Accuracy of High-Resolution CT in Diagnosing Lung Diseases

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OBJECTIVE. The purpose of our study was to determine if high-resolution CT facilitates the diagnoses of three diseases that cause cystic air spaces in the lungs: pulmonary eosinophilic granuloma, pulmonary lymphangiomyomatosis, and emphysema.

MATERIALS AND METHODS. Retrospective review of high-resolution CT findings in patients with pathologically proven pulmonary eosinophilic granuloma (n = 10), pulmonary lymphangiomyomatosis (n = 9), and emphysema (n = 10) and five control patients without cystic air spaces was conducted by two thoracic radiologists unaware of the pathologic diagnosis. After reviewing the scans, the radiologists made a diagnosis and indicated their level of confidence in the diagnosis on a three-point scale.

RESULTS. High-resolution CT allowed the two radiologists to be confident of the diagnosis of pulmonary eosinophilic granuloma in 84% of CT scans, lymphangiomyomatosis in 79%, and emphysema in 95%. When confident, the observers were correct in 100% of the cases. Agreement between observers was good for confident diagnoses based on high-resolution CT scans of pulmonary eosinophilic granuloma (κ = .77), lymphangiomyomatosis (κ = .88), and emphysema (κ = 1). Distribution of cystic changes differed on high-resolution CT scans for lymphangiomyomatosis and pulmonary eosinophilic granuloma. No consistent distribution pattern was observed for emphysema. Lack of a perceptible cyst wall was unique to cases of emphysema. All patients with lymphangiomyomatosis lacked nodules in the intervening lung parenchyma, whereas most patients with pulmonary eosinophilic granuloma had parenchymal nodules.

CONCLUSION. High-resolution CT can help radiologists reliably diagnose pulmonary eosinophilic granuloma, lymphangiomyomatosis, and emphysema.

Several diseases cause cystic or cystlike lung parenchyma abnormalities, including pulmonary eosinophilic granuloma, lymphangiomyomatosis, emphysema, end-stage interstitial lung disease, and cystic bronchiectasis [1]. Interstitial lung disease and cystic bronchiectasis have characteristic appearances and distributions that distinguish them from other diseases [1]. Overlapping clinical and radiographic features among pulmonary eosinophilic granuloma, lymphangiomyomatosis, and emphysema, however, can make differentiation of these diseases difficult [2–5].

Pulmonary eosinophilic granuloma is a lung disease of unknown cause characterized by lung infiltrates composed of Langerhans' histiocytes [6, 7]. A strong association with cigarette smoking exists [6, 8]. Lymphangiomyomatosis is a rare disease characterized by progressive proliferation of atypical smooth muscle cells in the walls of lymphatic vessels, bronchioles, and small pulmonary vessels [4, 5]. The disease is seen almost exclusively in women of childbearing age. Emphysema is a common lung disease; cigarette smoking is a major causative factor in the development of centrilobular emphysema, the most common subtype [9–11].

Pulmonary eosinophilic granuloma and lymphangiomyomatosis both cause lung parenchyma cysts, which are defined as air-containing lesions surrounded by a thin wall that is not shared. Emphysema produces cystlike changes in the lung parenchyma due to destruction of the alveolar walls, with resultant increase in the size of air spaces distal to terminal bronchioles [9–11].

Experience with high-resolution CT (HRCT) over the past several years has established its usefulness in defining the characteristic features

