Received: 18 November 2023 | Accepted: 4 January 2024

DOI: 10.1002/rcr2.1279

CASE REPORT

Respirology Case Reports OPEN ACCESS APSR WILEY

Successful discontinuation of corticosteroids through remission induction therapy with benralizumab for chronic eosinophilic pneumonia

Yoshiro Kai[1] | Ryosuke Kataoka[1] | Kentaro Suzuki[1] | Eriko Nakamura[2] | Masato Takano[3] | Shigeo Muro[2]

[1]Department of Respiratory Medicine, Minami-Nara General Medical Center, Nara, Japan

[2]Department of Respiratory Medicine, Nara Medical University, Nara, Japan

[3]Department of Diagnostic Pathology, Minami-Nara General Medical Center, Nara, Japan

Correspondence
Yoshiro Kai, Department of Respiratory Medicine, Minami-Nara General Medical Center, 8-1 Fukugami, Oyodo-cho, Yoshino-gun, Nara 638-8551, Japan.
Email: y-kai@eco.ocn.ne.jp

Associate Editor: Kazuyuki Nakagome

Abstract

Chronic eosinophilic pneumonia (CEP) is an eosinophilic lung disease. Treatment for CEP includes corticosteroids; however, CEP often recurs. A 53-year-old woman was referred to our hospital because of poorly controlled asthma. She was treated with combination of moderate-dose inhaled corticosteroid (ICS), a long-acting β2-agonist (LABA), and betamethasone/dexchlorpheniramine. She was switched to single-inhaler triple therapy, after which her asthma control improved; thus, betamethasone/dexchlorpheniramine was discontinued. Ten weeks later, she was diagnosed with CEP due to marked eosinophilia and pulmonary eosinophilic infiltrates. Oral corticosteroid treatment was initiated, symptoms improved, and peripheral blood eosinophilia decreased with improved infiltrative shadows. Remission induction therapy was initiated with benralizumab combined with corticosteroid therapy. Eosinophilia and inflammatory responses decreased. After 7 months, corticosteroid was discontinued, and she was treated with benralizumab alone. She remained in remission for 4 months. This case suggests that benralizumab may be useful as a remission induction therapy in patients with CEP.

KEYWORDS
Benralizumab, chronic eosinophilic pneumonia, corticosteroid, remission, severe asthma

INTRODUCTION

Chronic eosinophilic pneumonia (CEP) is a lung disorder characterized by marked accumulation of eosinophils in the pulmonary interstitium and alveolar spaces. Standard treatment for CEP includes systemic corticosteroids. However, patients often experience CEP recurrence and require repeated and prolonged courses of corticosteroids that are associated with many adverse effects, such as osteoporosis, myopathy, and increased risk of infection. A recent literature review revealed that biological treatments such as humanized monoclonal antibody against interleukin-5 (IL-5) (mepolizumab) and humanized monoclonal antibody against IL-5 receptor α (benralizumab) are novel approaches for CEP with severe asthma.[1] There are a few reports of benralizumab treatment for CEP[2,3] We present a case of successful discontinuation of corticosteroids through remission induction therapy with benralizumab.

CASE REPORT

A 53-year-old woman with a 16-year history of oral medication treatment for depression was referred to our hospital for poorly controlled asthma. She was a never-smoker and had been diagnosed with bronchial asthma for >10 years. She was treated with a combination of inhaled corticosteroid (ICS)/a long-acting β2-agonist (LABA) (fluticasone propionate) [FP; 250 μg]/salmeterol [SM; 50 μg] and betamethasone 0.25 mg/dexchlorpheniramine 2 mg (Celestamine®) at

