# Simple Pulmonary Eosinophilia (Loeffler's Syndrome):
## Chest Radiographic and CT Findings[1]

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**Purpose :** The purpose of our study is to describe the chest radiographic and CT findings of simple pulmonary eosinophilia.

**Materials and Methods :** Twenty-six patients with simple pulmonary eosinophilia underwent chest radiography and CT scanning; the results were analyzed retrospectively by two chest radiologists, focusing on the patterns and distribution of the parenchymal abnormalities.

**Results :** The chest radiographs were normal in eight patients (31%), while among the remaining 18 patients, they showed subtle opacity (n= 9), nodules (n= 8), consolidation (n= 2), and mass (n= 1). Follow-up chest radiographs (n= 18) demonstrated complete (n= 16) or partial (n= 1) resolution of parenchymal lesions or migratory lesions (n= 1). On CT, nodule(s) (n= 19) were most commonly seen, followed by ground-glass opacity (n= 16), consolidation (n= 3), and mass (n= 1). A peripheral halo surrounding a nodule or an area of consolidation was seen in 18 patients. The nodules(s) (n= 19) were subpleural (n= 13) or random (n= 6). Areas of ground-glass opacity (n= 16) were subpleural (n= 13), random (n= 2), or central (n= 1). All lesions were patchy rather than diffuse. Follow-up CT in nine patients showed complete (n= 7) or partial (n= 2) resolution of parenchymal lesions.

**Conclusion :** Chest radiographs of patients with simple pulmonary eosinophilia often reveal no abnormality. The most common finding is subtle opacity or nodule(s), while CT reveals transient nodule(s) with a surrounding halo or transient areas of ground-glass opacity.

**Index words :** Lung, abnormalities
Lung, CT
Lung, diseases
Lung, nodule
Pneumonia, eosinophilic

Simple pulmonary eosinophilia, also known as Loeffler's syndrome, is characterized by the presence on chest radiographs of transient or migratory pulmonary abnormalities, and by peripheral eosinophilia, minimal or no pulmonary symptoms, and rapid spontaneous resolution (1-5). Pathologically, eosinophils and histiocytes accumulate in alveolar spaces and on alveolar walls (1-4, 6).

Chest radiographic findings of the disease have been described in several reports; most commonly, unilateral or bilateral nonsegmental areas of consolidation are seen, and these are usually transient and migratory (1, 3, 5). The CT findings of the disease have not, however, been well described. The purpose of this study is to describe both the radiographic and CT findings of simple pulmonary eosinophilia.

## Materials and Methods

Between August 1994 and October 1998, 49 consecutive patients with simple pulmonary eosinophilia were diagnosed at our institution. Inclusion criteria (1, 2) for the diagnosis of simple pulmonary eosinophilia were peripheral eosinophilia with peripheral blood eosinophil counts greater than 500 cells/microliter (ranging from a 6.7 to 72 percent of white blood corpuscle count [540 to 28,706 cells/microliter]) and positive findings of parenchymal abnormalities on chest radiographs (n= 43) or CT scans (n= 26). Both chest radiographic and CT studies of the thorax were available for 26 of these 49 patients . There were 19 men and seven women whose ages ranged from 18 to 74 years (mean, 46 years). CT scans were obtained within one to 13 (median, 7 ) days of chest radiographs. After a detailed and rigorous review of the patients' medical records (including the two whose imaging studies were obtained in outside institutions), the possibility that the pulmonary lesions were caused by the use of certain drugs or by parasitic infestations was discounted. All drugs used for chemotherapy were evaluated for potential causes of eosinophilia, but none were related to peripheral blood eosinophilia. No patient had a history of asthma. Cases satisfying the diagnostic criteria of acute eosinophilic pneumonia (n= 6), chronic eosinophilic pneumonia (n= 3) and idiopathic hypereosinophilic syndrome (n= 4) were also excluded (1, 2).

Only seven patients (27 %) complained of mild chest pain (n= 3), dyspnea (n= 3), or cough (n= 2), while the remaining 19 (73 %) were symptom-free. No patient underwent treatment for the alleviation of symptoms related to simple pulmonary eosinophilia.