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of a variety of diffuse interstitial pulmonary diseases [12, 13]. For many of these diseases, the features shown on HRCT correlate well with the gross and histopathologic abnormalities. Therefore, HRCT can be used to diagnose certain pulmonary diseases without also obtaining a tissue specimen. Conventional CT and HRCT findings for pulmonary eosinophilic granuloma, lymphangiomyomatosis, and emphysema have been described previously [3, 4, 14–18]. Many authors speculate on distinguishing characteristics seen on HRCT, although the cystic changes caused by these diseases may be indistinguishable, particularly with regard to lymphangiomyomatosis and pulmonary eosinophilic granuloma [4, 14, 17]. Müller et al. [4] point out that pulmonary eosinophilic granuloma might be distinguished from lymphangiomyomatosis on the basis of cyst distribution and presence of parenchymal nodules rather than on the basis of features of the cysts themselves, although no studies to date have directly examined this. The purpose of our study was to determine if radiologists' interpretation of HRCT scans can reliably distinguish between pulmonary eosinophilic granuloma, lymphangiomyomatosis, and emphysema in pathologically proven cases and to determine which features shown on HRCT were consistently helpful in the differentiation. To our knowledge, this is the first study to assess how accurately these three pulmonary diseases can be identified using HRCT and to determine what features seen on HRCT are useful in making diagnoses.

Materials and Methods

A computerized search of records of patients with a clinical diagnosis of pulmonary eosinophilic granuloma or lymphangiomyomatosis was performed for the period 1987–1995, and the patients' charts were reviewed. Of the 103 cases of pulmonary eosinophilic granuloma and 32 cases of lymphangiomyomatosis found, 10 patients with pulmonary eosinophilic granuloma and nine patients with lymphangiomyomatosis had undergone chest HRCT and had corresponding pathologic proof of pulmonary disease. A similar search and review of the records of 920 patients with a clinical diagnosis of emphysema identified only 10 patients with suitable chest HRCT (HRCT scans at three levels or more) and corresponding pathologic proof. The scans of five patients whose chest HRCT findings were normal were added as control subjects.

Pathologic diagnosis was confirmed by open-lung biopsy in 12 patients, transbronchial biopsy in seven patients, autopsy in one patient, and from the analysis of the surgical specimen from lung-volume reduction surgery in nine patients (all with emphysema). On average, the pathologic diagnosis was made within 6 months of the first HRCT scan (range, 1 day–40 months).

Clinical information including age, sex, date and type of biopsy, and date of HRCT scans were recorded for each patient. The mean age for patients with pulmonary eosinophilic granuloma was 36 (range, 24–46); with lymphangiomyomatosis, 42 (range, 21–62); and with emphysema, 59 (range, 37–70). The mean age for the control subjects was 47 (range, 40–55). All the patients with lymphangiomyomatosis were women; 40% of the patients with pulmonary eosinophilic granuloma and emphysema were women. Sixty percent of the control subjects were women.

Radiologic Evaluation

Because the study was retrospective, the imaging protocol was not standardized, and a variety of CT scanners were used. HRCT scans (1.0- to 1.5-mm collimation with high-spatial-frequency reconstruction algorithm) were obtained every 10 mm in 19 patients. In five patients, HRCT scans were obtained every 2 cm. In five patients with emphysema, HRCT scans were obtained at the level of the aortic arch, tracheal carina, and 1 cm above the diaphragm. In the five control patients, HRCT scans were obtained every 10 mm. All CT scans, both conventional and high-resolution, were available to the observers. No clinical information was available except the age and sex of the patients, which was included on many of the HRCT scans. IV contrast material was not used for any of the scans.

Two experienced thoracic radiologists independently reviewed the studies without being aware of the pathologic diagnosis. They made diagnoses and rated their level of confidence in those diagnoses on a three-point scale (definite, probable, possible), where definite represented the highest degree of confidence [19]. Diagnoses were based on the typical appearance of lymphangiomyomatosis and emphysema as previously described in the literature [1, 3, 10, 11, 16–18].

The radiologists recorded the following features seen on HRCT for each study: cyst configuration (rounded, lobulated, or confluent), cyst wall appearance (not identifiable; thin, <1 mm; or thick, ≥1 mm), and the location of vascular structures (central, within the cystic space; or noncentral, peripherally located). The distribution of disease was visually estimated and recorded for the following lung regions: apex to aortic arch, aortic arch to inferior pulmonary vein, inferior pulmonary vein to top of lower diaphragm, and extreme base (the lowest level). Extent of involvement was defined as normal (no evidence of disease), less than 30% involvement, 30–60% involvement, or greater than 60% involvement. Other findings, including parenchymal nodules, pleural and pericardial fluid, pneumothorax, and skeletal lesions, were recorded if present.

