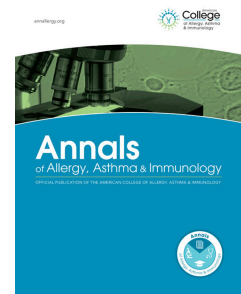


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Relapsing Chronic Eosinophilic Pneumonia Treated Successfully with Benralizumab

Peter A. Ricketti, DO, Anthony J. Ricketti, MD



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Title Page

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Authors: Peter A. Ricketti, DO, Anthony J. Ricketti, MD

Corresponding Author Information:

Peter A. Ricketti, DO
Mercer Allergy and Pulmonary Associates, LLC
1544 Kuser Road, Suite C-6
Trenton, New Jersey 08619
Telephone: (609)-581-9900
Fax: (609)-581-9905
Email: peter.ricketti@gmail.com

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Abbreviations/Acronyms:

Chronic eosinophilic pneumonia – CEP
Computed tomography – CT
Complete blood count – CBC
Total eosinophil count – TEC
Bronchoalveolar lavage – BAL
Chest x-ray – CXR

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Chronic eosinophilic pneumonia (CEP) is a rare, idiopathic inflammatory disease characterized by eosinophilic infiltration in the lung. CEP is a clinical and laboratory diagnosis. It presents with pulmonary symptoms, abnormal chest imaging, peripheral eosinophilia and eosinophils in pulmonary tissue (1). The condition has a 2:1 female predominance and a mean age of 45 years at time of diagnosis. Two-thirds of patients have a prior history of asthma and approximately half a history of atopy, including eczema, urticaria and nasal polyposis (2). Asthma typically is present prior to CEP but occasionally develops during the course of disease.

Concomitant asthma is often severe and sometimes progressive despite treatment with corticosteroids (3). The main treatment of CEP is corticosteroids and the response is usually excellent. About half of the patients relapse during or after tapering corticosteroid therapy (4). Since prolonged systemic corticosteroid therapy may be needed, adverse side effects from therapy are common. Therefore, new treatments are needed for CEP. We report the first case of CEP successfully treated with multiple doses of benralizumab.

The patient was a 57 year-old Caucasian male who initially presented to the hospital in November 2014 for cough, dyspnea, night sweats, fever, fatigue and anorexia with a 7 kg weight loss. He had a history of asthma which started one year prior to this admission. He denied signs or symptoms of neuropathy, hypertension, abdominal pain, voice changes or vasculitis. His past medical history included anxiety with depression, flexural eczema, benign prostatic hypertrophy, and seasonal allergic rhinitis. He denied any prior smoking history and environmental or occupational exposure to chemicals, dusts, or antigens associated with hypersensitivity pneumonitis. He reported homosexual relations for the past several years but had a negative HIV screening test. His medications included tamsulosin for benign prostatic hypertrophy and fluticasone propionate/salmeterol 250/50 mcg diskus twice daily. He denied any recreational

drug use, over-the-counter medications, or recent antibiotic use. On physical examination, the temperature was 101.4°F, pulse 122/min, oxygen saturation 89% on room air and BP 111/69 mm Hg. The lungs revealed bilateral crackles. There was no organomegaly, lymphadenopathy or skin lesions.

The computed tomography (CT) scan of the chest revealed multisegment, right-sided infiltrates and a left upper lobe infiltrate (Figure 1). The complete blood count (CBC) revealed a white blood count of 31.8×10^9 cells/L with 43% eosinophilia (total eosinophil count (TEC) 13.7×10^9 cells/L). The antinuclear cytoplasmic antibody (p-ANCA and c-ANCA) tests were both negative. The patient underwent bronchoscopy and the bronchoalveolar lavage (BAL) was negative for fungi, acid-fast bacilli, microorganisms or parasites. The cell distribution from the lavage revealed 68% eosinophils, 20% macrophages, 5% lymphocytes, and 7% neutrophils. A stool sample for ova and parasites was negative. A screening HIV test was non-reactive. His IgE level was 78 IU/mL. The sedimentation rate was 41 mm/hr.

The patient was placed on prednisone 40 mg/day and had a significant improvement in his symptoms. His chest x-ray (CXR) and eosinophilia (TEC undetectable) improved. The patient remained on moderate doses (10-15 mg) of daily prednisone and eventually weaned off of corticosteroids in February 2017. He remained well until January 2018 when he developed malaise, cough, wheeze, dyspnea, mild anorexia, and nasal congestion. He was noted to have a patchy infiltrate in the right upper lobe on CXR. The CBC revealed an eosinophil count of 8% (TEC 700 cells/ μ L), and the patient was receiving another course of prednisone 40 mg/day for 5 days prior to the CBC. The patient weaned off corticosteroids after 4 months. He had a repeat exacerbation in July 2018 with a CT scan revealing bilateral infiltrates, and the CBC showed an eosinophil count of 13.4% (TEC 900 cells/ μ L).

