A case of chronic eosinophilic pneumonia successfully treated with mepolizumab

Masako To, MD, PhD[a,b], Yuta Kono, MD, PhD[a], Satoshi Yamawaki, MD[a], Seiko Soeda, MD, PhD[a], Otohiro Katsube, MD[a], Hirohisa Kishi, MD, PhD[c], and Yasuo To, MD, PhD[a]

Clinical Implications

- Mepolizumab may be a good treatment option for chronic eosinophilic pneumonia when the disease relapses and/or adverse effects of corticosteroid therapy occur. The therapy has fewer adverse events and is more easily sustainable than conventional corticosteroid therapy.

TO THE EDITOR:

Chronic eosinophilic pneumonia (CEP) is an inflammatory disease characterized by eosinophilic infiltration in the lung of unknown etiology. It is also characterized by the progressive onset of symptoms, including cough and increasing dyspnea.[1] For the treatment of CEP, systemic corticosteroid therapy is recommended, and the response to corticosteroids is usually very good. However, approximately 50% of patients with CEP relapsed after termination of corticosteroid therapy or while corticosteroids were being tapered.[2-4] When prolonged systemic corticosteroid therapy is needed, adverse events caused by corticosteroids, including diabetes mellitus, osteoporosis, and infections, are a serious issue.[2] Therefore, novel alternative therapeutic strategies are urgently needed for CEP. A case of CEP successfully treated with mepolizumab is presented.

A 65-year-old man visited our hospital because of a chronic cough and abnormal chest X-ray findings. He did not have high fever, dyspnea, massive sputum production, or wheezing. He had no history of lung disease, except for an approximately 20-year history of bronchial asthma. He was a never smoker, and he had no obvious history of occupational dust inhalation. The laboratory data showed an elevated leukocyte count with marked eosinophilia (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). Proteinase 3 antineutrophil cytoplasmic antibody (PR-3 ANCA), myeloperoxidase antineutrophil cytoplasmic antibody (MPO-ANCA), and angiotensin-converting enzyme (ACE) were all negative. Krebs von den Lungen-6, surfactant protein D, and surfactant protein A levels were slightly elevated (Table E1). Chest computed tomography (CT) showed infiltrative shadows in the left upper and lower lobes (Figure 1, *A*). Fiberoptic bronchoscopy showed no abnormal findings in the bronchial lumen. Bronchoalveolar lavage fluid (BALF) showed an elevated eosinophil percentage (72%; normal range, $\leq$1%) (Figure E1, *A* and *B*). Bacterial culture of BALF detected only normal flora. On the basis of the high percentage of eosinophils in the BALF, the marked peripheral eosinophilia, the infiltrative shadows on chest CT, and the negative findings for other potential causes of cough and pulmonary infiltrates, the diagnosis of CEP was established.

Treatment with prednisolone 30 mg/d (0.5 mg/kg/d) was given, with biweekly tapering of the dosage (Figure 2). The patient responded well to corticosteroid therapy, and his symptoms disappeared with the decrease in peripheral blood eosinophil counts (Figure 2). However, after termination of systemic corticosteroid therapy, his symptoms worsened, with increased peripheral eosinophil counts (Figure 2). Infiltrative shadows were newly developed in the right upper lobe, whereas the infiltrative shadows in the left upper and lower lobes had disappeared (Figure 1, *B*); the CEP had relapsed. Because serious adverse events sometimes occur with prolonged systemic corticosteroid therapy, mepolizumab 100 mg/d every month was administered instead of systemic corticosteroid therapy. He responded well to the therapy. His symptoms decreased several days after the administration of mepolizumab. About 1 month after the administration of mepolizumab, his symptoms disappeared, and his peripheral blood eosinophil counts decreased to the normal range (Figure 2). The infiltrative shadows disappeared on his chest CT taken 3 months after the start of mepolizumab therapy (Figure 1, *C*). The patient has had no relapse of CEP up to now with the continuation of mepolizumab therapy. No adverse events potentially attributed to mepolizumab therapy were observed. We are planning to continue mepolizumab therapy with careful observation of patients.