Statistical Analysis

The chi-square test was performed to compare the HRCT features of each disease. Agreement between the two observers for the diagnosis made with the highest level of confidence was assessed using the kappa statistic [20].

Results

Accuracy of HRCT Diagnosis

All 10 cases of pulmonary eosinophilic granuloma and nine cases of lymphangiomyomatosis were correctly identified by one of the radiologists. The second radiologist identified all cases of lymphangiomyomatosis and nine of 10 cases of pulmonary eosinophilic granuloma correctly, incorrectly diagnosing one case as lymphangiomyomatosis. The mistaken case had cystic changes extending into the lung bases and lacked parenchymal nodules. One radiologist misread as normal a scan showing emphysema with minimal disease in the upper lungs. The second radiologist made the correct diagnosis of emphysema in this case but with an intermediate (probable) level of confidence. The scans of the control subjects were correctly identified by both radiologists. No cases of lymphangiomyomatosis or pulmonary eosinophilic granuloma were mistaken for emphysema or normal by either observer. No cases of emphysema were confused with lymphangiomyomatosis or pulmonary eosinophilic granuloma.

An average 88% of the time, a high degree of confidence (definite) was reached in HRCT scans. The observers were confident in their diagnoses of 84% of the HRCT scans showing pulmonary eosinophilic granuloma, and when confident were correct in 100%. The observers were confident in their diagnoses of 79% of the HRCT scans showing lymphangiomyomatosis, and when confident were correct in 100%. Similarly, the radiologists were confident in their diagnoses of 95% of HRCT scans showing emphysema, and when confident were correct in 100%. All diagnoses of scans showing normal findings were definite, but because one observer interpreted a scan showing emphysema as normal, the average percentage correct was 91%. Agreement was good between observers for confident (definite) diagnoses based on HRCT scans of pulmonary eosinophilic granuloma ($\kappa = .77$), lymphangiomyomatosis ($\kappa = .88$), and emphysema ($\kappa = 1$), as well as for confident diagnoses in the study overall ($\kappa = .89$).

HRCT Features

Distribution of disease involvement and HRCT features in patients with pulmonary eosinophilic granuloma, lymphangiomyomatosis, and emphysema are listed in Tables 1 and 2, respectively. All cases of lymphangiomyomatosis involved the lung diffusely, with disease involving the costophrenic angles equally (Fig. 1). Of the cases of pulmonary eosinophilic granuloma, none of the HRCT

TABLE 1 Distribution of Disease in 29 Patients as Shown by High-Resolution CT

Pattern of Involvement	Disease		
	Pulmonary Eosinophilic Granuloma	Lymphangiomyomatosis	Emphysema
Diffuse[a]	0	9 (100%)	5 (50%)
Diffuse with upper lung predominance[b]	1 (10%)	0	2 (20%)
Diffuse with lower lung predominance	0	0	0
Lung bases spared[c]	9 (90%)	0	2 (20%)
Upper lung spared[d]	0	0	1 (10%)

[a] Equal extent of disease, including costophrenic angles.
[b] Equal extent of disease until costophrenic angles. Disease at costophrenic angles <30%.
[c] Tapered pattern of involvement between regions 2 and 3 with no involvement of the bases. Region 2 = aortic arch to inferior pulmonary vein. Region 3 = inferior pulmonary vein to top of lower hemidiaphragm.
[d] Normal or <30% involvement, regions 1 and 2. Region 1 = apex to aortic arch.

scans showed disease equally distributed at all levels. The lung bases were completely spared in nine patients (Fig. 2). One case of pulmonary eosinophilic granuloma had involvement of the costophrenic angles but involved the upper lung predominantly (Fig. 3). The extent of disease at the level of the costophrenic angles was significantly less than the disease in the rest of the lung in this case.