The patient requested different therapy because of corticosteroid induced weight gain, osteopenia, and new-onset diabetes mellitus type II. He was placed on benralizumab 30 mg every 4 weeks for 3 doses, and then once every 8 weeks. The prednisone dosing was tapered over the next 3 weeks. The patient had a clinical response to benralizumab with no respiratory symptoms for the past 30 months of observation. His TEC has remained undetectable over this time interval and his pulmonary function testing and CXR have remained normal.

Eosinophils interact with multiple cellular pathways, including T_H2 cells, mast cells, basophils, macrophages and multiple interleukins, but recruitment of the eosinophil to the lung is most likely directed by IL-5 and the eotaxin subfamily of chemokines. BAL fluid from affected areas of the lung has elevated IL-5 levels correlating with disease activity in CEP (5).

In an attempt to minimize corticosteroid usage in CEP, biologic agents have been utilized to treat symptoms and prevent relapse of CEP. Omalizumab was used in a patient with CEP after a second relapse in 2 years. This patient had an elevated IgE and was disease-free with 15 months of omalizumab treatment (6). Reslizumab at a dose of 3 mg/kg was initiated every 4 weeks in a patient with CEP and resulted in discontinuation of corticosteroids and remission for 6 months (7). Mepolizumab was used effectively in another patient with CEP and a 20-year history of asthma during his second relapse at 100 mg every month for several months (8). Benralizumab was used in a patient with eosinophilic pneumonia with multiple relapses. The patient was given 30 mg and remained symptom-free for 8 weeks (9).

Benralizumab neutralizes IL-5 function by binding the alpha subunit of the IL-5 receptor and induces apoptosis of target cells via antibody-dependent cell-mediated cytotoxicity (10). The patient described responded well to therapy and has been disease-free for 30 months with q8 week benralizumab therapy. Although long-term safety of benralizumab in patients with CEP is

70 unknown, this medication has far fewer toxicities than systemic corticosteroids and can possibly
71 be used long-term for the treatment of CEP to prevent relapses of the condition. This is the first
72 case report utilizing benralizumab in a patient with CEP treated with multiple doses of the
73 monoclonal antibody over 30 months. This monoclonal antibody may be a good treatment option
74 for CEP especially in patients with frequent relapses or patients with relapses when the
75 corticosteroid dose is reduced.

References

1. Rose DM, Hrnclir DE. Primary eosinophilic lung diseases. *Allergy Asthma Proc* 2013;34(1):19-25.
2. Cottin V. Eosinophilic lung diseases. *Clin Chest Med* 2016;37(3):535-536.
3. Ishiquro T, Takayanagi N, Uozumir R, Tada M, et al. The long-term clinical course of chronic eosinophilic pneumonia. *Intern Med* 2016;55:2373-2377.
4. Suzuki Y, Suda T. Long-term management and persistent impairment of pulmonary function in chronic eosinophilic pneumonia: a review of the previous literature. *Allergol Int* 2018;334-340.
5. Kita H, Sur S, Hunt LW, Edell ES, et al. Cytokine production at the site of disease in chronic eosinophilic pneumonitis. *Am J Resp Crit Care Med* 1996;153:1437-1441.
6. Kaya H, Gumus S, Ucar E, et al. Omalizumab as a steroid-sparing agent in chronic eosinophilic pneumonia. *Chest* 2012;142(2):513-516.
7. Sarkis E, Patel S, Burns K, et al. Anti-interleukin (IL-5) as a steroid-sparing agent in chronic eosinophilic pneumonia. *J Asthma* 2018:1-5.
8. To M, Kono Y, Yamawki S, et al. A case of chronic eosinophilic pneumonia successfully treated with mepolizumab. *J Allergy Clin Immunol Pract* 2018;6(5):1746-1748.e1.
9. Isomoto K, Baba T, Sekine A, et al. Promising effects of benralizumab on chronic eosinophilic pneumonia. *Intern Med* 2020;59:1195-1198.
10. Vanricchi G, Bagnasco D, Borriello F, et al. Interleukin-5 pathway inhibition in the treatment of eosinophilic respiratory disorders: evidence and unmet needs. *Curr Opinion Allergy Clin Immunol* 2016;16(2):186-200.

Figure 1: CT of the chest demonstrating multisegment right sided infiltrates and a left upper lobe infiltrate.

