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The Distribution Pattern of Disseminated Small Lung Nodules

— Comparative Study of Radiological and Pathological Findings of Bronchogenous and Hematogenous Spread Lesions —

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ABSTRACT **The distribution pattern of disseminated small lung nodules was radiologically studied with special reference to the relationship between lesions and the bronchial branching system using inflated and fixed lungs of 6 cases obtained from autopsy. The bronchogenous spread lesions, which were seen in endobronchial tuberculosis and bronchopneumonia, were located in the centriacinar portion of the secondary lobule. Their distribution patterns were regular and corresponded to the bronchial branching pattern. On the other hand, the hematogenous spread lesions, which were seen in miliary tuberculosis and pulmonary metastasis of carcinoma, had no relation to airway structures. They were randomly distributed regardless of bronchial branching. Recognition of these different distribution patterns is important for evaluating diffuse lung diseases by computed tomography.**
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Keywords: Diffuse lung disease, Centriacinar lesion, Centrilobular lesion, Computed tomography

1. INTRODUCTION

Computed tomography (CT) has been used increasingly for evaluating pulmonary parenchymal diseases[1)2)]. CT provides thin-section transaxial images without superimposition, therefore it can demonstrate disease processes not identifiable on chest radiographs. In several recent CT-pathologic correlative studies[3)~6)], pulmonary parenchymal abnormalities on CT were analyzed in relation to lung structures, including the secondary pulmonary lobule. These studies provided useful information for interpreting CT images of pulmonary parenchymal diseases. Radiographic patterns of pulmonary parenchymal diseases reflect various pathologic conditions. One of the important factors of these conditions is the pathway by which the pathogen spreads through the lung. Although endobronchial tuberculosis and miliary tuberculosis are caused by the same pathogen, the distribution patterns of the disseminated noduldes are different on CT[7)]. This seems to be due to differences in the spread of the pathogens.

In this study, we performed comparative analysis of radiological and pathological findings of bronchogenous spread and hematogenous spread lesions using inflation-fixed lungs obtained from autopsy.

2. MATERIALS AND METHODS

Six lungs were obtained from 6 autopsied cases. All of them had pathologically confirmed diagnosis: endobronchial tuberculosis (2 cases), miliary tuberculosis (2 cases), bronchopneumonia (1 case), and hematogenous pulmonary metastasis of lung carcinoma (1 case).

The lungs were prepared by the method described by Markarian and Dailey[8)]. The lungs were fixed in distention for 48 hours in a fixative fluid containing polyethylene glycol 400, 95% ethyl alcohol, 37% formaldehyde, and water in proportions of 10 : 5 : 2 : 3. Following fixation, the lungs were dried by forcing air through the mainstem bronchus at a pressure of 10 cm H_2O. The lungs were cut into axial or frontal slices with 5 mm thicknesses. All slices were radiographed in contact with a fine resolution and high contrast film (Fuji FR for soft X-ray, Fuji photo film, Tokyo) at 14 kVp, 3 mA, and 60 cm focus-film distance with soft X-ray apparatus (CSM-2, Softex, Tokyo). Furthermore, selected slices were cut into 2 mm thick slices and radiographed at 11 kVp, 3 mA, and 60 cm focus-film distance. Microscopic sections of these selected slices were prepared for hematoxylin and eosin staining. Radiographs of the slices were correlated with pathological findings including observation of the surface of the specimens under a dissecting microscope.

In one case of endobronchial tuberculosis, three dimensional reconstruction of the lesion and the bronchial branching system was performed by observation of both the surface of specimen and the radiographs under dissecting microscope using contiguous 2 mm thick slices. The secondary lobules and the size of their distributed area were determined by the bronchial branching pattern according to Reid's lobular concept[9)10)]. The relation between the lesions and bronchial branching system, including lobular structure, was analyzed.

3. RESULTS

3·1 Bronchogenous spread lesions

3·1·1 Endobronchial tuberculosis

Radiographs of the specimens with endobronchial tuberculosis showed multiple nodular shadows with airbronchiologram or their coalescences (Fig. 1). These lesions were correlated with peribronchiolar alveolar filling lesions at the submacroscopic level which could be observed under the dissecting microscope. Histopathologic findings of the lesions demonstrated peribronchiolar tuberculous nodules with caseous necrosis (Fig. 1). Both cases of endobronchial tuberculosis showed almost the same radiological and pathological findings.