No significant differences in the characteristics of the predominant cysts were noted between pulmonary eosinophilic granuloma and lymphangiomyomatosis regarding the cyst configuration, thickness of cyst wall, or location of vascular structures. No scans of lymphangiomyomatosis showed nodules in the intervening lung parenchyma, whereas seven of 10 scans of pulmonary eosinophilic granuloma showed these findings.

Only HRCT scans of emphysema showed the lack of a perceptible cyst wall. Lymphangiomyomatosis and pulmonary eosinophilic granuloma both showed thin cyst walls. The cyst configuration in emphysema was more likely to be lobulated, large, and confluent than the other disease entities were (Fig. 4). Similarly, vascular structures tended to be central in cases of emphysema and noncentral in lymphangiomyomatosis and pulmonary eosinophilic granuloma. No consistent pattern of distribution was observed in the case of emphysema.

In our series, one patient with lymphangiomyomatosis had a left apical pneumothorax. This finding did not help to distinguish it from the other two diseases. No patient in our series had skeletal lesions or pleural or pericardial effusions.

TABLE 2 High-Resolution CT Features in 29 Patients with Pulmonary Eosinophilic Granuloma, Lymphangiomyomatosis, or Emphysema

Features	Number (%) of Scans		
	Pulmonary Eosinophilic Granuloma (n = 10)	Lymphangiomyomatosis (n = 9)	Emphysema (n = 10)
"Cyst" configuration[a]			
Rounded	7 (70)	9 (100)	2 (20)
Lobulated	3 (30)	0	8 (80)
Confluent	2 (20)	0	8 (80)
Discrete	8 (80)	9 (100)	2 (20)
Small (<10 mm)	5 (50)	6 (67)	2 (20)
Medium (10–20 mm)	5 (50)	3 (33)	0
Large (>20 mm)	0	0	8 (80)
"Cyst" wall[a]			
Imperceptible	0	0	10 (100)
Thin (<1 mm)	10 (100)	9 (100)	0
Thick (≥1 mm)	0	0	0
Vascular structures			
Central	0	0	8 (80)
Noncentral	10 (100)	9 (100)	2 (20)
Other findings			
Parenchymal nodules[b]	7 (70)	0	0

[a] Not significant. Chi-square lymphangiomyomatosis versus pulmonary eosinophilic granuloma.
[b] In four patients with pulmonary eosinophilic granuloma, parenchymal nodules were the predominant manifestation of the disease.

Discussion

Pulmonary eosinophilic granuloma, lymphangiomyomatosis, and emphysema are three lung diseases producing cystic or cystlike parenchymal changes that can be seen on HRCT scans. The HRCT appearance of the parenchymal cysts in pulmonary eosinophilic granuloma and lymphangiomyomatosis can be virtually identical, although some authors believe that bizarre, irregularly shaped cysts are more common in pulmonary eosinophilic granuloma [21]. The range of cyst sizes observed is also similar for these two diseases, commonly in the range of 10 to 20 mm but possibly up to several centimeters [14, 15, 17, 18]. In contrast to emphysema, the cysts in these two diseases have perceptible walls. Wall thickness varies, ranging from almost imperceptible to a few millimeters thick [14, 15, 17, 18], although in our study all were less than 1 mm. The cystlike changes due to emphysema are seen on HRCT scans as rounded areas of low attenuation without perceptible walls and with a central location of vascular structures [10, 11]. With advanced disease, the air space changes become more confluent.

In this study, both observers arrived at a confident diagnosis on the basis of predominant findings in 88% of the HRCT scans. When the radiologists were confident in their diagnosis, they correctly identified pulmonary eosinophilic granuloma, lymphangiomyomatosis, and emphysema 100% of the time.

