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Letter to the Editor

Benralizumab as initial treatment for chronic eosinophilic pneumonia

Dear Editor,

Chronic eosinophilic pneumonia (CEP) is an eosinophilic inflammatory disease of unknown etiology, characterized by the infiltration of eosinophils into the interstitium and alveoli of the lung. Although CEP usually resolves with systemic corticosteroid treatment (SC), about half of CEP patients relapse after reduction or discontinuation of SC, and long-term SC is often required.¹ We report on a case of CEP successfully treated with benralizumab at initial diagnosis, without the use of SC, and discuss the possibility of anti-interleukin-5 treatment for CEP as an alternative to SC.

A 70-year-old woman with a 1-month history of cough and dyspnea was referred to our hospital for a detailed examination. She was a lifelong non-smoker with a history of bronchial asthma since age 60, treated with budesonide/formoterol 640/18 µg twice daily. She had received a 5-day course of oral prednisolone (30 mg/day) for asthma exacerbation 4 months earlier. Her temperature was 36.9 °C and physical examination revealed no abnormalities. Laboratory data showed peripheral eosinophilia (1400/mm³), elevated serum levels of immunoglobulin E (260 IU/mL), and hypoxemia (PaO₂, 68.4 Torr on room air). Serum anti-myeloperoxidase and anti-proteinase 3 antibodies, and specific immunoglobulin E antibody against *Aspergillus fumigatus* were negative. The results of respiratory function testing were as follows: vital capacity 1.77 L (80.5% predicted), forced vital capacity 1.73 L (78.6% predicted), forced expiratory volume in 1 s 1.22 L (78.2% predicted), and diffusion capacity of the lung for carbon monoxide 15.24 mL/min/mmHg (100.1% predicted). Chest radiography showed an infiltrative opacity in the right apex (Fig. 1A). Computed tomography (CT) of the chest showed ground-glass opacities in the right upper lobe (Fig. 1B) and consolidation in the left lower lobe (Fig. 1C). Bronchoalveolar lavage fluid analysis showed pulmonary eosinophilia (a cell count of 5.01×10^5 /mL, with a cell differential of 66.0% macrophages, 29.5% eosinophils, 4.0% lymphocytes, and 0.5% neutrophils, and a CD4/CD8 ratio of 3.5). A transbronchial lung biopsy specimen obtained from the right upper lobe showed eosinophilic infiltration in the interstitium and alveoli of the lung, consistent with chronic eosinophilic pneumonia (Fig. 2). CEP was diagnosed, but the patient refused

long-term SCs due to their harmful side effects. Benralizumab 30 mg was therefore administered as alternative treatment. The off-label use of benralizumab for CEP in this patient was approved by the ethics committee of Hamamatsu Rosai Hospital (201904C1) and implemented in compliance with the Declaration of Helsinki. Written informed consent was obtained from the patient. One week post treatment, the patient was asymptomatic and her peripheral eosinophilia and hypoxemia had resolved. The infiltrative opacity was no longer visible on chest radiography (Fig. 1D). The ground-glass opacities in the right upper lobe disappeared (Fig. 1E) and the left lower lobe consolidation began to resolve on chest CT (Fig. 1F). A month after administration of benralizumab, a chest radiograph showed no abnormalities (Fig. 1G) and CT showed that the right upper lobe abnormality (Fig. 1H) as well as the consolidation in the left lower lobe (Fig. 1I) had almost completely resolved. Her respiratory function testing normalized as follows: vital capacity 2.17 L (98.6% predicted), forced vital capacity 2.19 L (99.5% predicted), and forced expiratory volume in 1 s 1.83 L (117.5% predicted). She has been receiving benralizumab treatment since diagnosis without any relapse of her CEP and without any need for SC for more than 12 months because she expressed concern about CEP relapse, asthma exacerbation, and side effects of long-term SC. We are continuing follow-up and offering discontinuation of benralizumab.

