

Effect of mepolizumab alone in chronic eosinophilic pneumonia relapse: A case report

Marcello Ciuffreda, MD^a, Cristiano Caruso, MD^b,
Antonino Romano, MD^c, and Antonella Sarni, MD^a



Clinical Implications

- Mepolizumab might be an excellent treatment for chronic eosinophilic pneumonia when relapses or serious complications occur. The effects related to a mepolizumab treatment might be as effective and long-lasting as the ones obtained with oral corticosteroids.

Chronic eosinophilic pneumonia (CEP) is a rare disorder characterized by the massive accumulation of eosinophils in the lungs and may be associated with blood eosinophilia. The response to steroids is common as well as a relapse after tapering or suspension; frequently long-term oral corticosteroid administration is needed. We described a clinical case successfully treated with mepolizumab alone during a relapse of CEP, instead of chronic systemic steroids or concomitant steroids therapy as it usually occurs. We observed an improvement of clinical symptoms, radiological thoracic computed tomography (CT) scan, and biological markers. This case confirms that mepolizumab might be an excellent treatment for CEP when relapses or serious complications occur. It is yet to be known if anti-IL-5 therapy could reduce the risk to develop systemic disorders as vasculitis in these patients.

CEP is a rare disorder characterized by the massive accumulation of eosinophils in the lungs and may be associated with blood eosinophilia.¹ In the evaluation of the differential diagnosis, it is necessary to rule out systemic disease, infectious (parasitosis), autoimmune (eg, eosinophilic granulomatosis with polyangiitis [EGPA]), and immunological disease (allergic bronchopulmonary aspergillosis, cryptogenic organizing pneumonia). The clinical presentation is characterized by symptoms such as dyspnea and cough, but also hypereosinophilia and compatible pulmonary infiltrates. Some cases might be misdiagnosed because of disease incidence, nonspecific clinical presentation, or overlap with other entities. Rapid improvement with systemic steroid therapy is typical. The response to steroids is common as well as a relapse after tapering or suspension; frequently long-term oral corticosteroid administration is needed. Alternative therapy has been described in case reports with biological agents.^{2,3} We described a clinical case successfully treated with mepolizumab alone during a relapse of CEP, instead of an initially concomitant therapy with systemic steroids, as it usually occurs. A 59-year-old nonsmoking woman had been diagnosed with allergic asthma from the age of 20. She came to our observation with a diagnosis of chronic eosinophilic pneumonia performed 8 years before. The symptoms had begun in 2011 with dyspnea due to minimal strain and chronic cough. CT showed bilateral lung infiltration as ground glass opacity (GGO).

Spirometry has documented mild functional restriction (forced vital capacity [FVC] 78%, total lung capacity 82%, forced expiratory volume in 1 second [FEV₁] 84%, FEV₁/FVC 74%). Pulmonary auscultation revealed bilateral wheezing during forced expiratory, no crepitations. Blood tests showed severe hyper-eosinophilia on peripheral blood, eosinophils at 32%, 3100 eosinophil μ L in total count, elevated C-reactive protein 50 mg/L, and IgE total 78 IU/mL. The skin prick test for respiratory inhalant (including *Aspergillus*) was negative. The patient underwent a bronchoscopy with bronchoalveolar lavage fluid (BALF). Microbiological examinations were negative, including fungi (PCR for *Aspergillus*). The alveolar cytogram documented 250,000 total cells with 60% of eosinophils, 35% of macrophages, 3% of lymphocytes, and 2% of neutrophils. Trans-bronchial biopsy (TBB) was not performed. The autoimmunity examinations (pANCA and cANCA, anticytoplasmic autoantibodies) were negative. Gastroscopy was normal. The patient has never presented signs or symptoms of neuropathy or gastrointestinal pain. She has never showed signs of vasculitis, skin lesions, or voice dysfunction. She has never lost weight or reported myalgias. She was not exposed to antigens that cause hypersensitivity pneumonitis. Parasitology stool samples were negative. Therapy with long-acting bronchodilators β_2 -agonists (salmetamol), inhaled steroids (fluticasone propionate 1000 μ g for a day), and leukotriene receptor antagonist (montelukast 10 mg) was started, associated with 32 mg of oral methylprednisolone.