In this group of patients, the most useful discriminating factor between pulmonary eosinophilic granuloma and lymphangiomyomatosis was the distribution of the cystic changes. The presence or absence of parenchymal nodules between the cysts also helped distinguish the two. The HRCT features of the cysts themselves did not help identify the disease. Several authors have previously alluded to the fact that pulmonary eosinophilic granuloma and lymphangiomyomatosis can be distinguished by the distribution of the cystic changes [3, 4, 14,

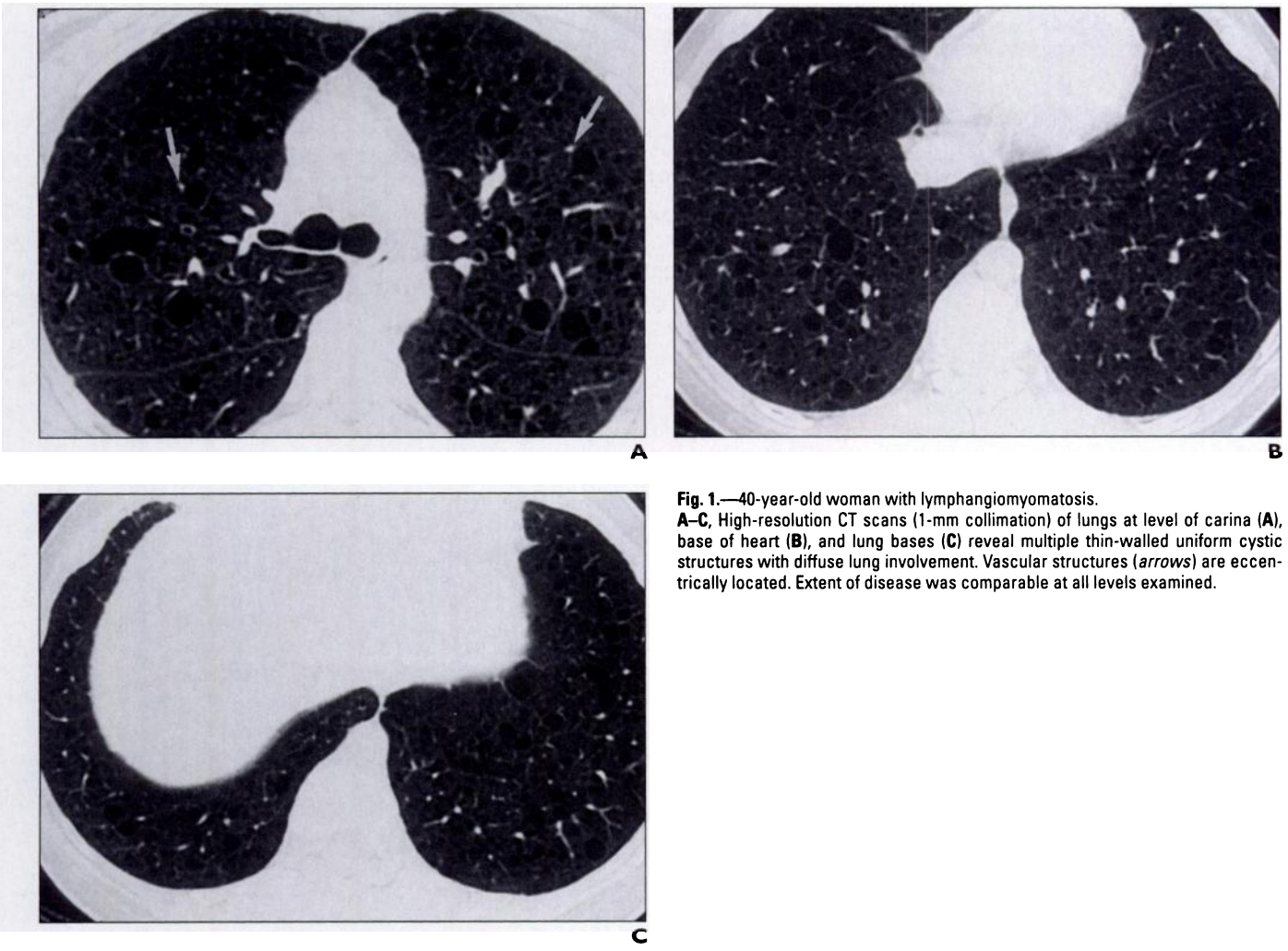
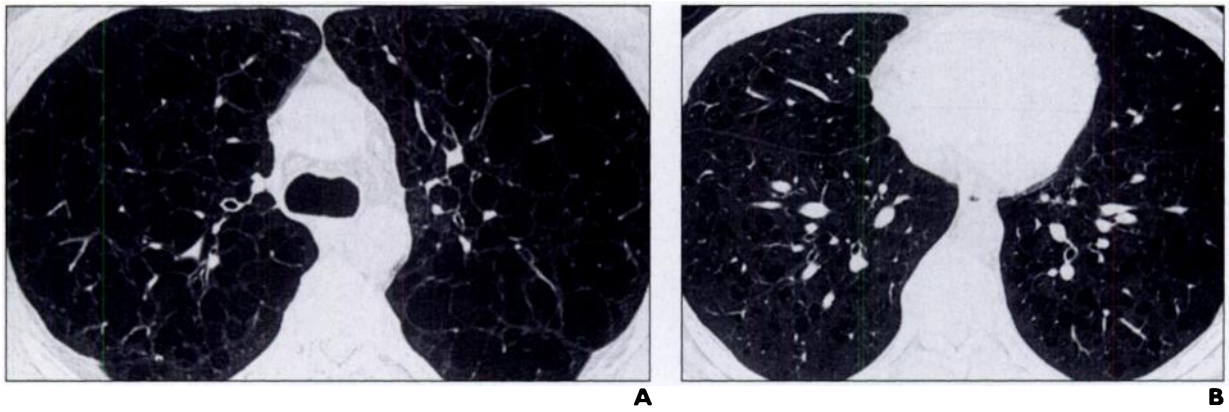


