

Focal Organizing Pneumonia: CT and Pathologic Findings

The purpose of this study was to describe the CT findings of focal organizing pneumonia and to compare the findings with pathology. CT findings of histologically proven focal organizing pneumonias in 26 consecutive patients were analyzed. In 17 patients who had undergone surgical resections, the findings were correlated with pathology. Focal organizing pneumonias appeared as a nodule (n=13) or a mass (n=13), ranging from 9 mm to 66 mm in diameter. Ground-glass opacity was seen in 6/13 (46%) nodules and 6.5/13 (50%) masses ($k=0.48$) with an extent ranging from 5% to 75% (mean, 16%). In 4/26 (15%) patients, the extent was more than 50% of the lesion. They showed smooth (n=4), lobulated (n=8), spiculated (n=1), or lobulated and spiculated margin (n=13). On correlative analysis, nodule or mass on CT consisted histologically of intraalveolar exudate or microabscess, chronic inflammatory cell infiltration, fibrotic nodules, and polypoid granulation tissue in the alveolar or bronchiolar spaces. Ground-glass opacity consisted of interstitial fibrosis and chronic inflammatory cell infiltration and intraalveolar polypoid granulation tissue. Focal organizing pneumonia may simulate a lung cancer with variable appearances on CT and the findings reflect underlying histopathology of the disease.

Key Words : Lung, CT; Lung, Infection; Lung, Nodule; Lung Neoplasms, Diagnosis

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INTRODUCTION

Focal organizing pneumonia is defined as unresolving pneumonia or pneumonia with a delayed resolution. With antimicrobial treatment, pneumonia usually resolves within four weeks after its initial manifestation on chest radiograph. However, in about 5-10% of patients, the pneumonia remains unresolved (1-4).

Focal organizing pneumonia consists histologically of polypoid granulation tissue in the alveolar spaces as well as in the bronchial lumen and thickening of the alveolar septa with chronic inflammatory change (2-6). It is one of the benign conditions that are often difficult to distinguish from bronchogenic carcinoma; therefore, patients with organizing pneumonia often undergo surgical resection (6, 7). The computed tomographic (CT) findings of focal organizing pneumonia have been described in a few papers (6, 8-10). In these papers, CT findings showed a wide variation and simulated a peripheral lung cancer. However, CT-pathologic correlation of the disease has not been reported in detail. Our study was aimed to describe the CT findings of focal organizing pneumonia and to compare them with pathology.

MATERIALS AND METHODS

Between April 1996 and April 2000, 26 consecutive

patients with pathologically proven focal organizing pneumonia visited our hospital. The patients were 18 men and 8 women (age range; 30-82 yr, mean; 55 yr). Focal organizing pneumonia was diagnosed with surgical resection in 17 patients (open lung biopsy [n=7], video-assisted thoracoscopic surgery [n=10]) and with percutaneous 21-gauge core-needle biopsy [Autovac, Angiomed, Karlsruhe, Germany] and transbronchial lung biopsy in the remaining nine patients. Surgical resection was performed due to a possibility of malignancy because the lesion was present persistently on chest radiographs at least for two months and percutaneous lung biopsy did not suggest a definite histologic diagnosis. Of nine non-surgical patients, follow-up chest radiographs (range of follow-up period, 20 days to 150 days; mean, 51 days) showed a disappearance of the lesion in two and decrease in size in seven. In five patients in whom follow-up CT scan was available, the lesions disappeared (n=2) or decreased in size (n=3) during the follow-up period (range, 22 days to 270 days; mean, 123 days). During the follow-up period, corticosteroids were not given in any patients.

Twenty patients complained of cough/sputum (n=9), chest discomfort (n=7), dyspnea (n=2), hemoptysis (n=1), and fever (n=1). The remaining six patients, in whom the lesion was detected incidentally, were asymptomatic. Five patients recollected that they had a previous history of pneumonia prior to the diagnosis of focal organizing pneumonia. In the

remaining 21 patients, previous history of pneumonia was not recorded. Smoking history was positive in 13 of 18 men (mean; 39-pack yr, range; 8-90-pack yr).