The clinical symptoms improved rapidly, and a thoracic CT scan after 1 month showed the disappearance of pulmonary infiltrates. Attempts to reduce and suspend steroids were without success, and steroids were continued until March 2019. Symptoms, particularly dyspnea, were controlled with 16 mg of methylprednisolone dosage. Dosage of steroids lower than 16 mg caused relapsed dyspnea and fatigue. In March 2019, 8 years after the beginning of the therapy, the patient decided by herself to reduce and suspend the steroids because of adverse effects: difficult-to-control hypertension, hyperglycemia, osteoporosis, and aesthetic changes (moon face). After several weeks, she had an unscheduled visit for a follow-up about respiratory parameters; we prescribed blood tests and a thoracic CT scan to redefine the diagnosis. The radiological examination (Figure 1) presented new GGO lung infiltrates in the lung segment associated with peripheral hypereosinophilia 1,800 per μ L. We decided not to perform again bronchoscopy with BALF and TBB because the diagnosis was clear. The patient refused to restart steroids because of the adverse effects that she had undergone (hyperglycemia, hypertension, and aesthetic changes). We discussed the case, and we decided to start mepolizumab, which is approved for the treatment of eosinophilic severe asthma and EGPA, without resuming steroid. The symptoms gradually improved. Pulmonary auscultation revealed normal sounds. CT scan after 3 months showed the disappearance of pulmonary infiltrates. Actually, after 10 months of therapy, the patient received mepolizumab monthly with a dosage of 100 mg, and she is now in complete wellness. Lung diffusion capacity (DLCO) and pulmonary function tests are normal (FVC 98%, total lung capacity 105%, FEV₁ 95%, FEV₁/FVC 93%, DLCO 91%). Compared with the clinical presentation at the beginning of the therapy, there was a

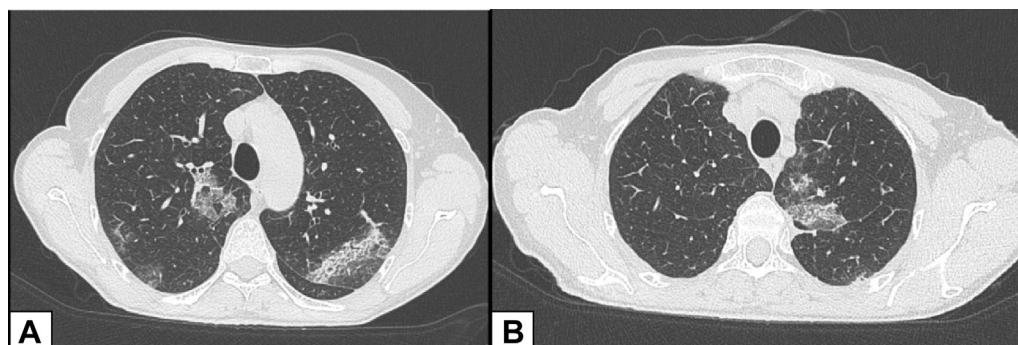


FIGURE 1. Thoracic computed tomography scan, lung windows. Ground glass opacity (A) and lung infiltrate prevalent in the apical regions, before mepolizumab treatment (B), March 2019.