CEP is an idiopathic pulmonary disease characterized by marked eosinophil accumulation in the pulmonary parenchyma. The mainstay of treatment of CEP is currently SC, and the prognosis is usually good with a favorable response to SC. However, relapse is common, and some patients require long-term SC,¹ resulting in significant side effects such as osteoporosis and opportunistic infection.² There is therefore a need for the development of an effective and safe alternative treatment for CEP. There have been recent reports on the successful treatment of CEP with mepolizumab or benralizumab post relapse after discontinuation of SC.^{3–7} However, to our knowledge, this is the first case of CEP being successfully treated with benralizumab as the initial treatment. Although the pathogenesis of CEP has not been fully elucidated, the possible involvement of interleukin-5 (IL-5) in the accumulation of eosinophils into the lung parenchyma has been reported.^{8,9} Mepolizumab binds to IL-5 and reduces eosino-

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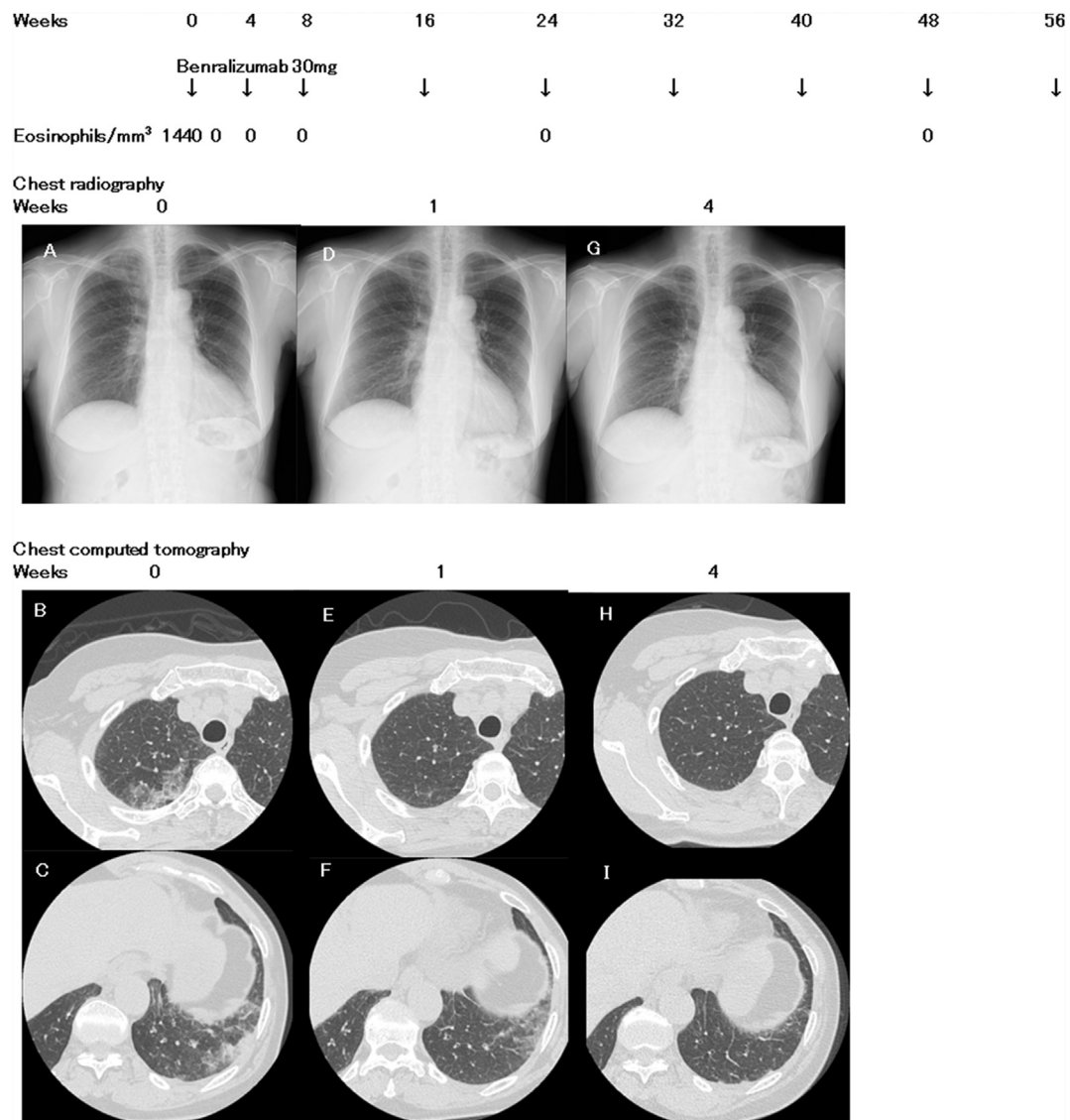


