Histiocytosis X*  
Unusual-Confusing Features of Eosinophilic Granuloma

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We report our experience with seven cases of eosinophilic granuloma in which unusual and/or confusing features were encountered. These features include: histologic confusion with desquamative interstitial pneumonitis, diffuse histiocytic lymphoma, eosinophilic pneumonia; cysts filled with air and/or fluid; radiographic onset in the eighth decade of life; intratracheal mass; and focal parenchymal consolidation.

Histiocytosis X is a term used to define three diseases with similar morphologic characteristics: Letterer-Siwe disease, Hand-Schuller-Christian disease, and eosinophilic granuloma (EG).1,2 In general, they differ in terms of their age of onset, severity of clinical course and sites of involvement. EG typically is seen in young adults and often involves lung and/or bone. Pathologically, the three diseases are characterized by histiocytes, eosinophils, and granulomatous infiltration of alveolar septa and bronchial walls.3

During the past few years, we have encountered seven instances of EG with unusual and/or confusing features.

CASE REPORTS

CASE 1

A 33-year-old white woman experienced recurrent bouts of pleuritic chest pain. In September 1980, a chest roentgenogram was normal except for patchy alveolar disease in the anteromedial right lung (Fig 1). A follow-up study one month later showed partial clearing. She continued to have recurrent bouts of pain with dyspnea on exertion, dry cough, and fatigue. A roentgenogram taken in May 1981 revealed multiple bilateral nodules with an upper zone predominance (Fig 2). Workup included skin testing and sputum study for tuberculous infection and serologic evaluation for histoplasmosis, angiotensin-converting enzyme levels, and rheumatoid factor determination. All results were negative. A gallium scan revealed uptake in both lungs.

Transbronchial biopsy in July 1981 was reported as showing desquamated type 2 pneumocytes, mild, patchy fibrosis of alveolar septal walls, and focal infiltration by histiocytes, eosinophils, and lymphocytes. No granulomas were observed. A diagnosis of desquamative interstitial pneumonitis was suggested. Subsequent open lung biopsy uncovered eosinophilic and histiocytic infiltrate, fibrosis, and histiocytic aggregates consistent with a diagnosis of EG.

A chest roentgenogram in August 1981 demonstrated small, irregular shadows, the nodular densities having become less apparent. The patient has subsequently done well without treatment.

CASE 2

A 47-year-old white woman with a history of ulcerative colitis was noted to have an enlarged thyroid gland in July 1981 and was given thyroxine therapy for several months. Since an ultrasound examina

**Figure 1.** Case 1. PA roentgenogram, normal except for patchy alveolar disease overlying right hilum, better seen on lateral view (not shown).

**Figure 2.** Case 1. PA roentgenogram showing bilateral nodules with upper zone predominance.

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Manuscript received April 22; revision accepted July 9.
study on admission demonstrated a left pneumothorax that was treated with chest tube drainage. The lungs showed bilateral focal cysts, some with air-fluid levels (Fig 5). An open lung biopsy resulted in a diagnosis of EG. The patient was followed up in a clinic for several months, was asymptomatic without treatment, and was subsequently lost to follow-up.

CASE 4
A 71-year-old white woman was admitted to the hospital for resection of gastric carcinoma. Her past medical history was remarkable in that she had undergone modified radical mastectomy 30 years earlier for carcinoma of the breast. Several years later she had a total abdominal hysterectomy and bilateral salpingo-oophorectomy for ovarian carcinoma.

The patient acknowledged dyspnea on exertion, persistent morning cough, and orthopnea, all of which had been labeled for several years as chronic obstructive pulmonary disease. An admission chest roentgenogram in May 1982 revealed in each lung a few nodules,
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with an upper zone predominance (Fig 6). Since these nodules were not present in December 1981, a metastatic workup ensued and included mammography, liver/spleen scan, bone scan, and skeletal survey. All results of examinations were negative. Sputum cytology, culture for acid-fast organisms and fungi, and transbronchial and needle biopsy were all nondiagnostic. In May 1982 the patient underwent open lung biopsy, and the tissue recovered was consistent with EG.

Because of the patient’s poor pulmonary function and nutritional status, her postoperative course was stormy. She eventually underwent esophagogastrectomy for adenocarcinoma in July 1982, tolerating the procedure well.