The indications of CT scans in these patients were as follows: evaluation of patchy areas of consolidation or subtle opacity on chest radiographs (n= 10); evaluation of the nature of solitary pulmonary nodule or mass seen on chest radiographs (n= 7); staging work-up or follow-up evaluation of underlying malignancy (n= 7) or benign lymph node disease (n= 2). The identified underlying malignancies (n= 7) included lung cancer in four patients and primary lymphoma (mucosa-associated lymphoid tissue origin) of the stomach, breast cancer, and squamous cell carcinoma of the buccal mucosa, each in one patient. Benign lymph node diseases included Kimura's disease (angiolymphoid hyperplasia with eosinophilia) and sarcoidosis, each in one. In all patients, CT scans were obtained before the peripheral eosinophil count was known. Peripheral eosinophilia was present a week before and after the time of initial CT, and as the causes of eosinophilia were not clear, patients with underlying diseases were diagnosed as having simple pulmonary eosinophilia.

Chest radiographs were obtained with an FCR 9000 or 9501 computed radiographic system (Fuji, Tokyo, Japan), using the following imaging parameters: 120 kVp, 0.6- or 1.2-mm nominal focus, 183-cm film-focus distance, 12:1 oscillating grid, and phototimed exposure. The default mode of image processing, including dynamic range compression, gradation enhancement, and edge enhancement, was used. All CT scans were performed with a HiSpeed Advantage Scanner (General Electric Medical Systems, Milwaukee, WI). Both helical (7-mm collimation, pitch of 1) and high-resolution CT scans(1-mm collimation, 10-mm intervals) were obtained in 18 cases, only high-resolution CT scans in eight patients, and only conventional CT scans from outside hospitals in two. Imaging data were reconstructed using a bone algorithm. Scans were imaged using the lung (window width, 1500 HU; window level, -700 HU) and the mediastinal (window width, 400 HU; window level; 20 HU) window.

Follow-up chest radiographs (range, seven days to six months; median, 18 days) were available in all patients (n= 18) in whom initial chest radiographs revealed abnormalities. In nine cases, follow-up CT scans (range, nine days to six months; mean, 20 days) were obtained after initial CT scans.

The radiologic findings were reviewed retrospectively by two chest radiologists, and final decisions were

