Pulmonary Involvement of Hypereosinophilic Syndrome: High-Resolution CT Findings in Three Patients

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Hypereosinophilic syndrome is a rare entity of eosinophilic lung disease characterized by idiopathic prolonged eosinophilia of marked degree and variable organ involvement. Pulmonary involvement of hypereosinophilic syndrome occurs in up to 40% of patients. We report HRCT findings of three patients with pulmonary involvement of hypereosinophilic syndrome diagnosed by clinical manifestation, bronchoalveolar lavage and transbronchial lung biopsy. On HRCT, several small nodules were seen in both lungs, especially in peripheral lung areas of the three patients. One had nodules with ground-glass attenuation halo and also focal areas of ground-glass attenuation in this area.

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Hypereosinophilic syndrome (HES) is an infiltrative disease of eosinophils affecting multiple organs, including the lung (1). The criteria for this diagnosis include persistent eosinophilia of 1500 eosinophils per cubic mm for longer than six months or death before six months, the absence of parasitic, allergic or other known causes of eosinophilia, and evidence of organ involvement (1, 2). Pulmonary involvement occurs in 40 percent of HES, mainly presenting with cough or dyspnea (3). Patients with HES and pulmonary infiltrates may pose certain diagnostic problems such as infection, infarction, congestive heart failure or HES itself (1, 3, 4). The authors report three HES patients with pulmonary involvement in whom high-resolution CT showed small nodules in peripheral lung areas.

CASE REPORTS

Case 1
A 51-year-old woman was admitted to hospital because for six months she had felt discomfort in the right upper quadrant of the abdomen. She had no specific medical history. Laboratory studies revealed an elevated leukocyte count of 15000 per cubic mm with marked eosinophilia (total eosinophil count, 8880). Focal lesions were found in her liver. Ultrasound guided biopsy of the focal lesion revealed eosinophilic abscess. A bone marrow biopsy was performed; it revealed 42% of mature eosinophils and no evidence of leukemia. She did not complain any neurologic symptoms or cardiac problems. Chest radiograph was normal, though HRCT showed several small nodules in the subpleural areas of both lungs (Fig. 1). The eosinophil content of bronchoalveolar lavage fluid was 26% and transbronchial lung biopsy on the right lower lobe lesion showed focal pneumonic infiltration with eosinophils and fibrous exudate. Steroid treatment was started and the liver lesions and eosinophilia improved within two months.

Case 2
A 44-year-old man was admitted for evaluation of a cough. His medical history was insignificant. Laboratory studies yielded leukocytosis (16000 per cubic mm) with marked eosinophilia (total eosinophil count, 7136). A chest radiograph showed no abnormalities of the lungs and heart; HRCT showed several small nodules with a ground-glass attenuation halo in both lungs (Fig. 2a) and peripheral focal areas of ground-glass attenuation in the lower lungs (Fig. 2b). Bronchoalveolar lavage (BAL) revealed 4% eosinophilia. Microbiologic cultures on BAL fluid for tuberculosis, bacteria and fungi were negative. Focal hepatic lesions were found and

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ultrasound-guided liver biopsy showed periportal eosinophilic infiltration with bridging hepatic necrosis. Gastroscopic biopsy revealed eosinophilic mucosal infiltrations in the stomach; a bone marrow biopsy revealed 39.5% of matured eosinophils. Steroid and busulfan treatment was started and ten months later the patient was doing well while receiving therapy; laboratory study, however still revealed eosinophilia of 8.6%.

**Case 3**

A 58-year-old woman was admitted for the evaluation of generalized myalgia. Laboratory study revealed eosinophilia (total count, 4100). Bone marrow biopsy revealed 16% of eosinophils; a chest radiograph showed no abnormalities but HRCT showed several small nodules in both lungs (Fig. 3). Bronchoalveolar lavage revealed 18% of eosinophils. Despite steroid and hydroxyurea treatment peripheral eosinophilia persisted. Eighteen months later, laboratory study still revealed eosinophilia of 21.6%.

**DISCUSSION**

The eosinophilic lung diseases are a diverse group of pulmonary disorders linked by common findings of an increase in circulating or tissue eosinophils. Although numerous classifications of these disorders have been proposed, there is no optimal way to classify these disorders (5). Hypereosinophilic syndrome is one characteristic entity of eosinophilic lung diseases and must be differentiated from all other causes of peripheral eosinophilia.

The term “hypereosinophilic syndrome” was first proposed by Hardy and Anderson (6) in 1968. They described three patients characterized by severe hypereosinophilia, cardiac or pulmonary symptoms, hepatosplenomegaly, constitutional symptoms, anemia, and diffuse organ infiltration by mature eosinophils.
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Eosinophilic syndrome represents a heterogeneous group of disorders characterized by a idiopathic prolonged eosinophilia of marked degree and, furthermore, by variable organ dysfunction. It may involve virtually any organ system, though bone marrow hypereosinophilia is common to all patients. The most severe clinicopathologic involvement is of the heart and nervous system (4).

Pulmonary involvement in HES occurs in up to 40% of patients, who typically present with cough or dyspnea (3, 5). In patients with HES and pulmonary infiltrates, the condition may be attributed to infection, infarction, congestive heart failure or HES-related pulmonary involvement (1–4). One half of these patients have significant pleural effusion, probably due to congestive heart failure or embolic phenomena (1–3). A chest radiograph shows focal or diffuse, interstitial or alveolar, and nonlobar infiltrates (1–3, 5–8). Winn et al (1) reported a patient who presented with ARDS that was thought to be a complication of HES. Hilar lymphadenopathy was noted, but the prevalence of intrathoracic lymphadenopathy had not been assessed. Histopathology demonstrates striking infiltration of involved organs by eosinophils, is associated with disruption of the architecture, and there are areas of necrosis. BAL fluid eosinophilia may suggest HES-related pulmonary involvement (3, 5).

To our knowledge, this is the first report of HRCT findings in patients with lung involvement of HES. In spite of no specific abnormalities on chest radiographs, several small nodules were seen in both lungs, especially peripheral lung areas on HRCT. One of them showed focal areas of ground-glass attenuation located subpleurally and ground-glass attenuation halo around nodules. In our patients, the eosinophil count in BAL fluid was elevated in all three patients, and TBLB that was performed in one patient showed focal pneumonic infiltrations with eosinophils. These results strongly suggest HES-related pulmonary involvement. Other organ systems involved in our patients included the stomach, liver and bone marrow. Early recognition of the syndrome is important because there is strong evidence that prognosis may be much improved if treatment is instituted promptly (9).

REFERENCES

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