the primary care clinic. She was switched to single-inhaler triple therapy (indacaterol [IND; 150 μg]/glycopyrronium [GLY; 50 μg]/mometasone furoate [MF; 160 μg]) due to poor control of bronchial asthma. We initiated triple therapy, asthma control test (ACT) score improved from 5 to 23, and chest x-ray was normal and systemic steroids were discontinued after 6 weeks. However, after discontinuing systemic steroid treatment, a worsening of bronchial asthma was observed. An uncontrolled asthma state was indicated by ACT score of 5. Laboratory data showed an elevated white blood cell count (10,400 cells/μL), with 60.2% eosinophils. C-reactive protein level was 0.28 mg/dL, and the total serum immunoglobulin (Ig)-E level was 1090 IU/mL (normal range: 0–148 IU/mL). The results of serum proteinase-3 antineutrophil cytoplasmic antibody (ANCA) and myeloperoxidase-ANCA were negative (<1.0 U/mL). The atrial blood examination under ambient air showed a pH of 7.419, partial pressure of carbon dioxide ($PaCO_2$) of 44.3 mmHg, partial pressure of oxygen (PaO_2) of 76.0 mmHg. Chest radiograph revealed reticular shadows in the bilateral lungs (Figure 1A). Chest computed tomography (CT) revealed ground glass opacity in bilateral lung fields. Bronchiolitis or centrilobular nodules or bronchial wall thickening were not detected (Figure 1B–F). Inflammatory markers indicated elevated fractional exhaled nitric oxide levels (FeNO, 127 ppb). Rheumatoid factor (RF) levels were elevated (34 IU/mL). Pulmonary function test revealed a forced expiratory volume in 1 s (FEV1) of 2020 mL (85.5% of predicted value) and FEV1/forced vital capacity of 61.0%. The patient also had sinusitis with slightly thickened mucosa and retained the secretions of maxillary sinuses. (Figure 1M,N). We performed bronchoscopy. By observation, mucus plugs were not detected. Bronchoalveolar lavage fluid (BALF) contained a high percentage of eosinophils (71.0%). The transbronchial lung biopsy specimens showed eosinophilic infiltration (Figure 1O,P). Charcot–Leyden Crystals were not detected. She was diagnosed with CEP accompanied with bronchial asthma. Figure 2 shows the clinical course of the patient.

After bronchoscopy, systemic prednisolone (PSL) 40 mg, were administered. Peripheral blood eosinophil counts decreased and chest radiograph findings showed improvement (Figure 1G–L). The ACT score improved