reached by consensus. The radiographs and CT scans were reviewed separately at four-week intervals, and analyzed for patterns and distribution of parenchymal abnormalities. The former were categorized as nodules, subtle opacity, air-space consolidation, reticular density, or mass, as seen on chest radiographs and as nodules, ground-glass opacity, consolidation, irregular linear opacity, or mass, as seen on CT scans. Subtle opacity on chest radiographs was defined as increased density without obscuration of underlying vascular structures,
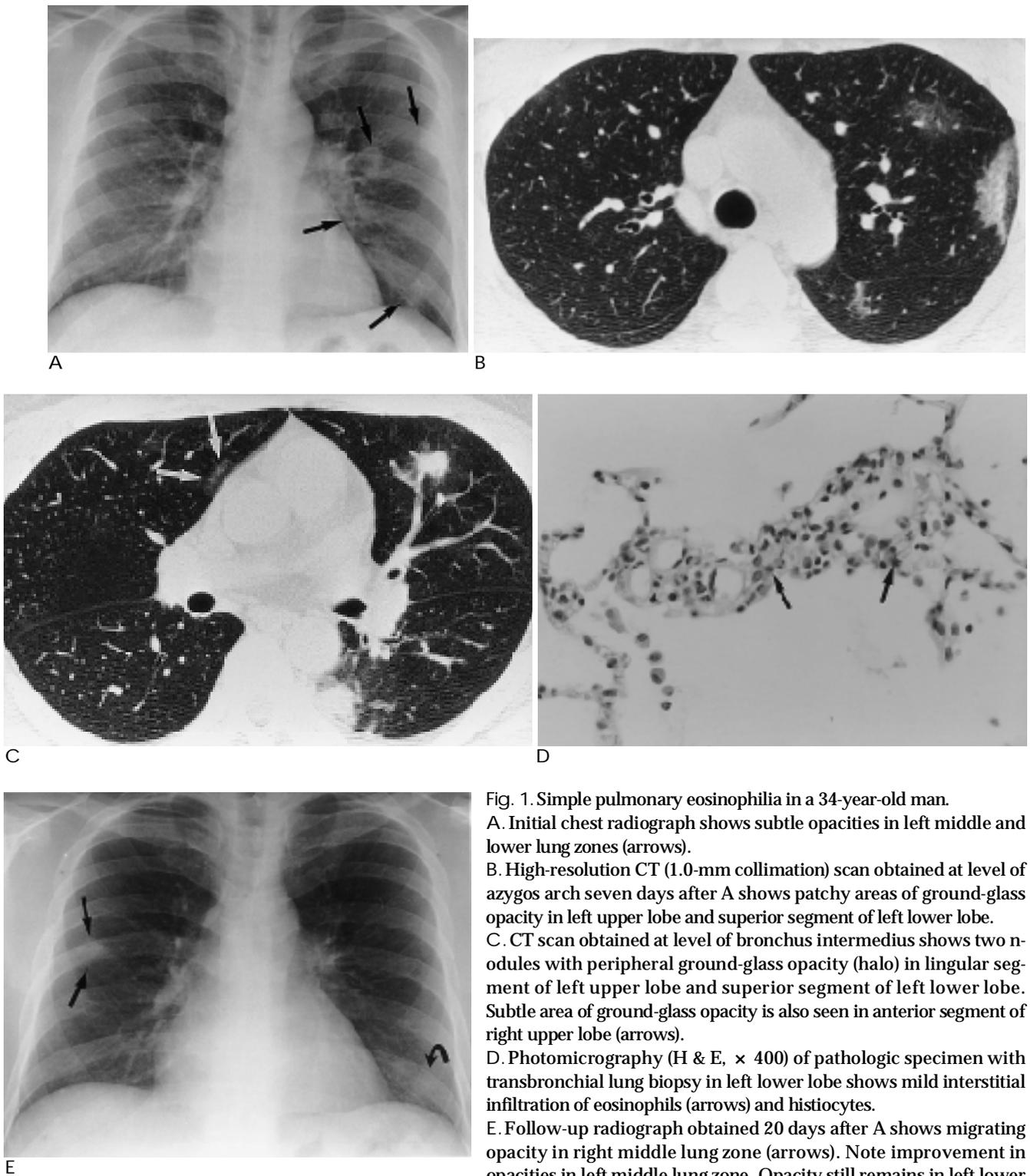


A



B



C



D



E

Fig. 1. Simple pulmonary eosinophilia in a 34-year-old man.
A. Initial chest radiograph shows subtle opacities in left middle and lower lung zones (arrows).
B. High-resolution CT (1.0-mm collimation) scan obtained at level of azygos arch seven days after A shows patchy areas of ground-glass opacity in left upper lobe and superior segment of left lower lobe.
C. CT scan obtained at level of bronchus intermedius shows two n-odules with peripheral ground-glass opacity (halo) in lingular segment of left upper lobe and superior segment of left lower lobe. Subtle area of ground-glass opacity is also seen in anterior segment of right upper lobe (arrows).
D. Photomicrography (H & E, × 400) of pathologic specimen with transbronchial lung biopsy in left lower lobe shows mild interstitial infiltration of eosinophils (arrows) and histiocytes.
E. Follow-up radiograph obtained 20 days after A shows migrating opacity in right middle lung zone (arrows). Note improvement in opacities in left middle lung zone. Opacity still remains in left lower lung zone (curved arrow).

whereas consolidation was defined as markedly increased density with obscuration of these structures. If a nodule, mass, or consolidation showed peripheral ground-glass opacity (halo) on CT scans (especially on high-resolution CT), this was recorded. The distribution of each pattern, as seen on radiographs, was divided into three zones on the chest radiographs; upper, middle, and lower. The upper lung zone was defined as an area superior to the aortic arch, the lower zone as inferior to the inferior pulmonary vein, and the middle zone as an area between the upper and lower zones. On CT, lesion location was divided into six lobes, the lingular segment being considered a separate lobe. Distribution was classified as predominantly central, subpleural, or random; and as patchy or diffuse. Lesions were regarded as central when located within one-third of the lung from the mediastinum, subpleural when they were located within the outer third of the lung from the chest wall, and random whey they did not fit either of these categories. Lesions were considered diffuse when scattered widely and uniformly in both lungs and patchy when inconsistent and not uniform.