Nineteen patients (73%) had no underlying illness. Four patients had concomitant malignant condition including acute myelogenous leukemia (n=2), breast cancer (n=1), and leiomyosarcoma (n=1). Two had diabetes mellitus. One underwent cardiac transplantation due to dilated cardiomyopathy. In patients with leukemia and cardiac transplantation, lung biopsy was performed for possible invasive pulmonary aspergillosis because CT showed a nodule or mass with surrounding ground-glass opacity. In patients with breast cancer and leiomyosarcoma, lung biopsy was performed with a presumed diagnosis of metastasis.

The interval between CT scanning and subsequent lung biopsy or surgery ranged from 2 to 36 days (mean, 13 days). CT scans were obtained with three different machines, but mainly with GE 9800 or HiSpeed Advantage scanner (General Electric Medical Systems, Milwaukee, WI, U.S.A.). The scans were obtained from the lung apices to the middle portion of both kidneys with 7-10-mm collimation. Both enhanced (after injection of 30 g of iodinated contrast medium, 100 mL of Iopamidol [Iopamiron 300; Bracco, Milan, Italy]) and unenhanced CT scans were obtained in 23 patients. In these patients, additional high-resolution (1-mm collimation, 3-5-mm intervals) CT scans were obtained at lesion sites. Only high-resolution CT scans were obtained in three patients.

All CT findings were analyzed retrospectively by two independent chest radiologists. Interobserver agreement was tested with κ (kappa) statistic (11). CT analysis included the location, distribution, size, shape, and margin of the focal lesion. Presence of calcification, internal necrosis, and cavitation was evaluated. Presence of enhancement more than 15 H of the lesion was also evaluated when both enhanced and unenhanced CT scans were available. The attenuation values within the lesions were measured by using a cursor, apart from a necrotic low-attenuation area. Location of the lesion was divided into five lobes (lingular segment as a portion of the left upper lobe). Distribution of the lesion was subcategorized into being subpleural, along the bronchovascular bundles, and random (no apparent relation with either the pleura or the bronchovascular bundles). The longest diameter of the lesion, where it appeared largest on axial images, was measured. When the lesion was 3 cm or less in diameter, it was classified into a nodule. When it was more than 3 cm in diameter, the lesion was classified into a mass. The shape of the lesions was subdivided into being round, oval, and trapezoidal. The margin was subdivided into being smooth, lobulated, spiculated, and lobulated and spiculated. Internal necrosis was presumed to be present when focal area of lower attenuation than the remaining large portion of the enhancing lesion was seen on enhanced scans. Ground-glass opacity was regarded to be present when hazy increased attenuation of

the lung, but with pre-preservation of bronchial and vascular margins, was seen in and around the lesion. The observers quantified subjectively and visually the percentage of necrosis and ground-glass opacity, respectively, within a tumor just on the equatorial image. The extent of necrosis and ground-glass opacity was calculated visually to the nearest 5%. Presence of satellite nodule was also described. Mediastinal lymph node enlargement (abnormal if the short axis was larger than 10 mm in diameter) was also recorded.

An experienced lung pathologist reviewed lung specimens in 17 patients in whom surgically resected lung specimens were available. On pathologic examinations, the presence of intraalveolar exudate or abscess, fibrotic nodules, polypoid granulation tissue in the alveolar or bronchial spaces, chronic interstitial inflammatory cell infiltration and fibrosis were analyzed. The pathologic findings were compared with CT findings.

RESULTS

CT Findings

Focal organizing pneumonias appeared as a nodule (n=13) or a mass (n=13). The lesions ranged from 9 mm to 66 mm in diameter. The organizing pneumonias were located in right upper lobe in seven patients, right middle lobe in three, right lower lobe in eight, left upper lobe in six, and left lower lobe in two. They were distributed in subpleural regions (n=16), along bronchovascular bundles (n=6), or randomly (n=4). They were round (n=3), oval (n=9), or trapezoidal (n=14) in shape and had smooth (n=4), lobulated (n=8), spiculated (n=1), or lobulated and spiculated margin (n=13) (Fig. 1-4). Enhancement more than 15 H (17.5/23 [76%], $k=.75$), ground-glass opacity within a lesion (12.5/26 [48%], $k=.48$) (Fig. 1, 2), necrotic low attenuation (10.5/23 [46%], $k=.75$), satellite nodule (10/26 [38%], $k=.62$), calcification (4/26 [15%], $k=.63$), and cavitation (4/26 [15%], $k=1$) (Fig. 4) were seen. Ground-glass opacity was associated in 6/13 (46%) nodules and 6.5/13 (50%) masses. The extent of ground-glass opacity ranged from 5% to 75% (mean, 16%). In 4/26 (15%) patients, the extent of ground-glass opacity was more than 50% of the lesion (Fig. 1, 2). The extent of necrosis ranged from 5% to 75% (mean, 15%). Mediastinal lymph nodes were enlarged in 5/26 (19%) patients. The nodes were enlarged in subcarinal (n=3), right lower paratracheal (n=2), aortopulmonary window (n=1), and retrotracheal (n=1) areas.