The radiographs of contiguous 2 mm slices for three dimensional reconstructive analysis are shown in Fig. 2, and the relation between the lesions and secondary lobules in one of these slices is shown in Fig. 3. The schema in Fig. 4 demonstrates the relationship between the lesions and bronchial branching system within the secondary lobules based on three dimensional reconstructive analysis of all slices.

There were basically 3 to 5 nodular lesions in each secondary lobule which was approximately 10-15 mm in diameter. Each nodule was found in the peribronchiolar area around a terminal bronchiole and respiratory bronchioles. This indicates that the nodules were located at the central por-

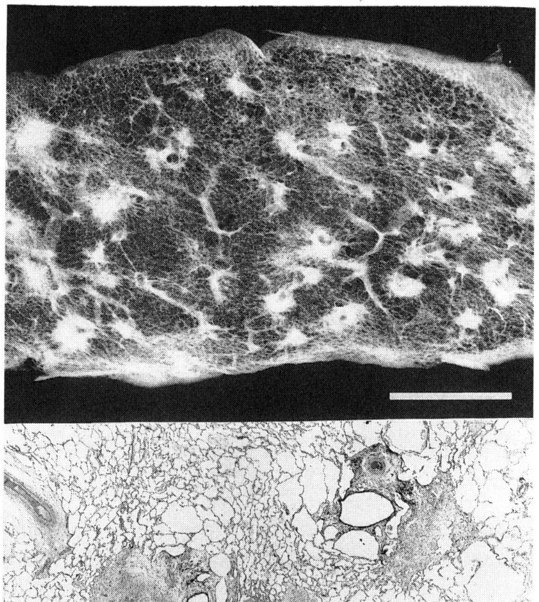

Fig. 1 Radiograph and photomicrograph of a specimen with endobronchial tuberculosis. Multiple nodular shadows with airbronchiologram and their coalescences are shown on radiograph (white bar represents 10 mm). The distribution pattern of nodules corresponds to the bronchial branching pattern. A microscopic section (H & E, 10×) demonstrates peribronchiolar tuberculous nodules with caseous necrosis.

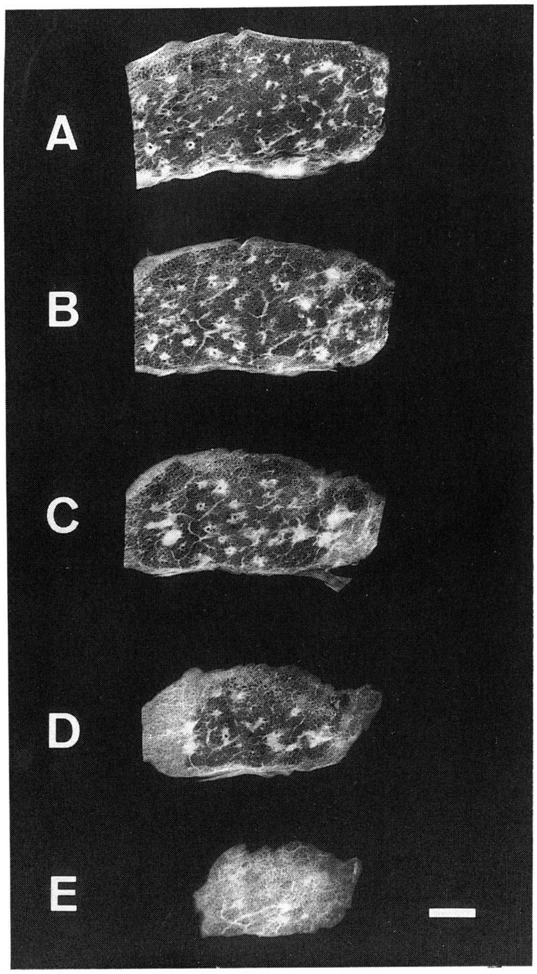

Fig. 2 Radiographs of contiguous 2 mm thick slices of specimen (A-E) with endobronchial tuberculosis for three dimensional reconstructive study (white bar represents 10 mm).

tion of an acinus (centriacinar lesion). In other words, the lesions were located at the core structure of the secondary lobule (centrilobular lesion). These basic lesions occasionally coalesced to form larger lesions, but normal parenchyma remained in the peripheral area of the lobules (Fig. 3, 4). The distribution pattern of these centriacinar nodules had a regularity that corresponds to the bronchial branching pattern, because the location of the centriacinar portion is determined by the bronchial branching system.

