

The Rapid Evolution of CT Findings in Pulmonary Langerhans Cell Histiocytosis: A Case Report¹

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Imaging findings of pulmonary Langerhans cell histiocytosis (PLCH) demonstrate evolving changes over time, and the radiological transitions shown by imaging tools may allow a prediction of histopathological activity in PLCH. However, there are no reports describing how rapidly CT findings change with time. We describe a case of PLCH that showed a rapid evolutionary change of the pulmonary lesions in a 48-year-old man, in which the nodular lesions showed cystic changes within two-month follow-up periods on chest CT scans.

Index words : Histiocytosis

Computed tomography (CT)

Lung, CT

Pulmonary Langerhans cell histiocytosis (PLCH) is a disease that shows evolving radiological changes. Initial nodular lesions often undergo cystic changes as seen by a chest CT (1). This radiological transition is regarded as a reliable tool for predicting the histopathological activity of PLCH (2). If it was possible to predict the speed of the evolutionary changes, the use of a chest CT could become an important tool for predicting disease stage, and for estimating the activity of PLCH. However, there are no reports describing how rapidly the CT findings change with time. Here, we report a case of PLCH in which rapid evolutionary CT finding changes were observed at two-month intervals during follow-up studies.

Case Report

A 48-year-old man was admitted to our hospital with abnormal findings as determined by a routinely performed low-dose (35 mA, 120 kVp) helical chest CT. The patient, a heavy smoker (30-packs years), denied having any symptoms or specific past medical history. The first low-dose chest CT (LDCT) showed no parenchymal abnormalities. However, a 6 months follow-up LDCT after the initial LDCT showed several newly developed small ground glass opacity (GGO) or solid nodules in both lungs. The nodules measured less than 5 mm in the longest diameter. Two months later, a third follow-up high-resolution chest CT (HRCT) was obtained, in which some of the GGO nodules had disappeared. However, a small solid nodule in the superior segment of the right lower lobe had changed into a cavitory nodule, and a small GGO nodule in the left upper lobe had changed into a discrete cystic lesion (Fig. 1A-D). A pulmonary function test and bronchoscopic findings were normal.

While considering several diagnostic possibilities,

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such as, PLCH, pulmonary tuberculosis, pulmonary metastases from an extra-thoracic malignancy, and fungal infections, we recommended that the patient undergo a surgical lung biopsy, fearing a cavitating metastatic malignancy. A video-assisted thoracoscopic lung biopsy was performed at the cavitating nodule located in the superior segment of the right lower lobe. The

histopathological diagnosis was cellular phase PLCH. A light microscopic examination disclosed that the nodule consisted of a mixed cellular population including variable numbers of Langerhans cells, eosinophils, lymphocytes, and fibroblasts (Fig. 1E, F). The patient did not receive any specific medication after the diagnosis. The patient remains asymptomatic and a further one-year