CT-Pathologic Correlation

Grossly, the lesions appeared as a nodule or mass with firm, slightly raised, tan-gray or yellow-gray appearance (Fig. 1). When CT findings were compared with pathologic

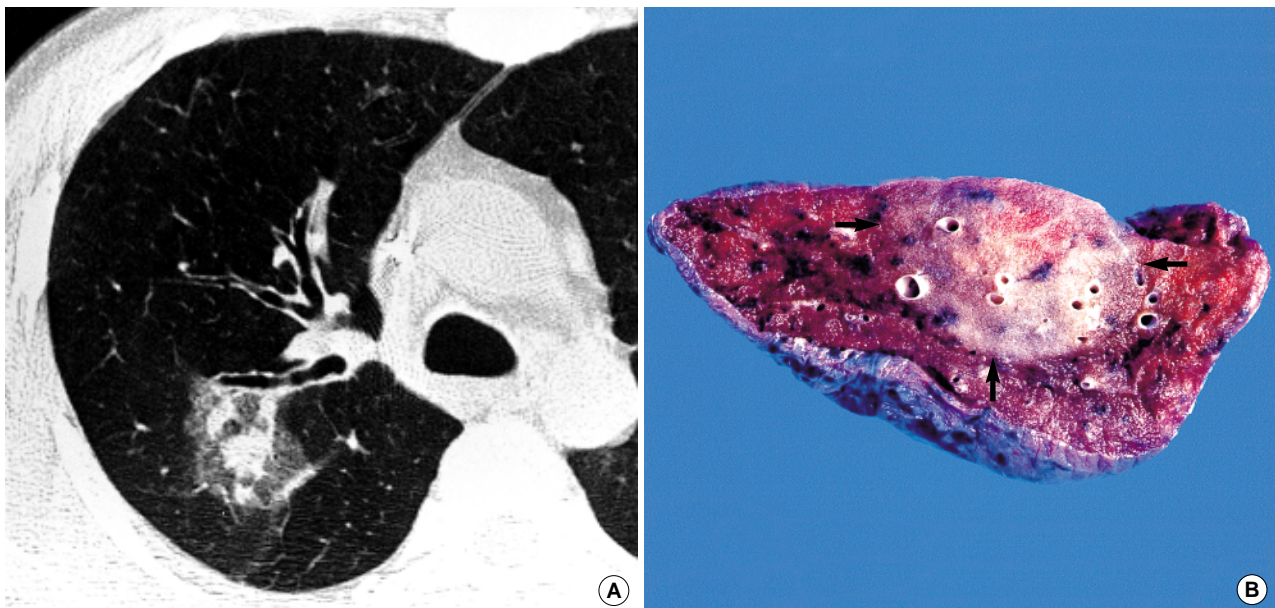


Fig. 1. Focal organizing pneumonia in a 36-yr-old man with acute myelogenous leukemia. (A) High-resolution (1.0-mm collimation) CT scan obtained at the level of azygos arch shows nodules with surrounding ground-glass opacity (65% involvement of lesion) in posterior segment of right upper lobe. (B) Gross pathologic specimen obtained with right upper lobectomy shows tan-gray, well-defined lesion with slightly elevated margin (arrows).