The lesions of endobronchial tuberculosis were basically centriacinar lesions, and thus their distribution pattern showed a particular regularity

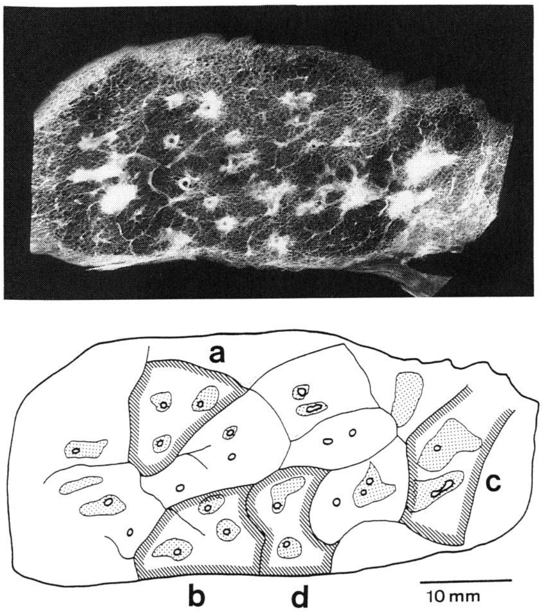

Fig. 3 Radiograph of slice C (in Fig. 2) and schema from observation of its surface under the dissecting microscope. There are 3-5 basic lesions in a secondary lobule (lobule a, b). All nodules are found in the peribronchiolar area. These basic lesions occasionally coalesce to form larger lesions, but normal parenchyma remains in the peripheral area of lobules (lobule c, d).

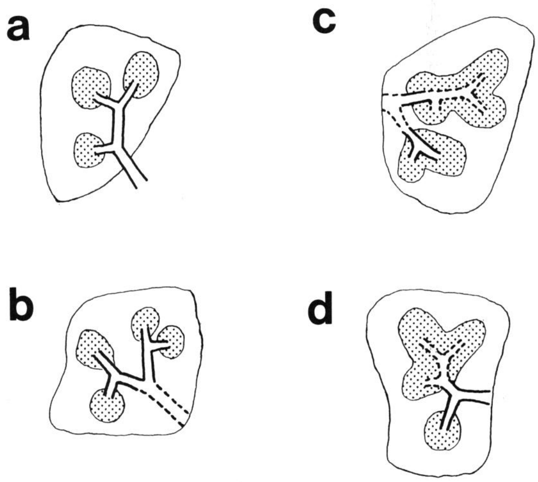

Fig. 4 The relationship between the lesion and the bronchial branching system within secondary lobules by three dimensional analysis of lobule a-d (in Fig. 3). The basic lesions are located in the centriacinar area which surrounds the terminal bronchiole and respiratory bronchioles. The distribution pattern of these centriacinar nodules corresponds to the bronchial branching pattern.

that corresponds to the bronchial branching pattern.

3·1·2 Bronchopneumonia

The radiographs of the specimen with bronchopneumonia showed multiple fluffy nodular shadows and their coalescences. Histopathologic findings of the lesions demonstrated intraalveolar infiltration by polymorphonuclear leukocytes and exudate (Fig. 5). There were 3 to 5 basic nodular lesions in each lobule, and they were located in the peribronchiolar or centriacinar area of each acinus which was approximately 6-10 mm in diameter. The distribution pattern of the lesions in bronchopneumonia also had a regularity that corresponds to the bronchial branching pattern. It was essentially the same pattern as that in endobronchial tuberculosis.