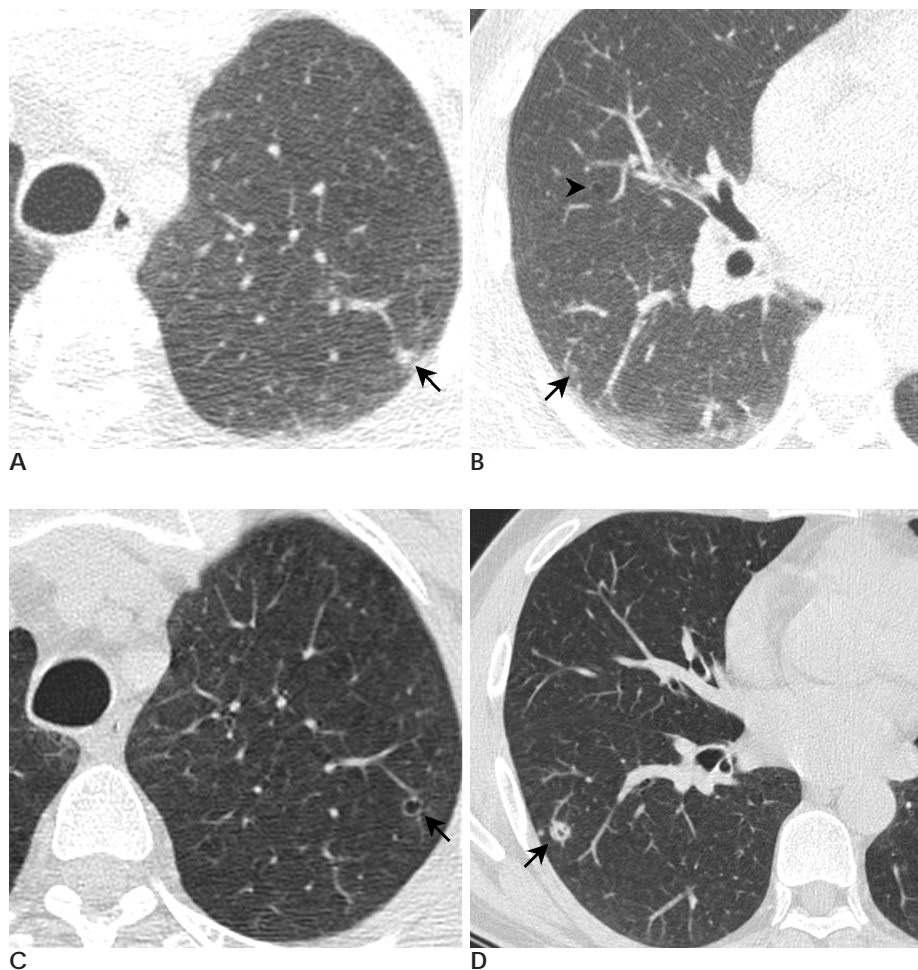


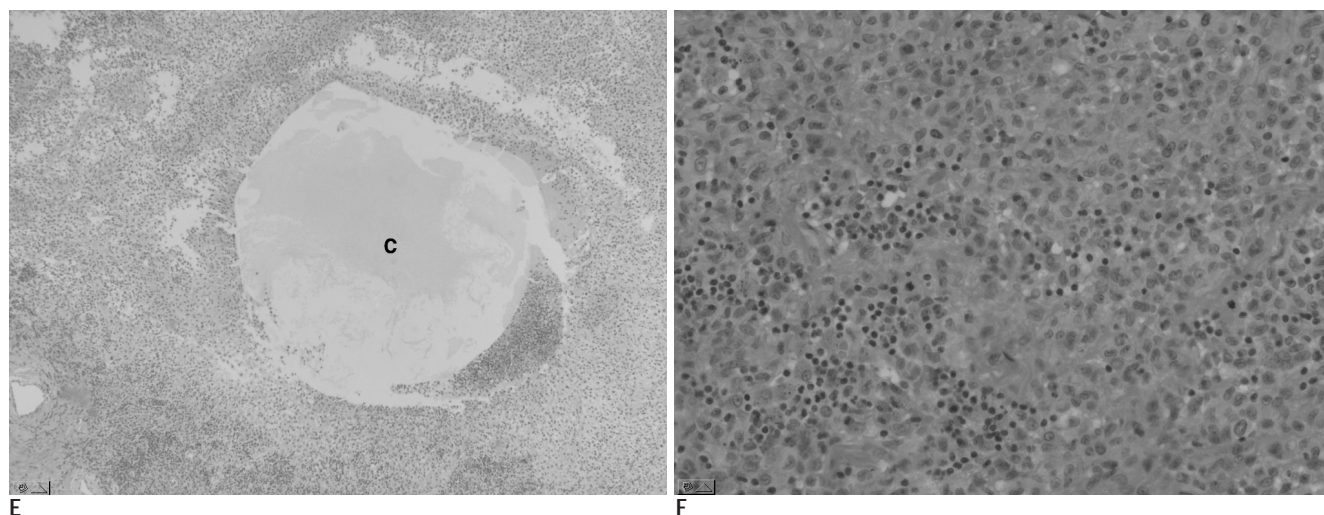
Fig. 1. Pulmonary Langerhans cell histiocytosis in a 48-year-old man.

A, B. Lung window setting low dose (section thickness; 5.0 mm, 35 mA, 120 kvp) CT scans obtained at levels of the thoracic inlet (**A**) and the right middle lobar bronchus (**B**), respectively, show small nodules (arrows) in the left upper lobe and the right lower lobe. Note also a small cystic lesion in the right middle lobe (arrowheads).