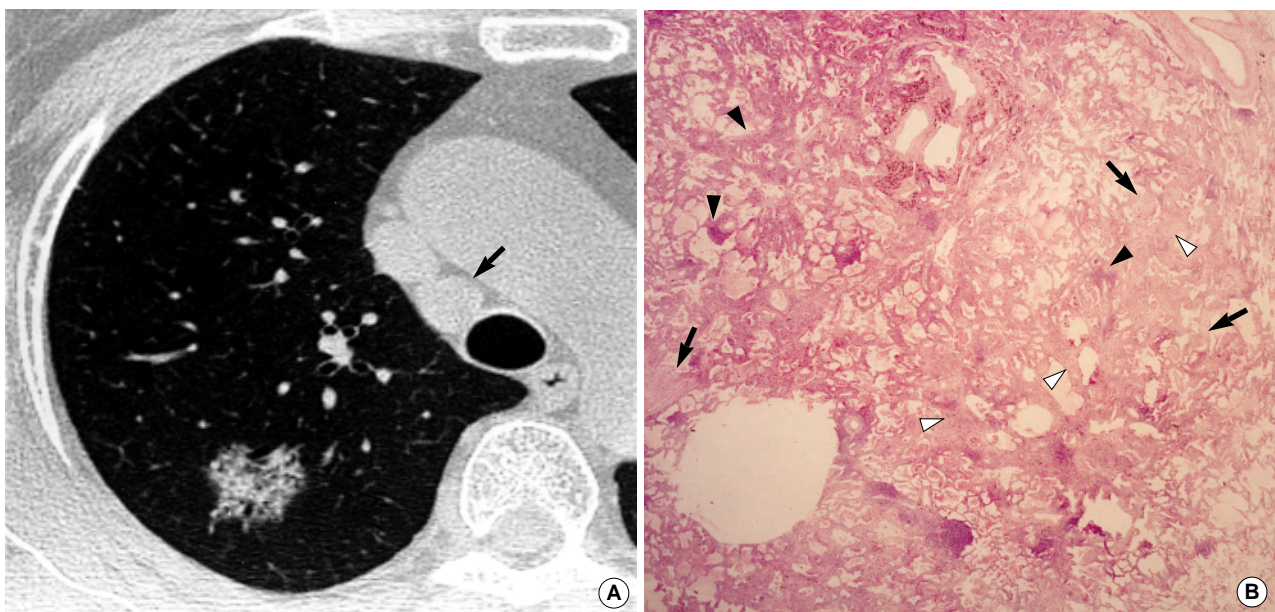


Fig. 2. Focal organizing pneumonia in a 65-yr-old woman with diabetes. (A) High-resolution (1.0-mm collimation) CT scan obtained at the level of aortic arch shows nodular ground-glass opacity (30% involvement of lesion) with bubble-like lucencies in posterior segment of right upper lobe. Also note enlarged right paratracheal lymph node (arrow). (B) Photomicrograph at a low magnification shows well-delineated nodular lesion consisting of polypoid granulation tissue (arrows) infiltrated by fibroblasts and inflammatory cells (arrowheads). Also note interstitial widening with fibrosis (open arrowheads) (H&E, $\times 40$).

findings, nodule or mass on CT corresponded histologically to a varying extent of intraalveolar exudate and microabscess, chronic inflammatory cell infiltration, fibrotic nodules, and polypoid granulation tissue in alveolar or bronchiolar space

(Fig. 3, 4). Internal necrotic low-attenuation on CT corresponded histologically to the areas of small abscess. Ground-glass opacity on CT corresponded to the areas of interstitial fibrosis and chronic inflammatory cell infiltration, mixed