Two patients underwent both transbronchial lung biopsy and BAL.

## Results

Transbronchial lung biopsy obtained in two patients demonstrated mild interstitial infiltration of eosinophils and histiocytes (Fig. 1). An increased number of eosinophils (32 % and 7 % of total cell counts, respectively) were present in bronchoalveolar lavage fluid.

Chest radiographs were normal in eight patients (31 %). The commonest radiographic finding among the remaining 18 was subtle opacity (n= 9, 50 %), followed by nodules (n= 8, 44 %), airspace consolidations (n= 2, 11 %) and mass (n = 1, 6 %) (Table 1). Follow-up chest radiographs in 18 patients showed complete resolution in 16 patients (including seven with underlying malignancy) within 7 days to 6 months (median, 20 days). In one patient, a migratory lesion was seen on a radiograph obtained 20 days after the initial radiograph (Fig. 1); another patient showed partial resolution on a radiograph obtained 14 days after the initial radiograph.

The commonest pattern of parenchymal abnormality observed on CT scans was nodules (n= 19; 73 %) (Figs. 1 - 3), followed by areas of ground-glass opacity (n= 16; 62 %) (Figs. 1, 3, and 4), consolidation (n= 3; 12 %) (Fig. 3), and mass (n= 1; 4 %) (Fig. 5). Peripheral halo of ground-glass opacity was seen in 48 (76 %) of 63 nodules in 18 patients and in all three areas of consolidation (Figs. 1-3). The distribution of nodules (n= 19) was subpleural (n= 13) or random (n= 6), that of ground-glass opacity (n= 16) was subpleural (n= 13), random (n= 2)

Table 1. Radiographic Findings of Simple Pulmonary Eosinophilia in 18 Patients

|  | Laterality | | Zonal distribution | | |
|---|---|---|---|---|---|
|  | Uni- | Bi- | Upper | Middle | Lower |
| Subtle opacity (n= 9; 50%) | 4 | 5 | 3 | 5 | 5 |
| Nodules (n= 8; 44%) | 5 | 3 | 3 | 7 | 2 |
| Consolidation (n= 2; 11%) | 1 | 1 | 1 | 0 | 2 |
| Mass (n= 1; 6%) | 1 | 0 | 1 | 0 | 0 |

Note- Uni:unilateral, Bi: bilateral



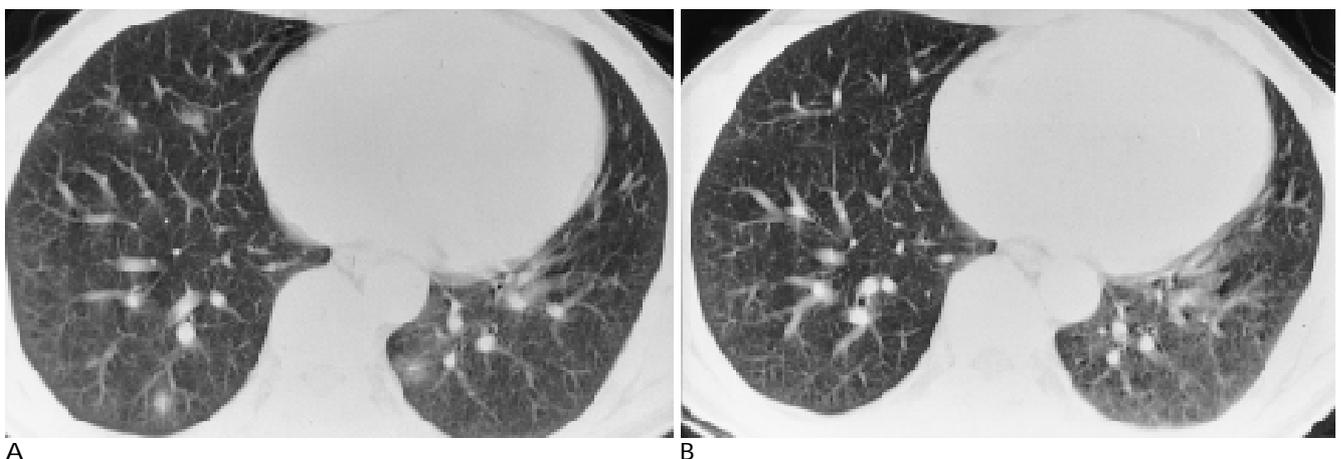A                                                                                    B