Fig. 1. Benralizumab treatment protocol, peripheral eosinophil counts, and chest radiological findings. The eosinophil count was 1440 at baseline and decreased to 0 immediately after the first administration. Chest radiograph taken at the initial visit to our hospital showed an infiltrative opacity in the right apex (A). Computed tomography (CT) of the chest showed ground-glass opacities in the right upper lobe (B) and left lower lobe consolidation (C). A week after administration of benralizumab, the right apical infiltrative opacity was no longer visible on chest radiograph (D). Chest CT showed that the ground-glass opacities in the right upper lobe had disappeared (E) and the consolidation in the left lower lobe had begun to resolve (F). A month after administration of benralizumab, chest radiograph showed no abnormalities (G). Chest CT revealed that the right upper lobe abnormality (H) and left lower lobe consolidation (I) had almost completely resolved.

phils. In contrast, benralizumab binds to the IL-5 receptor α chain and depletes eosinophils through enhanced antibody-dependent cell-mediated cytotoxicity.⁵ From these observations, anti-IL-5 antibodies or anti-IL-5 receptor α chain antibodies that can reduce or deplete eosinophils are expected to be effective and safe alternative treatments for CEP. In previous reports on CEP in which benralizumab was administered, CEP remission was induced and sustained with a single dose,^{6,7} while in CEP cases treated with mepolizumab, administration was continued for more than a

year.^{3–5} Treatment duration between benralizumab and mepolizumab may differ due to the different pharmacological effects of the two drugs. In the present case, benralizumab treatment was continued for more than 12 months because the patient expressed concern about CEP relapse, asthma exacerbation, and side effects of long-term SC. However, a few administrations of benralizumab might be sufficient for the treatment of CEP if resolution of symptoms, peripheral eosinophilia, and chest radiological findings have been obtained. Further studies involving a large number of

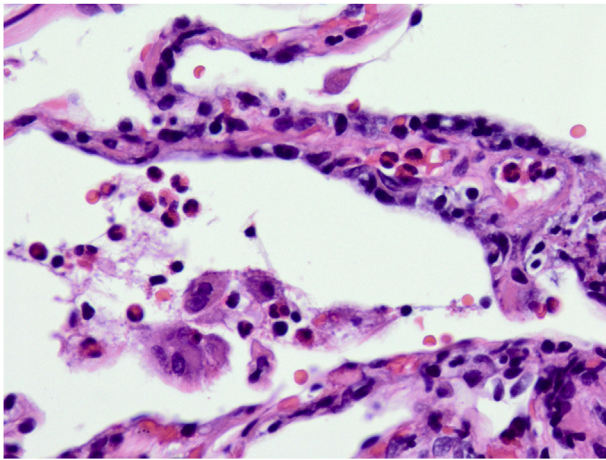


Fig. 2. A transbronchial lung biopsy specimen obtained from the right upper lobe showed eosinophilic infiltration into the interstitium and alveoli of the lung (hematoxylin eosin stain, $\times 400$).

patients are now needed in order to investigate the usefulness and appropriate duration of anti-IL-5 treatment for CEP.

Conflict of interest

The authors have no conflict of interest to declare.

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