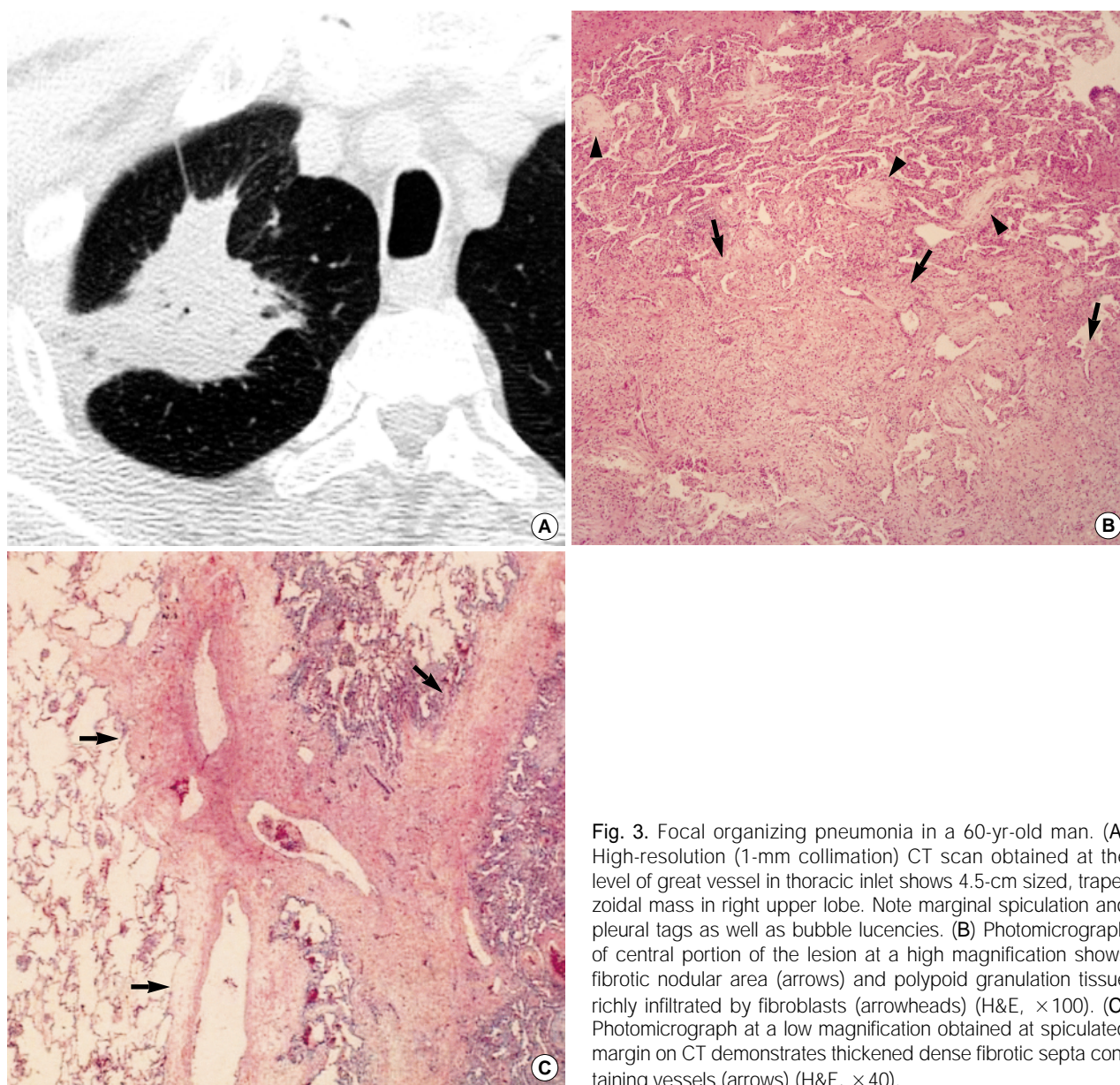


Fig. 3. Focal organizing pneumonia in a 60-yr-old man. (A) High-resolution (1-mm collimation) CT scan obtained at the level of great vessel in thoracic inlet shows 4.5-cm sized, trapezoidal mass in right upper lobe. Note marginal spiculation and pleural tags as well as bubble lucencies. (B) Photomicrograph of central portion of the lesion at a high magnification shows fibrotic nodular area (arrows) and polypoid granulation tissue richly infiltrated by fibroblasts (arrowheads) (H&E, $\times 100$). (C) Photomicrograph at a low magnification obtained at spiculated margin on CT demonstrates thickened dense fibrotic septa containing vessels (arrows) (H&E, $\times 40$).

with patchy areas of polypoid granulation tissue (Fig. 1, 2). Interstitial fibrosis was composed of mature collagen deposition rather than fibroblastic proliferation. As ground-glass opacity increased in extent in a nodule or mass on CT, pathologic specimens had a tendency to show interstitial processes (fibrosis and chronic inflammatory cell infiltration) rather than intraalveolar processes (exudate and microabscess, fibrotic nodules, and polypoid granulation tissue). Desmoplastic reactions were responsible for the marginal irregularity.