3·2 Hematogenous spread lesions

3·2·1 Miliary tuberculosis

The radiographs of the specimens with miliary tuberculosis showed multiple nodular shadows. Histopathologic findings of the lesions demonstrated tuberculous nodules with caseous necrosis (Fig. 6). In contrast to endobronchial tuberculosis, the lesions were randomly distributed and had no relation to

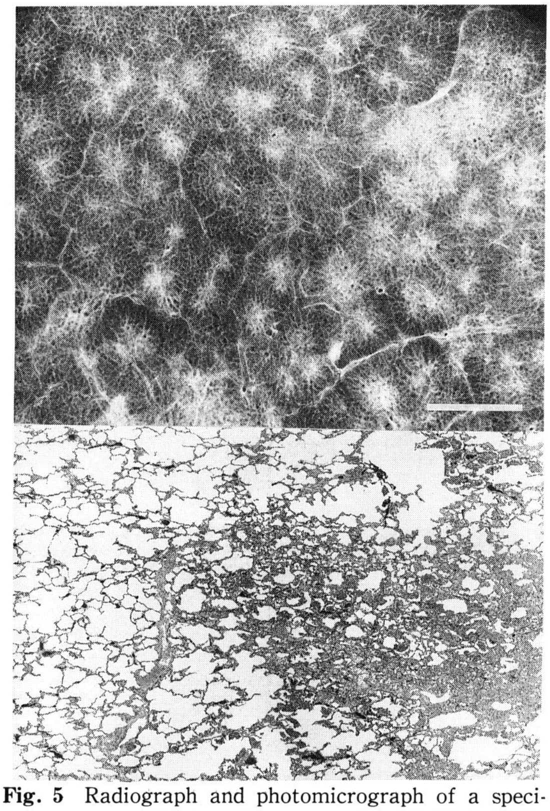

Fig. 5 Radiograph and photomicrograph of a specimen with bronchopneumonia. Multiple fluffy nodular shadows and their coalescences are shown on radiograph (white bar represents 10 mm). The lesions are located in the peribronchiolar or centriacinar areas of each acinus which is approximately 6-10 mm in diameter. The distribution pattern of the lesions corresponds to the bronchial branching pattern. A microscopic section (H & E. 10×) demonstrates intraalveolar infiltration by polymorphonuclear leukocytes and exudate in the peribronchiolar area.

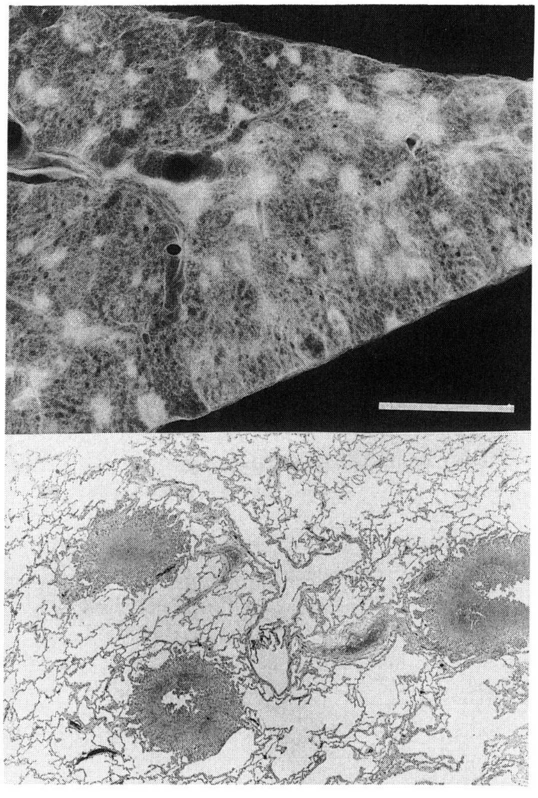

Fig. 6 Radiograph and photomicrograph of a specimen with miliary tuberculosis. Multiple nodular shadows are shown on radiograph (white bar represents 10 mm). A microscopic section (H & E, 10×) demonstrates three tuberculous nodules with caseous necrosis. In contrast to endobronchial tuberculosis, the lesions are randomly distributed and have no relation to the bronchial branching pattern.

the bronchial branching system. For example, some lesions were located in contact with pleura or interlobular septi. Both cases of miliary tuberculosis showed similar radiographic findings.

3·2·2 Hematogenous metastasis of lung carcinoma

The radiographs of the specimen with hematogenous metastasis of pulmonary adenocarcinoma showed multiple nodular shadows. Histopathologic findings of the lesions demonstrated neoplastic cells growing along the alveolar walls and thickening of the alveolar septi (Fig. 7). The lesions showed a randomly distributed pattern similar to miliary tuberculosis and also had no relation to the bronchial branching pattern.

