Long-Term Treatment With Anti-Interleukin 5 Antibodies in a Patient with Chronic Eosinophilic Pneumonia

Shimizu Y1, Kurosawa M2, Sutoh Y3, Sutoh E3
1 Division of Respiratory Medicine, Kaminakai Family Clinic, Takasaki, Gunma, Japan
2Department of Allergy and Respiratory Medicine, Sutoh Hospital, Annaka, Gunma, Japan
3Department of Surgery, Sutoh Hospital, Annaka, Gunma, Japan


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Chronic eosinophilic pneumonia (CEP), which was first reported by Carrington et al [1], is an insidious lung disease that was traditionally diagnosed based on a triad of pulmonary symptoms, blood eosinophilia, and chest radiographic abnormalities [2]. It is now typically diagnosed based on the combination of pulmonary symptoms (>2 weeks), bronchoalveolar lavage fluid (BALF) and/or blood eosinophilia (usually with a BALF cell count differential >25 % or blood eosinophils >1000/µL.), and infiltrations on chest radiography [3,4]. Interleukin 5 (IL-5) is an essential cytokine in the development, maturation, activation, and proliferation of eosinophils [5]. Consequently, it could be a key element in the pathogenesis of CEP [6,7]. We present the case of a patient with CEP treated with anti–IL-5 antibodies over a 3-year period.

A 58-year-old woman, who had been diagnosed with asthma 1.5 years earlier, visited the clinic because of increasing dyspnea on November 6, 1997. Since a few months earlier, she had been experiencing cough, chest pain, anorexia, fatigue, malaise, and weight loss. On December 12, 1997, the laboratory data showed blood eosinophilia (1040/µL) and an elevated C-reactive protein (CRP) level (40.0 mg/L). Her regimen was changed to prednisolone 10 mg/d and montelukast 10 mg/d orally and daily inhaled budesonide/formoterol 160 µg/4.5 µg at 4 puffs/d. Oral prednisolone was stopped 5 months after initiation of therapy because her symptoms had improved. Her regimen had been constant except for occasional treatments with systemic corticosteroids.

Neither BALF nor TBLB specimens contained malignant cells. The patient was diagnosed with CEP.

Treatment was started with oral prednisolone 30 mg/d, which was tapered to 10 mg/d. Her blood eosinophil count decreased (55/µL), and her CRP level dropped to normal levels. A chest CT scan showed that the ground-glass opacities had cleared. The patient declined to continue with prednisolone therapy and was discharged from the clinic on December 22, 1997. Nine years later, she returned to the clinic to receive treatment for CEP. She was treated with pranlukast 450 mg/d and prednisolone 10 mg/d orally and daily inhaled budesonide/formoterol 160 µg/4.5 µg at 2 puffs/d. Oral prednisolone was stopped 5 months after initiation of therapy because her symptoms had improved. Her regimen had been constant except for occasional treatments with systemic corticosteroids.

On October 15, 2015, the patient was admitted to hospital by an experienced pulmonologist because of unstable respiratory symptoms, such as cough and increasing dyspnea, although not fatigue, malaise, or weight loss. Her blood eosinophil count was 400/µL. The serum total IgE level was 262 IU/mL, and serum specific IgE for *Dermatophagoides* species was positive. Her regimen was changed to prednisolone 10 mg/d and montelukast 10 mg/d orally and daily inhaled budesonide/formoterol 160 µg/4.5 µg at 4 puffs/d.

On April 28, 2016, she visited the emergency department. Her blood eosinophil count was 1071/µL, and she was given an aminophylline and hydrocortisone infusion (Figure). Budesonide/formoterol was prescribed at 160 µg/4.5 µg at 8 puffs/d. On May 6, the blood eosinophil count was 1112/µL. The patient continued to take oral prednisolone because of unstable respiratory symptoms. Her inhaler technique was deemed adequate.

Mepolizumab was the first approved anti–IL-5 antibody for use in patients with severe eosinophilic asthma. It was launched in December 2015 in the 31 European countries.

Figure. Clinical course of a patient diagnosed with chronic eosinophilic pneumonia and allergic refractory asthma. Prednisolone was withdrawn after initiation of monthly mepolizumab on June 6, 2016. In parallel with a sustained reduction in blood eosinophil count, the FEV1 (%) values and ACT scores gradually improved with mepolizumab. Benralizumab was started on May 24, 2018. The pulmonary symptoms have since been controlled with anti–IL-5 antibodies.
covered by the European Medicines Agency. Recent case reports indicated favorable responses to mepolizumab in CEP [8,9]. However, the duration of mepolizumab therapy in these patients remains unclear.

Mepolizumab was administered subcutaneously every 4 weeks, and drug safety was assessed at each visit. CEP and asthma were monitored by automatic counting of eosinophils in peripheral blood combined with measurement of forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) using the Asthma Control Test (ACT) every 4 weeks. Chest CT examinations were performed as necessary.

Mepolizumab was started at 100 mg mepolizumab on June 9, 2016. The blood eosinophil count was 231/µL. The percentages of predicted FVC and FEV1 and the ACT score were 100.9%, 73.3%, and 12. Chest CT showed ground-glass and nodular opacities in the right lower lobe (Figure 1-B supplementary), suggesting relapse of CEP. On July 7, the blood eosinophil count decreased to 14/µL, although FEV1 and the ACT score were 74.6% and 14. On October 27, her FEV1 improved to 76.7% and her ACT score increased to 21. Chest CT showed no infiltrative shadows. She successfully stopped daily use of oral prednisolone. On June 22, 2017, the blood eosinophil count, FEV1, and the ACT score were 7/µL, 78.1%, and 25. She reduced her daily dose of budesonide/formoterol 160 µg/4.5 µg to 4 puffs/d. The fact that she had been taking mepolizumab for 2 years indicated successful long-term management and persistent improvement in pulmonary function. No adverse effects have been observed.

Benralizumab is a monoclonal antibody that targets the α chain of the IL-5 receptor and enables a longer dosing interval than mepolizumab [10]. On May 24, 2018, the blood eosinophil count, FVC, and FEV1 were 12/µL, 115.0%, and 80.0%. Given the benefits of this regimen, she hoped to be given 30 mg benralizumab every 4 weeks for the first 3 doses followed by a fixed-dose injection every 8 weeks. She had mild cough attacks in March 2019, although she rejected systemic corticosteroids. Her blood eosinophil count, FEV1, and ACT score were 112/µL, 74.3%, and 20. Chest CT showed no abnormal findings (Figure 1-E, Supplementary). Therefore, she was given an aminophylline infusion for 4 days. Since then, her pulmonary symptoms have been controlled, and she will receive benralizumab every 8 weeks.

Although recent case reports indicated favorable responses to mepolizumab in CEP [8,9], there is no evidence in favor of the recommended duration of anti–IL-5 antibody therapy for either CEP or asthma. This is the first report of CEP with asthma controlled with long-term IL-5 antibody treatment.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

References