DISCUSSION

Acute pneumonias resolve spontaneously or after antimi-

crobial chemotherapy with resorption of the inflammatory exudate and reconstitution of the normal underlying structure. In some cases, however, stimulation of fibroblasts by the inflammatory response brings in proliferation of connective tissue (12). The resulting intraalveolar and interstitial organization and fibrosis produce organizing pneumonia. The prevalence of organizing pneumonia is thought to be 5-10% of all patients with pneumonia (2, 6, 13, 14). Old age, diabetes mellitus, chronic bronchitis, and overuse of antibiotics have been presumed to be the predisposing factors for organizing pneumonia (6, 13, 15, 16). Auerbach *et al.* (15) reported that the frequency of pulmonary fibrosis secondary to pneumonia is increasing in their necropsy study. They speculated that use of antibacterial agents had con-

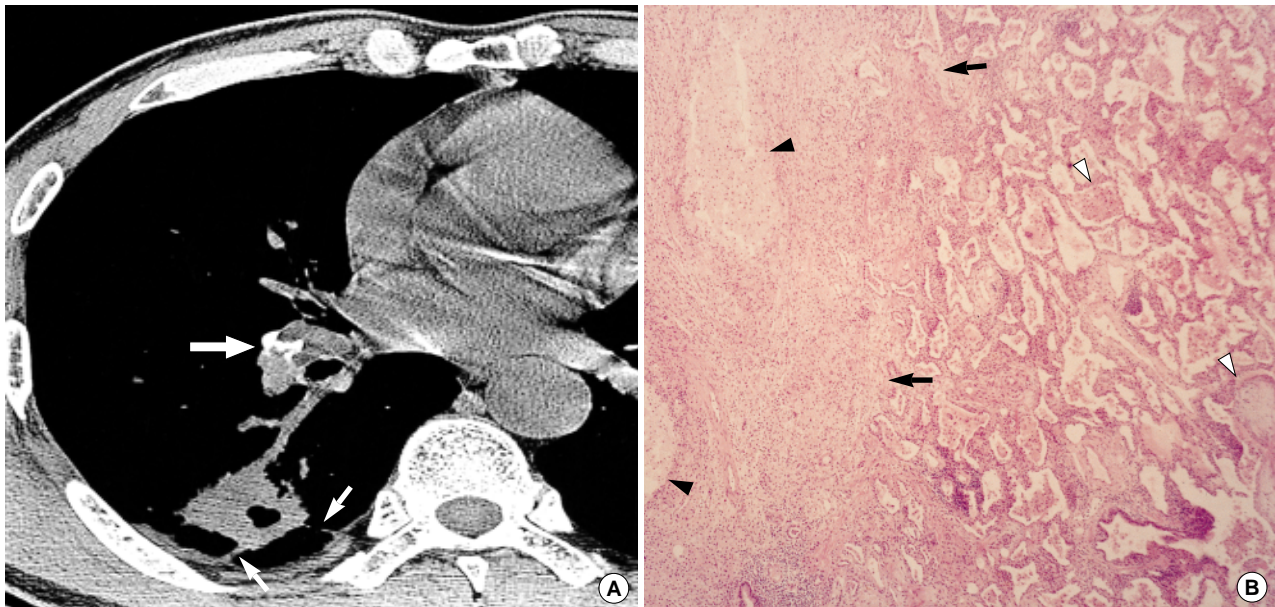


Fig. 4. Focal organizing pneumonia in a 68-yr-old man. (A) Mediastinal window of high-resolution (1-mm collimation) CT scan obtained at the level of basal trunk shows cavitating, trapezoidal mass in right lower lobe. Note spiculated pleural tags (small arrows), pleural thickening, and calcified hilar nodes (arrows). (B) Photomicrograph at a high magnification shows central fibrotic nodular area (arrows) with several cystic foci (arrowheads) containing foamy macrophages. Also note surrounding polypoid granulation tissue with intraalveolar macrophages (open arrowheads) (H&E, $\times 100$).

tributed to this increasing frequency.

At least four pathologic processes take part in remodeling of the lung in organizing pneumonia. They are interstitial thickening, deposition of connective tissue matrix within the airspaces, collapse of the airspaces, and contraction of the injured lung (19). Intraalveolar proliferation and plugging of fibroblasts produce nodular structures called Masson bodies (intraalveolar polypoid granulation tissue). Pulmonary myofibroblasts participate in the contractile phase of pulmonary fibrosis (20-22).