Fig. 2. Simple pulmonary eosinophilia in a 53-year-old man.
A. Initial CT (10-mm collimation) scan obtained at ventricular level shows several nodules with peripheral ground-glass opacity (halo) in both lower lobes and right middle lobe, which are predominantly subpleural in distribution.
B. Follow-up CT (10-mm collimation) scan obtained at same level and 20 days after A shows that nodules disappeared.

or central (n= 1), and that of areas of consolidation was subpleural (n= 2) or random (n= 1). For mass, distribution was subpleural. The distribution of all lesions was patchy, and none showed diffuse abnormalities. The predominant lobar distribution was not demonstrated (Table 2).

Follow-up CT scans (n= 9) showed complete resolu-

tion of the parenchymal lesions in seven patients within 1 to 6 months (median, 75 days). One patient showed partial resolution of nodules within 20 days, and the other showed almost complete resolution of the pre-existing mass lesion and small new nodules on the CT scans obtained 9 days later (Fig. 5).

Table 2. CT Findings of Simple Pulmonary Eosinophilia in 26 Patients

| | Laterality | | Zonal distribution | | | Transverse plane | | | Uniformity | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Uni- | Bi- | Upper | Middle | Lower | Central | Subpl. | Random | Diffuse | Patchy |
| Nodules (n= 19; 73%) | 9 | 12 | 11 | 12 | 15 | 0 | 13 | 6 | 0 | 19 |
| Ground-glass opacity (n= 16; 62%) | 8 | 8 | 12 | 7 | 7 | 1 | 13 | 2 | 0 | 16 |
| Consolidation (n= 3; 12%) | 3 | 0 | 2 | 0 | 1 | 0 | 2 | 1 | 0 | 3 |
| Mass (n= 1; 4%) | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |

Note - Uni: unilateral, Bi: bilateral, Subpl: subpleural
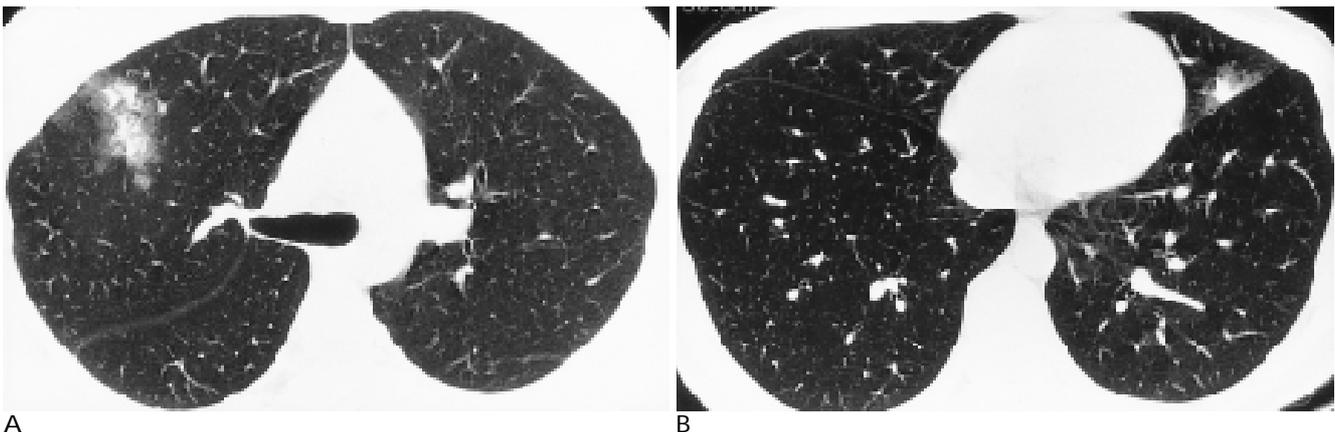