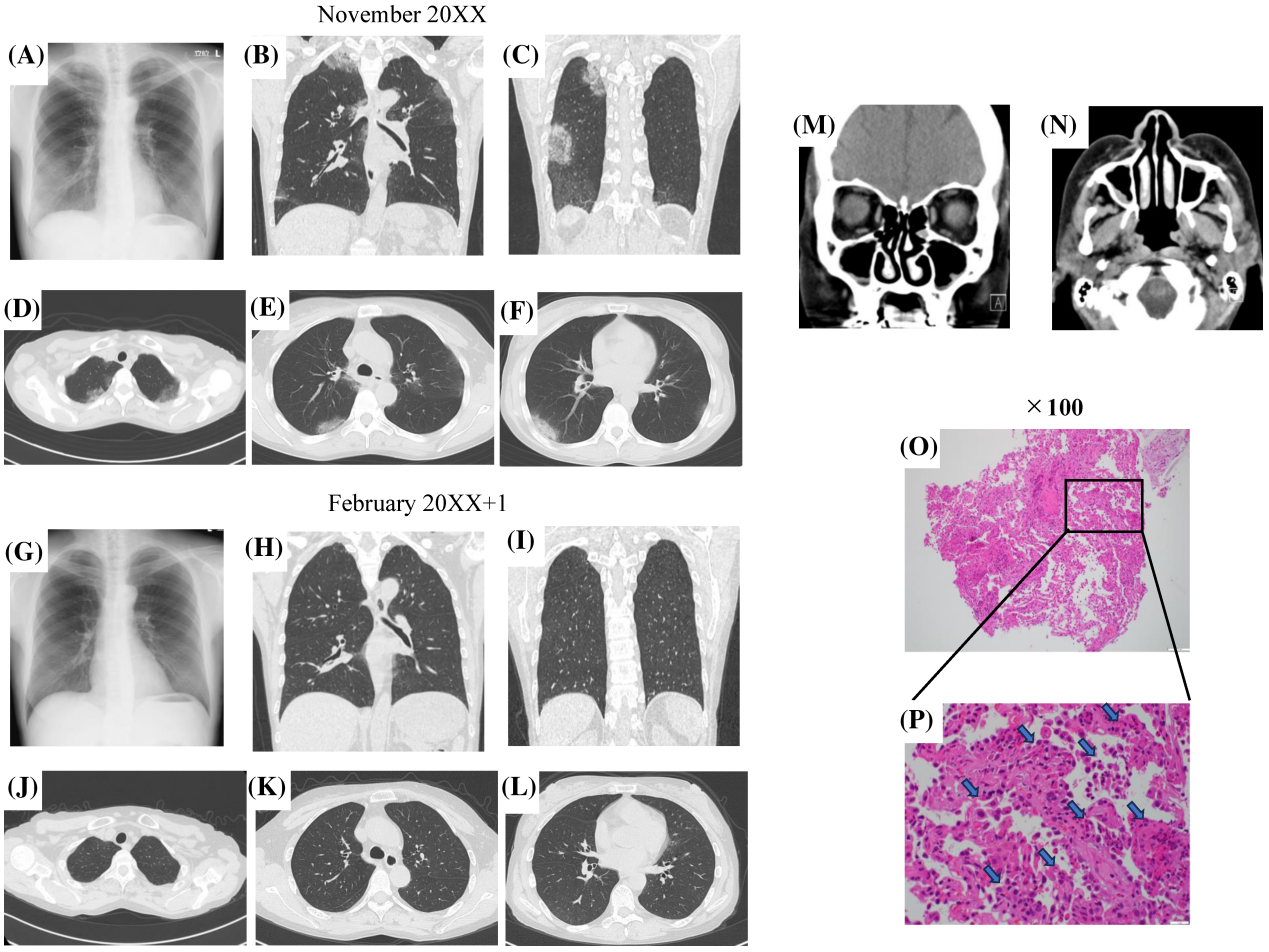

FIGURE 1 Imaging findings and histology of the patient. (A) Chest radiograph showing bilateral ground glass opacity shadows and (G) a significant improvement after treatment with corticosteroids. Chest CT showing (B–F) nonsegmental bilateral consolidation and (H–L) significant improvement after treatment with corticosteroids. (M, N) Paranasal CT showing slight sinus shadows. Lung biopsy samples (O, P) with haematoxylin and eosin staining indicating eosinophilic infiltration (arrowheads).