Focal organizing pneumonia is an intraalveolar pattern of organization similar to bronchiolitis obliterans organizing pneumonia. There are subtle features that allow separation between these two entities. There is a greater degree of residual acute inflammation in focal organizing pneumonia than in bronchiolitis obliterans organizing pneumonia. In focal organizing pneumonia, polypoid granulation tissues are identified predominantly in the alveolar spaces rather than in the small bronchioles (23). Still, however, there is a considerable overlap between these two entities and some cases may be difficult or even impossible to distinguish with histologic diagnosis alone.

Reported CT findings of focal organizing pneumonia show a wide range of variations. The pneumonias may appear on CT as benign-looking parenchymal abnormalities with oval, spindle-shaped, or trapezoidal lesions of subpleural areas or along the bronchovascular bundles. Satellite nodules may also be seen. Conversely, the pneumonias may appear as malig-

nant-looking abnormalities with lobulated and spiculated margins, pleural tagging, and convergent peripheral vessels (6, 8). In addition, enhancement more than 15 H is seen in about three fourths (76%) of the patients in the current study. Furthermore, when focal organizing pneumonia appears predominantly and persistently as a focal area of ground-glass opacity (in the current study, 48% of lesions showed ground-glass opacity within them ranging in extent from 5 to 70%), the lesion may mimic bronchioloalveolar carcinoma, solitary metastatic nodule, or mucosa-associated lymphoid tissue-lymphoma (24, 25). Therefore, on some occasions, the diagnosis of focal organizing pneumonia is difficult even with the use of many imaging modalities including CT. In these situations, surgical resections are performed for both diagnosis and treatment. However, as suggested in the current study and in the study of Kohno et al. (6), oval or trapezoidal shape and presence of satellite nodule in focal organizing pneumonia may be the differential diagnostic points from bronchogenic carcinomas. Other important differential feature is the gradual improvement of the CT findings on follow-up scans.

In our correlative study, nodule or mass on CT consisted histologically of a variable extent of concurrent acute (intraalveolar exudate and microabscess) and chronic (aggregates of proliferative granulation tissue: Masson bodies) intraalveolar inflammation, fibrotic nodules with collapse of airspaces and contraction of the injured lung, and chronic interstitial inflammation. Ground-glass opacity correspond-

ed pathologically to the areas of interstitial fibrosis and chronic inflammatory cell infiltration, mixed with some areas of intraalveolar polypoid granulation tissue. When a large area of ground-glass opacity was present with a nodule or mass on CT, pathologic specimens had a tendency to show interstitial processes rather than intraalveolar processes. Necrotic low-attenuation area on CT histologically represented intraalveolar exudates and microabscesses.

Patient with organizing pneumonia is regarded to have had a preceding episode of pneumonia (13, 16-18). However, in clinical practice, such episodes are not found in all patients. In previous reports, symptoms and signs such as cough, sputum, fever, and/or hemoptysis are often present in patients with organizing pneumonia (4, 14). In our series, 5/26 (19%) patients had a previous history of pneumonia.

Obviously there is a selection bias in our study. The current study included more cases with surgically resected specimens than the previous report (8), which might have resulted in more cases simulating lung cancer. Our study also suffers from retrospective review. Although we evaluated the degree of enhancement with administration of contrast medium, the injection method is not uniformly applied because CT studies were obtained from several institutions. The fact may have hampered the exact evaluation of the extent of contrast enhancement of lesions.

In summary, focal organizing pneumonia appears on CT as variable features from nodular area of ground-glass opacity to necrotic mass. Because CT findings may simulate a lung cancer, surgical resection may be performed to exclude malignant condition. The appearance of the lesion as an oval or trapezoidal abnormality, especially when the lesion is associated with satellite nodules on CT, suggests a benign nature. When imaging findings are inconclusive, short-term follow-up radiologic evaluation for change in size may be helpful. The CT findings of focal organizing pneumonia reflect a variable extent of underlying pathology including intraalveolar exudate, fibrotic nodules, fibroblast plugging in alveolar or bronchiolar spaces, and chronic interstitial inflammatory cell infiltration and fibrosis.

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