Fig. 1.—40-year-old woman with lymphangiomyomatosis.
A–C, High-resolution CT scans (1-mm collimation) of lungs at level of carina (**A**), base of heart (**B**), and lung bases (**C**) reveal multiple thin-walled uniform cystic structures with diffuse lung involvement. Vascular structures (*arrows*) are eccentrically located. Extent of disease was comparable at all levels examined.

17]. Specifically, pulmonary eosinophilic granuloma has an upper-lung predominance and tends to spare the costophrenic angles, whereas lymphangiomyomatosis involves the entire lung diffusely. Our study supports this contention. In our study, all patients with lymphangiomyomatosis had diffuse lung involvement to an equal extent at all levels. In contrast, nine of 10 patients with pulmonary eosinophilic granuloma lacked disease involvement of the costophrenic angles, and most of these patients had a tapering pattern of lung involvement, with the greatest involvement in the upper lungs. One patient with pulmonary eosinophilic granuloma had involvement of the costophrenic angles, although to a significantly lesser extent than in the remainder of the lungs. This case was misdiagnosed as lymphangiomyomatosis by one radiologist partly because of cystic changes in the lung bases and the absence of parenchymal nodules. Because of the atypical features, neither radiologist categorized the diagnosis as definite, however. Thus, the absence of disease at the level of the costophrenic angles is useful in differentiating pulmonary eosinophilic granuloma from lymphangiomyomatosis; however, the presence of disease at this level does not preclude a diagnosis of pulmonary eosinophilic granuloma. In cases of disease involving the costophrenic angles, the distribution throughout the entire lung must be examined. Pulmonary eosinophilic granuloma will have a relative decrease in involvement of the lung bases, while in lymphangiomyomatosis involvement is uniform throughout the entire lung. It is therefore important to obtain scans of the lungs in the costophrenic angle region, placing the patient prone if necessary.