A          B

Fig. 3. Simple pulmonary eosinophilia in a 25-year-old woman with breast cancer.
A. High-resolution CT (1.0-mm collimation) scan obtained at level of main bronchi shows nonsegmental area of consolidation with peripheral ground-glass opacity in right upper lobe.
B. CT scan obtained at level of inferior vena cava shows small nodule with halo in lingular segment of left upper lobe. Follow-up chest radiograph (not shown here) 20 days after A and B showed complete disappearance of consolidation and nodule.
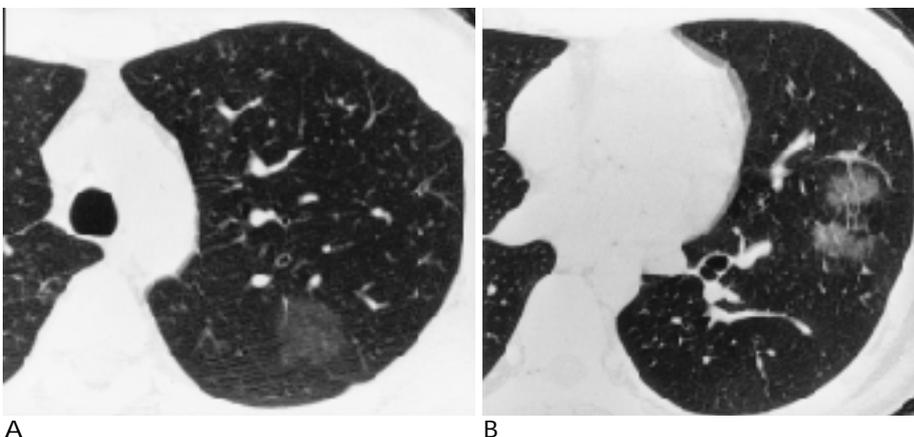


A          B

Fig. 4. Simple pulmonary eosinophilia in a 33-year-old man.
A. High-resolution CT (1.0-mm collimation) scan obtained at level of aortic arch shows area of ground-glass opacity in left upper lobe.
B. CT scan obtained at level of inferior pulmonary vein and on same day with A shows areas of ground-glass opacity in left lower lobe.
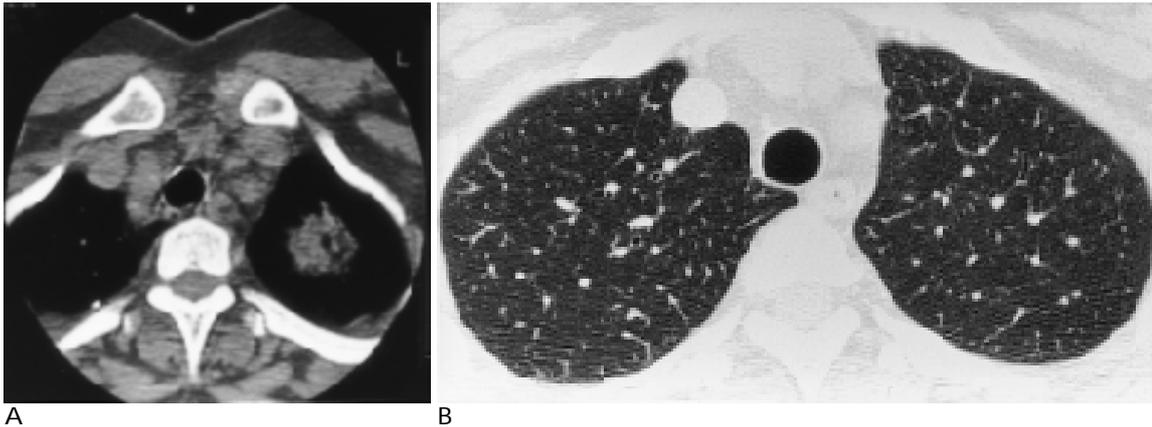
A                    B

Fig. 5. Simple pulmonary eosinophilia mimicking lung cancer in a 56-year-old woman.
A. Mediastinal window setting of CT (10-mm collimation) scan shows about 3-cm sized mass with a small area of air attenuation simulating cavitating mass in left upper lobe. Initially lesion was diagnosed as peripheral lung cancer.
B. Follow-up high-resolution CT (1.0-mm collimation) scan obtained 9 days after A, owing to disappearance of mass on fluoroscopy during percutaneous needle aspiration biopsy, shows almost complete disappearance of mass. Small new nodules in right middle and lower lobes were seen (not shown here).