Patients with CEP have been reported to show a good response to systemic corticosteroid therapy. However, a substantial percentage of patients suffered relapse of the disease after finishing corticosteroid therapy or while the corticosteroid was being tapered.[2-4] The present case of CEP also had a relapse of CEP after termination of systemic corticosteroid therapy. In contrast, he has had no relapse with continued mepolizumab therapy.

Chronic accumulation of eosinophils in the alveolar space induced by IL-5 is suggested to play a major role in the development of CEP. Although the triggering factors for CEP are usually unknown, the selective migration of T_H2 cells to the lungs, mediated by thymus and activation-regulated chemokine and RANTES, and the chronic release of IL-5 from T_H2 cells have been reported to be evident in CEP lung. The released IL-5 induces accumulation of eosinophils in the lungs. In fact, it has been reported that BALF from the affected area of the lung area has high IL-5 levels, but BALF from the normal area of the lung does not.[5] Blood IL-5 and BALF IL-5 levels were elevated in CEP, and they were decreased after treatment.[6] The BALF IL-5 concentration of patients with CEP was higher than that of controls.[7] Thus, IL-5 seems to play an important role in the pathogenesis of CEP.

Mepolizumab is an mAb to human IL-5 used for the treatment of severe eosinophilic asthma.[8] Mepolizumab binds to free IL-5 to inhibit it from interacting with IL-5 receptors on the surface of eosinophils. As mentioned in the previous paragraph, IL-5 seems to play an important role in the pathogenesis of CEP. Therefore, it is reasonable to conclude that the administration of mepolizumab suppresses local levels of IL-5 and infiltration of eosinophils, resulting in the resolution of CT findings and decreased symptoms. In addition, mepolizumab therapy can be