C, D. Follow-up HRCT scans (section thickness; 2.5 mm, 200 mA, 120 kvp) obtained at identical levels. Two months later, the same lesions have changed from nodules to a cavitary granuloma and cyst (arrows).

E. Low-magnification photomicrograph shows nodular cellular infiltrates with central cavitation (**C**) (H & E stain, $\times 40$).

F. A high-magnification photomicrograph demonstrates a mixed population of cells with variable numbers of Langerhans giant cells, eosinophils, lymphocytes, plasma cells, and fibroblasts (H & E stain, $\times 200$).



follow-up CT did not show any significant change in the parenchymal lung lesions.

Discussion

Pulmonary Langerhans cell histiocytosis is an uncommon disease of adult smokers with accompanying significant morbidity. PLCH is characterized histologically by the peribronchiolar proliferation of Langerhans cells (3). The cellular lesions expand to form nodules, which include a mixed population of cells with variable numbers of eosinophils, lymphocytes, plasma cells, fibroblasts, and pigmented alveolar macrophages as well as Langerhans cells.

The nodular lesions frequently form cavity and thick- and thin-walled cysts, which are thought to represent enlarged airway lumen. PLCH lesions display temporal microscopic heterogeneity with progression from dense cellular nodules to apparently cavitory nodules, followed by increased degrees of fibrosis that may extend along the alveolar walls. In advanced cases, fibrotic scars are surrounded by enlarged and distorted air spaces (4).

The histopathology of PLCH evolves from cellular nodules, via cavitory nodules, to entirely fibrotic and cystic nodules. As the lesions develop, they become less cellular, whereas the fibrotic components are prominent. Later stages are characterized by cystic lesions that are thought to represent airway lumen enlarged because of inflammation of the bronchiole wall, coalescence of adjacent affected airways, and para-cicatricial airspace enlargement (5). In its early stages, the disease is characterized by the presence of granulomatous nodules, but in later stages, these nodules are replaced with cystic lesions (1, 3).

Soler et al. (2) suggested that high-resolution (HR) CT is a reliable tool for predicting the histopathological activity of PLCH. These investigators classified the evolution of PLCH by histopathological analysis, i.e., florid granuloma (solid nodule) and inflammatory cavitory lesions (cavitory granuloma), and late-stage cystic lesions (fibrous cysts). The histopathology was then correlated with the HRCT findings, and it was demonstrated that during the evolution of PLCH, a nodular CT pattern represents histopathologically active disease, and that a cystic CT pattern, although frequently associated in part with inflammatory lesions, generally represents late-stage disease.

Despite the above-mentioned correlative study be-

tween the histopathological and HRCT findings (2), we cannot predict how rapidly nodular lesions will be converted into cystic lesions. However, if the precise timeline of radiological evolutionary changes could be correlated with the histopathological changes, the disease stage could be determined from the CT patterns.

An limitation of this study includes the applicability of data from serial different chest CT scan protocols between the initial LDCT scan for screening and the follow up HRCT scan for diagnosis.

From this case, it is clear that a nodule can evolve into a cavitating nodule and a nodule or nodular area of ground-glass opacity can evolve into a cystic lesion within a two-month period. Therefore, we consider that this cystic evolution does not necessarily represent late fibrotic stage PLCH, particularly when imaging findings are heterogeneous, i.e., mixed cystic and nodular lesions, as the disease may be still be in the inflammatory stage. Furthermore, in histopathological studies, the full range of cellular granulomatous nodules and cystic fibrotic scars separated by relatively normal lung can be observed in a single biopsy specimen obtained from a patient (5). Thus, the disease is likely to be in the fibrotic stage only when the cystic lesions are predominant findings with a bizarre appearance on CT.

In summary, we describe a case of PLCH that demonstrated rapid cystic evolution of pulmonary nodular lesions as seen from a chest CT over two month follow-up periods. In previous reports, cystic changes of the pulmonary nodules in PLCH have been regarded to appear in late stage disease. However, a cystic change of the CT findings may appear as mixed lesions with cavitory nodules in the histopathologically cellular disease stage. Studies based on a large number of cases are needed to determine how rapidly the imaging findings of lung lesions in PLCH evolve. Such studies would allow one to predict accurately the histopathological stage from the CT findings of the pulmonary lesions.

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