## Discussion

Although numerous classifications of eosinophilic lung diseases have been proposed, there is currently no optimal way of classifying these disorders. They may be classified as entities of unknown causes (simple pulmonary eosinophilia, acute eosinophilic pneumonia, chronic eosinophilic pneumonia, and idiopathic hypereosinophilic syndrome), known causes (allergic bronchopulmonary aspergillosis, bronchocentric granulomatosis, and eosinophilic lung disease with parasitic infection and drug reaction); or eosinophilic vasculitis (allergic angiitis and granulomatosis or Churg-Strauss syndrome) (1). Diagnostic criteria for each of these entities have recently been suggested (1, 2).

The eosinophil is a bone marrow-derived polymorphonuclear leukocyte containing granules within which are a variety of proteins. When released, these proteins are potentially cytotoxic, resulting in pathologic processes (5, 7 - 9). The term eosinophilia denotes an absolute eosinophil count above 500 cells/microliter (8). In simple pulmonary eosinophilia, the degree of eosinophilia varies, ranging between 1,000 and 50,000 cells/microliter (10), but does not appear to correlate with the amount, duration, or intensity of pulmonary infiltration (11, 12). Symptoms are usually lacking and physical findings are often absent (11). In our study, 19 of 26 patients had no symptoms, and in the remaining seven, symptoms were mild. The number of peripheral eosinophils ranged from 540 to 28,706 cells/microliter.

The pathologic changes seen in patients with simple pulmonary eosinophila have been described as areas of pneumonic consolidation consisting of alveolar exudate filled with many eosinophils, mononuclear cells, and occasional foreign body giant cells. Eosinophils and other round cells can also be found in the interstitium, but associated vasculitis is not seen (1 - 4, 6). Because most lesions are transient and mild, lung biopsy is not performed.

The radiographic finding commonly reported in patients with simple pulmonary eosinophilia is nonsegmental consolidation varying in size and either unilateral or bilateral. Abnormalities are usually transient and migratory (1-3, 11, 12), are often peripheral in nature, and may appear to be subpleural (2, 3). Neither cavitation in consolidation nor findings of pleural effusion, lymph node enlargement, or cardiomegaly have been reported (1). Hennell et al (12) described the radiographic findings of five patients with transient eosinophilic lung infiltration as confluent and patchy in appearance which may be radiating from the hilum, and often symmetric in two lungs. In fact, a patient with probable hypereosinophilic syndrome was included in his study and three patients were asthmatics. In our study, the predominant radiographic findings were ground-glass opacity and nodules. Areas of consolidation were infrequent.

The diagnostic criteria of simple pulmonary eosinophilia include abnormality on chest radiographs, with peripheral eosinophilia. Such abnormality has been a finding in almost all patients with simple pulmonary

eosinophilia (5). Our study showed normal chest radiographs in eight (31 %) of 26 patients. In simple pulmonary eosinophilia, pulmonary infiltration might not be visible on chest radiographs. In other words, negative chest radiographic findings in patients with peripheral eosinophilia do not always exclude the possibility of pulmonary infiltration. Under such circumstances, pulmonary infiltration is revealed by CT.

CT findings of simple pulmonary eosinophilia have rarely been described. We described recently the CT findings of the disease in few patients. The lesions appeared as single or multiple pulmonary nodules with or without a peripheral halo (1). In the present study, the predominant pattern of parenchymal abnormality seen on CT scans was nodules, distributed mainly in subpleural regions. About 76 % of the nodules were accompanied by a peripheral halo of ground-glass opacity. Patchy areas of ground-glass opacity were the second most frequent finding.