Parenchymal nodules, when present, are also helpful in distinguishing pulmonary eosinophilic granuloma from lymphangiomyomatosis. Other authors have suggested that a diagnosis of pulmonary eosinophilic granuloma is certain if nodules are present in the lung parenchyma between the cysts [14, 15, 18]. Parenchymal nodules have not been identified with lymphangiomyomatosis, and none were present in any patient with lymphangiomyomatosis in this study. However, parenchymal nodules are not always present in pulmonary eosinophilic granuloma. Nodules were absent in two of 10 patients with pulmonary eosinophilic granuloma in our series. Similarly, Moore et al. [3] reported three of 13 patients in their series of pulmonary eosinophilic granuloma with cysts only, and Brauner et al. [14] reported four of 18 patients with only cysts. Thus, in those instances of pulmonary eosinophilic granuloma in which parenchymal nodules are absent, scans showing the distribution of the cystic changes should aid in the diagnosis.

Cyst configuration may help distinguish pulmonary eosinophilic granuloma from lymphangiomyomatosis when the predominant findings consist of lobulated cyst contour, bi-



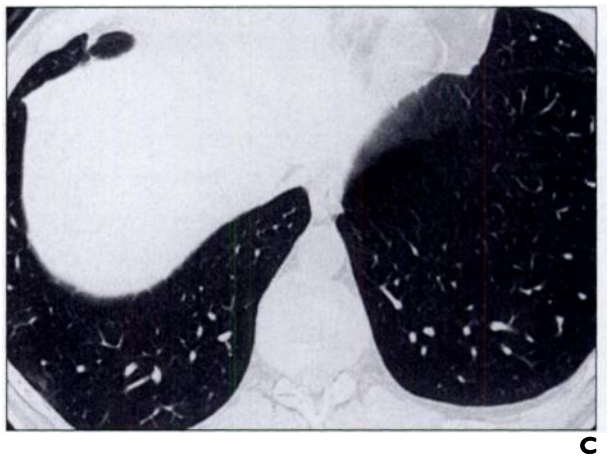


Fig. 2.—23-year-old man with pulmonary eosinophilic granuloma.
A–C, High-resolution CT scans (1-mm collimation) of lungs at level of carina (**A**), base of heart (**B**), and lung base (**C**) reveal multiple thin-walled cystic structures involving lungs, with sparing of lung bases. In **A**, many cysts are confluent and superficially resemble emphysema. Note, however, presence of discrete cyst walls and eccentric location of vascular structures. No lung parenchymal nodules are visible. Note similarity of cyst morphology to lymphangiomyomatosis in **B**.

zarre shapes, or confluence of the cysts. These types of cysts were present in a minority of patients with pulmonary eosinophilic granuloma in our study. Most patients with pulmonary eosinophilic granuloma, like patients with lymphangiomyomatosis, had predominantly rounded discrete cyst configurations. Thus, in our study, cyst configuration was not as useful in identifying pulmonary eosinophilic granuloma as distribution or parenchymal nodules.

Emphysema could be reliably distinguished from pulmonary eosinophilic granuloma or lymphangiomyomatosis by the cystic lung changes seen on HRCT. The most important distinguishing features were the lack of a perceptible cyst wall and the central location of vascular structures. Our findings are not unexpected because other authors have suggested