4. DISCUSSION

Chest radiography has been widely used in image diagnosis of diffuse lung disease. However the analysis of radiologic-pathologic correlation on radiographs has been limited to the shape, size and imprecise distribution of shadows because of superimposition.

Recently the diagnostic value of CT in peripheral lung disorder has been reported[1)2)5)6)]. CT can provide a thin-section image without superimposition, and its contrast resolution is inherently higher than that of conventional radiographs. It is easier to recognize peripheral lung structures by CT than by radiographs. Additionally, detailed CT-pathologic correlative studies[3)~6)], which clarified the relationship between lesions and peripheral lung structures, have provided useful knowledge for interpreting CT images. Itoh *et al*[3)~5)]. reported that CT can be valuable for localization of pathologic change within the acinus or secondary lobule. Murata *et al*[6)]. also reported the classification of parenchymal abnormalities on CT based on secondary lobular structure.

The relationship between the lesions and lung structures reflects various pathological conditions. However, the analysis of the factors which influences this relationship has not been satisfactory, so we analyzed the difference in the relation-

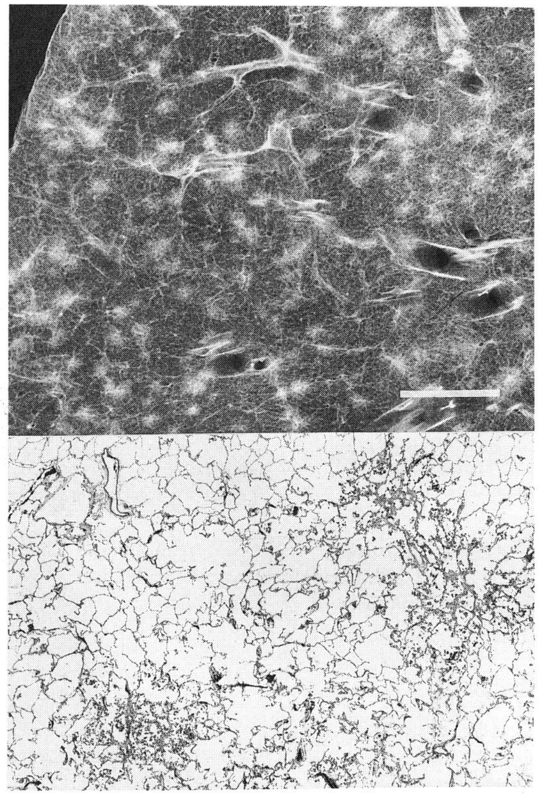

Fig. 7 Radiograph and photomicrograph of a specimen with hematogenous metastasis of lung carcinoma. Multiple nodular shadows are shown on radiograph (white bar represents 10 mm). A microscopic section (H & E, 10×) demonstrates neoplastic cells growing along the alveolar walls and thickening of the alveolar septi. The lesions have no relation to bronchial branching and are randomly distributed same as in miliary tuberculosis.

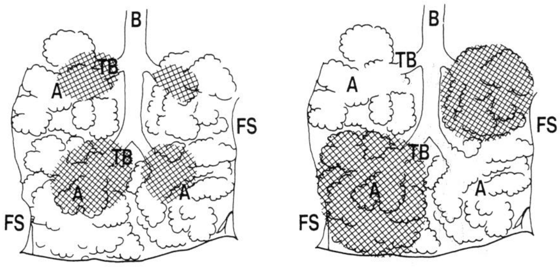

Fig. 8 Concepts of centriacinar lesion (left) and acinar shadow (right)[7)]. Acinar shadow on chest radiography is defined by size and shape, for example, a poorly marginated spherical lesion ranging from 4-10 mm, whereas centriacinar lesion on CT is defined by the relation to the lung structure.