Patients with simple pulmonary eosinophilia have an excellent prognosis and because pulmonary infiltrates and blood eosinophilia resolve spontaneously within one month, do not need treatment(1, 2, 6). The condition can, however, also be associated with parasitic or other infestation, drug reaction, environmental exposure, or malignancy. Infections may be parasistic (amebiasis, ascariasis, trichomosis, filariasis, paragonimiasis, strongyloidiasis), fungal (histoplasmosis, coccidioidomycosis, brucellosis), or protozoan (*Entamoeba histolytica, Entamoeba coli*), while the drugs involved in adverse reactions include acetylsalicylic acid, para-aminosalicylic acid, penicillin, mephensen carbonate, nitrofurantoin and potentially almost all classes of pharmaceuticals. Examples of environmental exposure are smoke inhalation, poison ivy desensitization, contact with nickel and pollen inhalation. About one half of the patients in whom simple pulmonary eosinophilia was initially diagnosed will eventually be shown to be affected by infestation, drug reaction, or environmental exposure (1, 2, 5). The etiology is quite obscure; the evidence to date suggests that an allergy is involved (3, 4, 6, 10, 12). In light of the above, the possibility of parasitic infestation, drug reaction, environmental exposure, and underlying malignancy should be carefully investigated (2).

It is also well known that malignant diseases (bronchogenic carcinoma, gastrointestinal tract tumors, Hodgkin's and non-Hodgkin's lymphoma), chronic granulomatous disorders (tuberculosis, sarcoidosis), and collagen vascular disease (rheumatoid arthritis, pol-

yarteritis nodosa, lupus erythematosus) can be associated with peripheral eosinophilia (3- 7, 10, 13). In the presence of these conditions, the cause of eosinophilia is not clear, however. In our study, simple pulmonary eosinophilia was associated with an underlying malignant disease in nine patients. In two patients, the disease was associated with a Kimura' s disease (angiolymphoid hyperplasia with eosinophilia) and a sarcoidosis, one in each patient. In these patients, chest radiograph revealed no abnormalities. Parenchymal abnormalities were seen only on CT scans, which were obtained in order to evaluate tumor staging or to search for pulmonary or mediastinal complications caused by underlying diseases. There are some diagnostic problems involved in detecting nodule(s) with or without a halo sign of simple pulmonary eosinophilia in patients with known underlying malignancies. The nodules should not be confused with metastatic pulmonary nodule(s), and to this end, an early differential leukocyte count and careful recording of any parasitic or fungal infestation and drug intake are required.

A peripheral halo surrounding the nodule or consolidation can be seen under a variety of conditions: hemorrhagic nodules of infectious (aspergillosis, mucormycosis, candidiasis, coccidioidomycosis) and noninfectious origin (Wegener' s granulomatosis, metastatic angiosarcoma, and Kaposi sarcoma); primary (bronchioloalveolar carcinoma or primary lymphoma) or secondary lung malignancy, and inflammatory disease such as organizing pneumonia (14, 15). We believe that the halo represents pathologically loose interstitial infiltration of eosinophils and histiocytes around dense eosinophilic consolidation. Diagnosis is usually possible on the basis of a complete history, a simple differential count of white blood cells in peripheral blood, and a follow-up radiologic study.

Our study was limited by several drawbacks. This suffers from the limitations of a retrospective study. Although we included patients (especially those with underlying malignancy) with increased peripheral blood eosinophil count and parenchymal abnormalities at CT, specific causes were not identified in these patients. Possible causes may have been unidentified parasitic or other infections, drug intake, and environmental exposure. Pathologic evaluation was performed in only two patients and not all patients underwent a follow-up radiologic examination. Radiologic-pathologic correlation would give detailed information, especially regarding the pathologic basis of the peripheral halo of ground-

glass opacity seen on CT. We included only 26/49 patients with simple pulmonary eosinophilia, for whom both chest radiographs and CT scans were obtained, and this may have led to a selection bias.

In summary, simple pulmonary eosinophilia is characterized clinically by no or minimal symptoms and spontaneous resolution within a month. The condition most commonly involves subtle opacity of nodules on chest radiographs. Pulmonary lesions are more readily detected by CT scans than by chest radiographs. The predominant CT findings of simple pulmonary eosinophilia are subpleural nodules of patchy distribution with surrounding ground-glass opacity (halo sign) or patchy areas of ground-glass opacity.

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