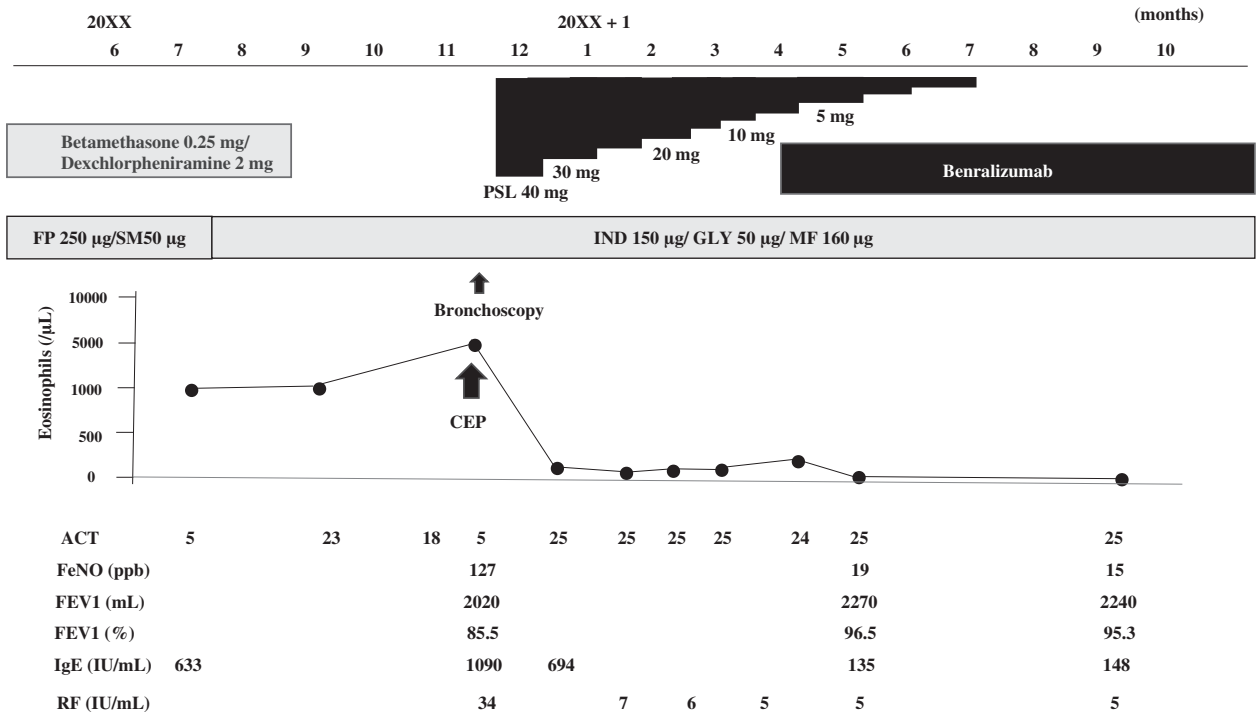

FIGURE 2 Clinical course of the patient. After the diagnosis of chronic eosinophilic pneumonia (CEP), remission induction therapy was initiated with benralizumab combined with corticosteroid therapy. After 7 months, corticosteroid was discontinued and she was treated with benralizumab alone without recurrence.

from 5 to 25. The RF levels were normalized. However, after starting corticosteroid treatment, her depression worsened. Therefore, corticosteroid dose was immediately tapered. Due to the risk of recurrence by rapid withdrawal of corticosteroid treatment, we obtained informed consent to initiate remission induction therapy with benralizumab, a humanized monoclonal antibody that targets the IL-5α receptor (30 mg every 4 weeks for 3 doses and then once every 8 weeks). After the initiation of benralizumab, the blood eosinophil count dropped to 0. The corticosteroid dose was subsequently reduced. Approximately 3 months later, corticosteroids were discontinued. After continued treatment with corticosteroids, the patient continued treatment with benralizumab alone and has remained in remission for approximately 4 months.

DISCUSSION

CEP is a progressive eosinophilic lung disease.[1] The standard treatment is systemic corticosteroids, which generally provide good responses in patients with CEP. However, CEP often recurs while tapering the dose and/or after discontinuing corticosteroids. Moreover, repeated and prolonged courses of corticosteroids are associated with many adverse effects. Recently, several case reports have shown that benralizumab, a humanized monoclonal antibody targeting the IL-5α receptor, is an alternative approach for CEP treatment.[2,3] In SIROCCO and CALIMA studies, benralizumab reduced the exacerbation rate and improved FEV1 in patients with severe eosinophilic asthma.[4] Furthermore, in the ZONDA study, benralizumab led to eosinophil depletion and decreased systemic corticosteroids in patients with severe eosinophilic asthma.[4] Benralizumab treatment resulted in a marked reduction in peripheral blood eosinophil counts.[4] Furthermore, benralizumab reduced eosinophil counts in the mucosa/submucosa of the airways and in the sputum.[5] IL-5-mediated eosinophil migration to the alveoli may play a pivotal role in CEP,[1] which may be suppressed by benralizumab. Benralizumab is reported to control eosinophilic bronchiolitis with (eosinophil extracellular trap cell death) EETosis with mucus plugs.[6] In this case, eosinophil counts in BALF increased, and the lung samples revealed an increase in eosinophil infiltration. Parallel to the increase in eosinophil count, the symptoms of asthma worsened. After the induction of corticosteroids and addition of benralizumab, asthma and lung infiltration symptoms also improved, followed by an improvement in lung airflow obstruction. Chest CT revealed a reduction in infiltration in the bilateral lung field. The RF is reported to increase in patients with eosinophilic granulomatosis with polyangiitis (EGPA).[7] In this case, the RF levels were elevated; however, vasculitis, which is characterized by EGPA, was not detected. After treatment with corticosteroid and benralizumab, the RF levels were normalized. Benralizumab controls diseases with eosinophil activation and has the potential to control other activated eosinophil-related diseases, including EGPA.

