung biopsy

Bronchioles are not usually directly visible on CT scans. However, when there is excessive soft tissue in or around the bronchioles, they can become visible at the center of the secondary pulmonary lobe.[1] The most common CT scan findings for bronchiolitis are centrilobular nodules and branching linear structures in secondary pulmonary lobules.

CT scan findings considered to represent bron-

Table 1—*Diagnostic Criteria for Each Lung Disease

Disease	Diagnostic Criteria
HTLV-1 carrier	Positive HTLV-1 antibody staining and polyclonal integration of proviral DNA in the peripheral blood or in biopsied tissue specimens
M pneumoniae pneumonia	Serologic tests (*ie*, complement fixation and indirect hemagglutination) with elevated single titers or a fourfold rise in titers
MTB	Presence of pathogen by examinations of sputum and BAL fluid
MAIC	Presence of pathogen by examinations of sputum and BAL fluid
M kansasii	Presence of pathogen by examinations of sputum and BAL fluid
ABPA	Asthma, peripheral blood eosinophilia; immediate positive skin test for Aspergillus antigens, increased serum IgE level, and pulmonary infiltrate seen on chest radiograph
DPB	Clinical, functional, and radiologic criteria of the grant-in-aid from the Ministry of Health and Welfare
FB	Histologic findings
DAB	Clinical features characterized by recurrent aspiration of foreign bodies
HP	Exposure history, clinical findings, radiologic findings, and histologic findings
Metastatic pulmonary calcification	Clinical features and bone scintigram
Diffuse pulmonary hemorrhage	Clinical findings, iron deficiency anemia, and pulmonary infiltrate on chest radiographs
RB-ILD	Histologic findings, clinical findings; and smoking history

*The diagnostic criteria are based on criteria from references 7, and 10 to 18.

chiolar diseases actually include a large variety of quite different pathologic entities that typically fall into the following two patterns on the CT scan: centrilobular nodules with tree-in-bud appearance; and ill-defined centrilobular nodules of ground-glass attenuation (GGA).[1–10] However, to the best of our knowledge, the clinical/pathologic correlations in patients with high-resolution CT (HRCT) scan findings presenting two patterns of centrilobular opacities remain unclear. We aimed to retrospectively evaluate and compare pulmonary CT scan findings of patients with predominant centrilobular nodules or preferential centrilobular disease with pathologic findings.

Materials and Methods

Patients

Our institutional review board approved this retrospective study, and waived informed consent. We retrospectively identified 648 patients who fulfilled each diagnostic criterion specific to each entity (Table 1)[7,10–18] and with predominant centrilobular nodules or preferentially centrilobular disease, who had undergone chest HRCT scans between January 1996 and December 2005 at three institutions. Thirty-one patients who were carriers of human T-lymphotropic virus type 1 (HTLV-1), 3 patients with *Mycoplasma pneumoniae* pneumonia, 8 with *Mycobacterium tuberculosis* (MTB), 7 with *Mycobacterium avium-intracellulare complex* (MAIC), 2 patients with diffuse panbronchiolitis (DPB), 2 patients with follicular bronchiolitis (FB), and 9 patients with alveolar hemorrhage were excluded from the study because of poor image quality on the HRCT scans, caused by motion artifacts or inadequate window-level settings, or because the hard copies of the CT film had been destroyed. Moreover, 10 HTLV-1 carriers, 8 patients with *M pneumoniae* pneumonia, 5 patients with DPB, 5 patients with diffuse aspiration bronchiolitis (DAB), and 5 patients with alveolar hemorrhage, in whom concurrent infectious diseases were diagnosed by serologic tests and clinical findings, were excluded from the study.

Thus, the study group comprised 553 patients (298 men; 255 women; age range, 15 to 86 years; mean age, 56 years) with centrilobular diseases whose cases were retrospectively reviewed. The patients included 243 HTLV-1 carriers, 52 patients with *M pneumoniae* pneumonia, 52 patients with MTB, 37 patients with MAIC, 33 patients *Mycobacterium kansasii* infection, 9 patients with allergic bronchopulmonary aspergillosis (ABPA), 12 patients with DPB, 7 patients with FB, 13 patients with DAB, 15 patients with subacute hypersensitivity pneumonitis (HP), 4 patients with metastatic calcification, 68 patients with alveolar hemorrhage, and 8 patients with respiratory bronchiolitis-associated interstitial lung disease (RB-ILD).

HTLV-1 is an etiologic retrovirus of adult T-cell leukemia/lymphoma (ATLL). HTLV-1 carriers were characterized by positive human T-lymphotropic virus type 1 antibody staining and polyclonal integration of proviral DNA in the peripheral blood or in biopsied tissue specimens. ATLL, on the other hand, was diagnosed by monoclonal integration of proviral DNA and the presence of abnormal lymphocytes with convoluted nuclei (ATLL cells) in the peripheral blood or from histologic findings compatible with a diagnosis of ATLL in biopsied tissue specimens. In patients with ATLL, ATLL pulmonary infiltration or opportunistic infections

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