**Case 5**

A 36-year-old white woman was admitted to the hospital for an elective uterine dilatation and curettage. She had been complaining of fatigue, with review of systems being remarkable only for mild dyspnea on exertion. An admission chest roentgenogram in February 1980 revealed bilateral air-filled cysts up to approximately 3 cm in diameter, the cysts predominating in the upper and middle zones.

(Fig 7). Six years earlier, the lungs had been normal. A liver/spleen scan was interpreted as showing possible splenomegaly. The patient had smoked one to two packs of cigarettes per day for four years. Her pulmonary function tests indicated an obstructive and more prominent restrictive deficit. A sweat chloride test was mildly abnormal, and the diagnosis of adult cystic fibrosis was entertained, although the roentgenographic pattern was not typical.

An open lung biopsy was performed, the initial interpretation of which was eosinophilic pneumonia in view of abundant eosinophils. Further review of the biopsy indicated that although eosinophils were abundant, diffuse nodular histiocytic aggregates with interstitial fibrosis were consistent with EG.

**Case 6**

A 13-year-old white boy presented with progressive shortness of breath, stridor, and an enlarging mass in the region of the thyroid gland. He was thought to have a nontoxic goiter. Thyroid scan and laboratory studies revealed no evidence of hyperthyroidism.

On admission, the patient’s lateral neck roentgenogram showed an intratracheal mass (Fig 8). A biopsy of anterior jugular nodes and a paratracheal infiltrative mass showed tissue consistent with EG. Bone marrow examination and a bone scan were normal. A chest roentgenogram demonstrated bilateral small opacities and bilateral hilar adenopathy. A course of therapy with prednisone and vinblastine was begun. Localized irradiation to the tracheal area resulted in a rapid response, with shrinkage of the mass and diminished stridor.

**Case 7**

A six-year-old black girl complained of gum tenderness and swelling. Over several months, she experienced gingival hemorrhage and subsequent extrusion of her primary teeth without pain.
lymphoma and eosinophilic pneumonia, respectively. Filer reported two cases of young women with prominent tissue eosinophilia on bone biopsy examination and striking peripheral eosinophilia. These findings and abnormalities on their chest roentgenograms suggested a diagnosis of Loeffler's pneumonia, until open lung biopsy revealed EG. Our patient showed no peripheral eosinophilia. Of further interest in our patient is that the chest roentgenogram revealed bilateral cysts predominating in the upper and middle zones. Such an appearance is associated with end-stage EG, when eosinophilic infiltration often is not a predominant histologic feature, although it was in our patient.4

Unlike case 5, the patient in case 3 showed larger and relatively few bilateral thin-walled cysts. Some of these cysts contained air-fluid levels. This uncommon appearance of eosinophilic granuloma has been reported elsewhere.8

The roentgenographic pattern in EG, from early to late stages, is said usually to progress from nodules (uncommonly cavitated) to irregular shadows to cystic areas with honeycombing. Alveolar consolidation is an uncommon manifestation. Pathologically the alveoli are filled with eosinophils and histiocytes. It is conceivable that the patchy alveolar disease seen initially in patient 1 may have represented such a manifestation, since an organism was never cultured. The patient was treated as if a bacterial pneumonia were present; and we have no biopsy proof of EG at that time. However, for the patient in case 7, the lingular consolidation was shown by biopsy to represent EG.

Mediastinal or hilar adenopathy is uncommon in adults with EG, even those with active disease,6,8,10 but may occur in children. Nakata et al14 recently reported a three-year-old boy with a large anterior mediastinal mass. The biopsy diagnosis of histiocytosis X was questioned until other classic lesions subsequently developed. Masson and Tedeschi15 described EG simulating sarcoidosis in a 17-year-old girl with hilar and paratracheal adenopathy as well as nodules in the lung. The patient in case 6 showed parenchymal abnormalities and bilateral hilar adenopathy consistent with EG. An unusual neck mass and an endotracheal mass causing stridor were also present, the biopsy specimen showing EG.

CONCLUSION

Our experience with these seven cases emphasizes that:

1. Bilateral upper zone predominance of nodules, irregular shadows, large cystic areas, or honeycombing should raise the suspicion of EG in patients with other factors that might lead one away from the diagnosis (female, black, older age group, underlying malignancy, biopsy diagnosis of entities sharing similar
histologic features).

2. EG may present with unusual features, such as thin-walled cysts with air-fluid levels, tracheal and neck mass, and alveolar consolidation.

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