This is the rare report to describe remission induction therapy using benralizumab in combination with corticosteroid therapy. Herein, we report the successful discontinuation of corticosteroids through remission induction therapy using benralizumab in patients with CEP. In conclusion, this report suggests that benralizumab may represent an induction treatment

option for cases of CEP with severe asthma requiring rapid discontinuation of corticosteroids due to serious corticosteroid-induced adverse effects. Additional studies are warranted to evaluate the effectiveness of benralizumab for treating CEP with severe asthma.

AUTHOR CONTRIBUTIONS

Y.K. wrote the manuscript. All authors contributed to the editing of the manuscript and approved the final version of the manuscript.

ACKNOWLEDGMENTS

We thank Enago (www.enago.jp) for English language editing.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

All data generated or analysed during this study are included in this article.Further enquiries can be directed to the corresponding author.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

ORCID

Yoshiro Kai https://orcid.org/0000-0001-6197-5176
Eriko Nakamura https://orcid.org/0000-0003-0913-2475
Shigeo Muro https://orcid.org/0000-0001-7452-9191

REFERENCES

1. Nakagome K, Nagata M. Possible mechanisms of eosinophil accumulation in eosinophilic pneumonia. Biomolecules. 2020;10(4):638.
2. Izhakian S, Pertzov B, Rosengarten D, Kramer MR. Successful treatment of acute relapse of chronic eosinophilic pneumonia with benralizumab and without corticosteroids: a case report. World J Clin Cases. 2022;10(18):6105–9.
3. Izumo T, Kuse N, Awano N, Tone M, Jo T, Yoshimura H, et al. Rapid and sustained effects of a single dose of benralizumab on chronic eosinophilic pneumonia. Respir Med Case Rep. 2020;30:101062.
4. Nagase H, Ueki S, Fujieda S. The roles of IL-5 and anti-IL-5 treatment in eosinophilic diseases: asthma, eosinophilic granulomatosis with polyangiitis, and eosinophilic chronic rhinosinusitis. Allergol Int. 2020;69(2):178–86.
5. Laviolette M, Gossage DL, Gauvreau G, Leigh R, Olivenstein R, Katial R, et al. Effects of benralizumab on airway eosinophils in asthmatic patients with sputum eosinophilia. J Allergy Clin Immunol. 2013;132(5):1086–1096.e1085.
6. Sasaki H, Miyata J, Irie A, Kuwata A, Kouzaki Y, Ueki S, et al. Case report: eosinophilic bronchiolitis with eosinophil ETosis in mucus plugs successfully treated with benralizumab. Front Pharmacol. 2021;12:826790.
7. Takahashi H, Komai T, Setoguchi K, Shoda H, Fujio K. A diagnostic score for eosinophilic granulomatosis with polyangiitis among eosinophilic disorders. Allergol Int. 2023;72(2):316–23.

How to cite this article: Kai Y, Kataoka R, Suzuki K, Nakamura E, Takano M, Muro S. Successful discontinuation of corticosteroids through remission induction therapy with benralizumab for chronic eosinophilic pneumonia. Respirology Case Reports. 2024;12(1):e01279. https://doi.org/10.1002/rcr2.1279