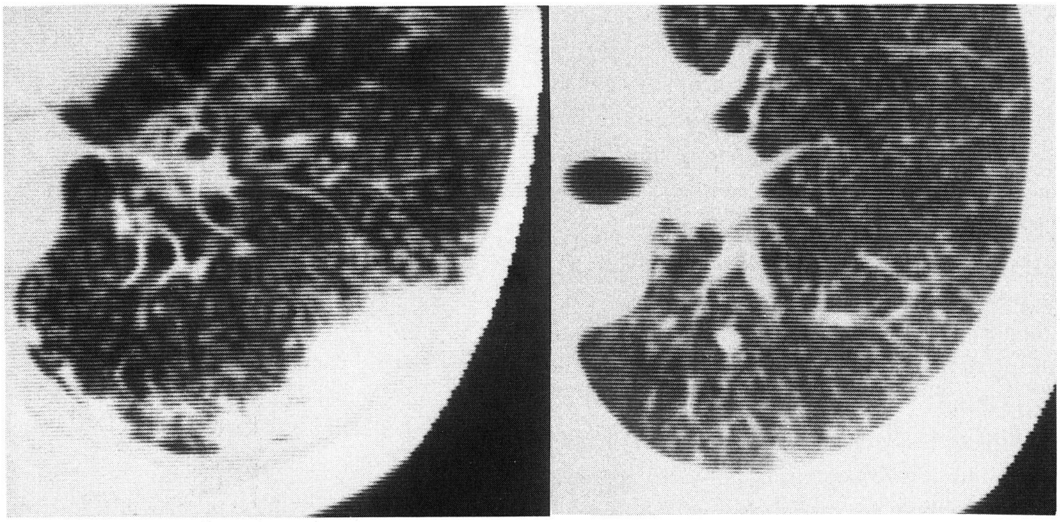

Fig. 9 CT images of cases with endobronchial tuberculosis (left) and miliary tuberculosis (right). CT image of endobronchial tuberculosis shows disseminated small nodules. Their distribution pattern has a regularity that corresponds to the bronchial branching pattern. On the other hand, CT image of miliary tuberculosis shows randomly distributed multiple small nodules.

ship between lesions and lung structures in bronchogenous spread and hematogenous spread lesions.

The bronchogenous spread lesions which were seen in endobronchial tuberculosis and bronchopneumonia were located in the centriacinar portion of the secondary lobule. Their distribution pattern had a regularity that corresponds to the bronchial branching pattern. Murata *et al*[5]. defined the centrilobular region on high-resolution CT (HRCT) images as an area surrounding the most visible peripheral branch of the pulmonary artery, which is located 3-5 mm away from the adjacent lobular border. They reported[5)6)] that centrilobular disease was characterized by ill-defined areas of increased attenuation in the centrilobular region on HRCT. Our study additionally emphasized that disseminated centriacinar or centrilobular nodules reveal a regular distribution pattern that corresponds to the bronchial branching pattern. Centriacinar or centrilobular lesions, that are not identifiable on radiographs, can be recognized by CT owing to more precise image analysis. The acinar shadow[11)], which is a traditional concept used for radiographs, is defined by size and shape, whereas centriacinar lesion which is defined by the relation to the lung structures is a new concept in CT (Fig. 8)[7)].

On the other hand, the hematogenous spread lesions which were seen in miliary tuberculosis and hematogenous metastasis of lung carcinoma had no relation to the airway structures. They were randomly distributed regardless of bronchial branching.

These differences in distribution patterns can be recoingzed with CT images of the in vivo lung. Fig. 9 shows CT images of patients with endobronchial tuberculosis and miliary tuberculosis. CT images demonstrated the difference of distribution pattern of nodules between endobronchial tuberculosis and miliary tuberculosis[7)].

Recognition of the distribution pattern of nodules on CT, in addition to directly locating individual nodules within the secondary lobules, is helpful to understand the relationship between the lesions and the airway structures. It leads to a better understanding of the CT appearance of diffuse lung disease.

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肺における散布性粒状病変の分布パターン

―気道散布性病変と血行散布性病変のX線病理学的研究―

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6例の剖検肺の伸展固定標本を用いて，病変と気道系との関係から，肺の散布性粒状病変のX線学的分布パターンを分析した．気道散布性結核及び気管支肺炎にみられる気道散布性病変は，小葉内の細葉中心部に認められ，その分布は気管支の分岐パターンに一致した規則的な分布を示した．一方，粟粒結核や癌の肺転移にみられる血行散布性病変は，気管支とは無関係なランダムな分布を示した．この二つの分布パターンの違いを認識することはCTによるびまん性肺疾患の評価に際して重要である．