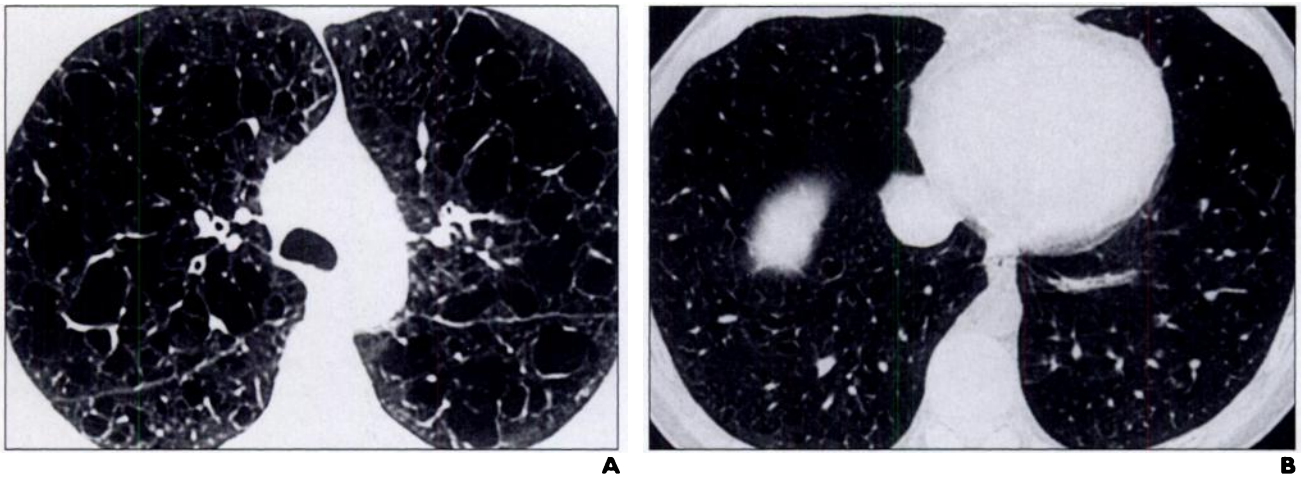


Fig. 3.—36-year-old woman with pulmonary eosinophilic granuloma.
A and **B**, High-resolution CT scan (1-mm collimation) of lungs. Scans at level of aortic arch (**A**) and lung base (**B**) show cystic changes present throughout lungs, including lung bases. However, upper lungs are involved to greater extent. Note superficial resemblance to lymphangiomyomatosis with cyst changes throughout lungs (including lung bases) and absence of parenchymal nodules.

Fig. 4.—63-year-old man with emphysema.
High-resolution CT scan (1-mm collimation) of lungs at level of lower trachea shows lungs involved with cystic process. No discrete cyst walls are seen. Note central location of vascular structures (*arrows*).

that cyst morphology might be a useful discriminating factor among emphysema, lymphangiomyomatosis, and pulmonary eosinophilic granuloma [10, 14, 18]. One possible pitfall could arise when diagnosing end-stage forms of either pulmonary eosinophilic granuloma or lymphangiomyomatosis, in which large confluent cysts mimicking bullae could potentially be mistaken for emphysema [14, 15, 17]. Distribution of the cystic changes was not helpful in distinguishing emphysema from pulmonary eosinophilic granuloma or lymphangiomyomatosis.

One limitation of our study is the small number of patients in each group. This small number is due in part to the fact that pulmonary eosinophilic granuloma and lymphangiomyomatosis are rare diseases and to the fact that few of the patients who underwent HRCT for emphysema had corresponding pathologic proof of disease. Not many patients fulfilled our requirement of definitive pathologic proof from open-lung or transbronchial biopsy in addition to HRCT scans. Our study is biased toward the more advanced stages of emphysema because of the lack of patients with less advanced emphysema who underwent HRCT and had subsequent correlative autopsy or pathologic proof. Thus, most patients with emphysema (nine of 10) had advanced disease and had undergone HRCT in preparation for lung-volume reduction surgery. In addition, the retrospective nature of this review precluded uniformity in scan technique.

In conclusion, when the radiologists' diagnoses were definite, a reliable distinction could be made among pulmonary eosinophilic granuloma, lymphangiomyomatosis, and emphysema. Certain features seen on HRCT allowed accurate distinction among these three diseases in the patients studied. HRCT features that aid in distinguishing pulmonary eosinophilic granuloma from lymphangiomyomatosis include distribution of the cystic changes and presence of parenchymal nodules. Distribution was the most important discriminating factor because parenchymal nodules were not always present. Particular attention should be paid to the lowermost (costophrenic angle) HRCT scans because the costophrenic angles are spared or have minimal disease compared with the rest of the lung in patients with pulmonary eosinophilic granuloma. Emphysema can be reliably distinguished from pulmonary eosinophilic granuloma or lymphangiomyomatosis by cyst features that can be identified on HRCT, including lack of a perceptible wall and central location of vascular structures. HRCT is a useful adjunct in the diagnosis of cystic pulmonary diseases and can preclude more invasive diagnostic steps.

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