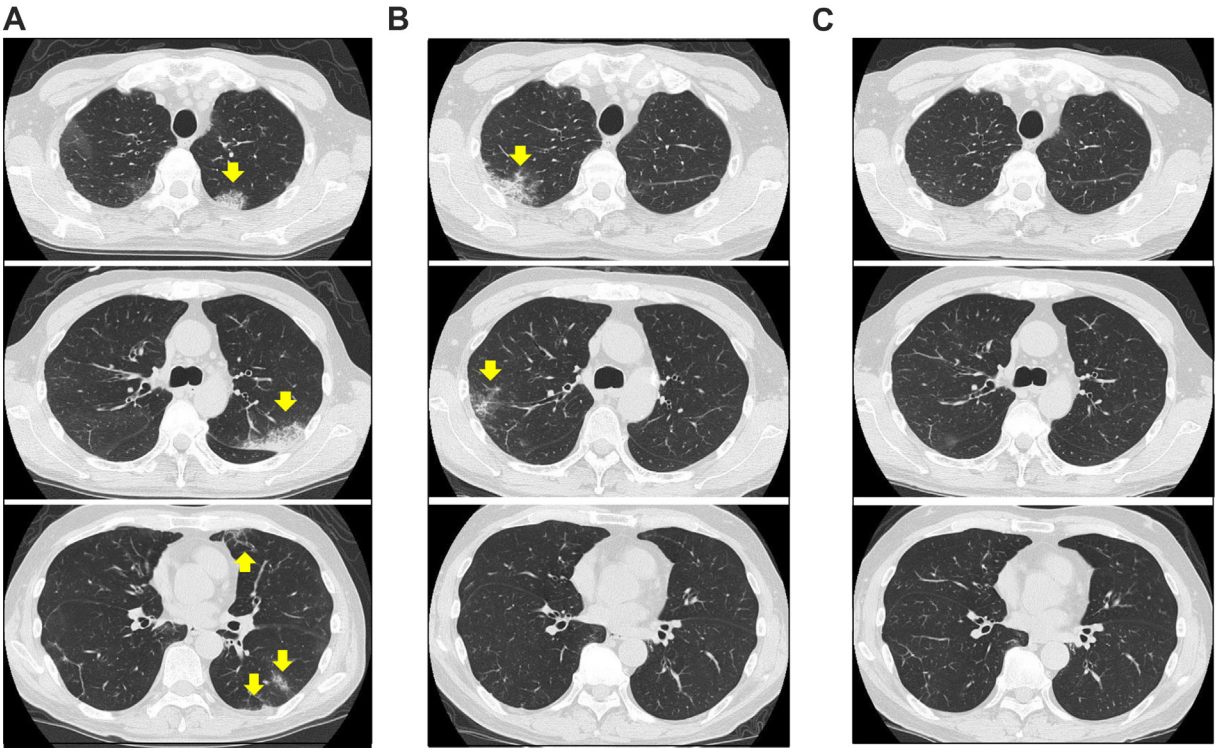

FIGURE 1. Chest CT findings. Chest CT findings on admission (**A**) showed infiltrative shadows in the left upper and lower lobes (indicated by yellow arrows). Chest CT taken at the time of relapse (**B**) revealed that infiltrative shadows were newly developed in the right upper lobe. Chest CT taken 3 months after the initiation of mepolizumab therapy (**C**) showed no infiltrative shadows.

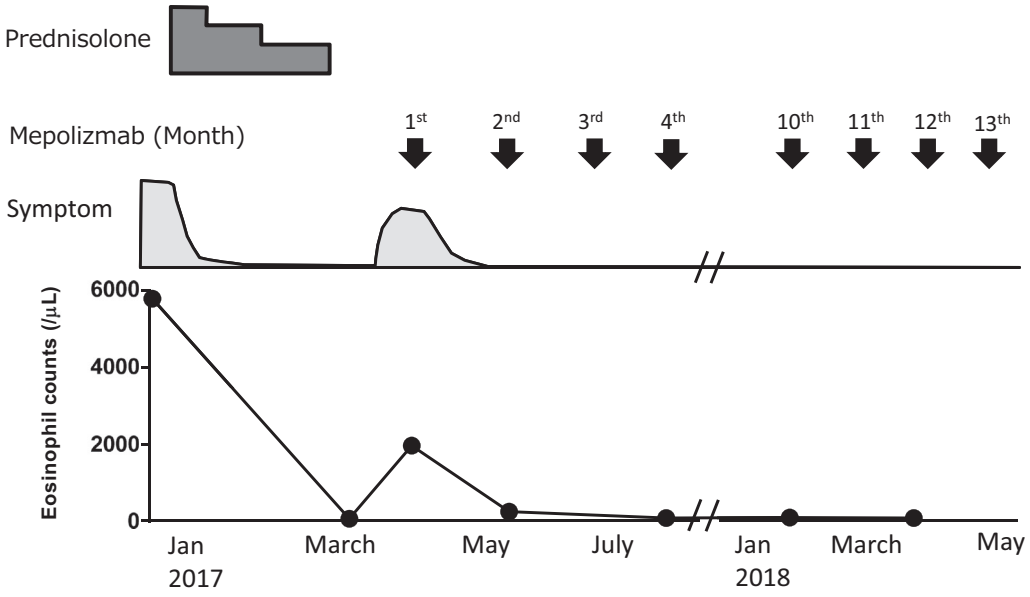

FIGURE 2. Treatment and clinical course. The patient responded to corticosteroid therapy, and his symptoms disappeared with the decrease in peripheral blood eosinophil counts, but his symptoms worsened, with increased peripheral eosinophil counts after termination of systemic corticosteroid therapy. After initiation of mepolizumab therapy, the patient's symptoms disappeared, and his peripheral blood eosinophil counts decreased to the normal range.