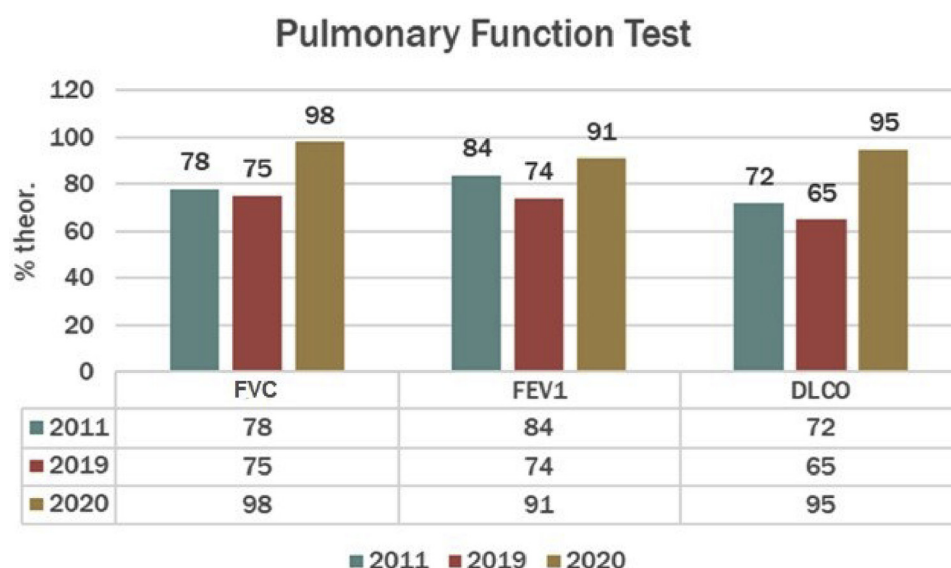


FIGURE 2. Pulmonary function test before treatment (2011, 2019) and after 10-month mepolizumab therapy (2020). There was improvement in lung volume, FEV₁, and lung diffusion capacity concordant with the disappearance of alveolar infiltrates at CT scan. CT, Computed tomography; DLCO, lung diffusion capacity; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

prevalent improvement in lung volume and DLCO with regard to maximal expiratory flow; this is in accordance with the disappearance of alveolar infiltrates at CT scan (Figure 2). Data for arterial blood gases are PaO₂ 78 mm Hg, PaCO₂ 43 mm Hg, pH 7.48. Eosinophils in peripheral blood are reduced to 8 per μ L with 1.3 in percentage counts, and Asthma Control Test (ACT) is improved (ACT equal to 10 before treatment and equal to 20 after treatment). Recent case reports documented a good response to mepolizumab in CEP;^{3,4} Masako⁴ reported a patient with relapsed CEP, which was successfully treated with mepolizumab only, confirming our findings that mepolizumab is an excellent treatment for CEP when serious adverse effects of corticosteroid administration occur. The long-term safety of anti-IL-5 antibody therapy was also reported by Shimizu.³ Compared with these studies, ours showed a more rapid improvement in the clinical symptoms, as well as in CT scans.

We decided to start mepolizumab because the patient refused corticosteroid therapy, which is usually maintained for several months after starting with biological drugs. Clinical symptom

improvement was obtained, and radiological evidence of GGO disappeared on the CT scan exactly as expected with corticosteroids. Biological agents are potential treatments for CEP, through the effect of IL-5 blocking molecules, or eliciting a natural killer cell-mediated antibody-dependent cellular cytotoxicity against eosinophils.

This case confirms that mepolizumab might be an excellent treatment for CEP when relapses or serious complications occur. This case is a “pure” CEP without systemic expression of vasculitis. There are case reports in literature in which CEP presents several years before the appearance of systemic vasculitis (polyarteritis nodosa).⁵ Patients with CEP are at risk to develop systemic disorders as eosinophilic granulomatosis with polyangiitis (up to 40%)^{6,7} according to dysregulation of the immunological pathway. Mepolizumab proved to be an excellent treatment for CEP, but it also improved the patient’s lung function compared with 2 years earlier, when the symptoms first presented. Mepolizumab reduces the activation and growth of eosinophils involved in both diseases; it is yet to be known if

anti-IL-5 therapy is able to prevent the onset of vasculitis, which is the commonly labeled use of the drug. It is also useful to confirm the results obtained from the case reports on a larger group of patients homogeneous for CEP, to evaluate the long-term outcome and to know how many patients treated with anti-IL-5 for chronic eosinophilic pneumonia will develop vasculitis such as EGPA. Mepolizumab might be an excellent treatment for CEP when relapses or serious complications occur.

^aUOSD Pneumology, S.M. Goretti Hospital, ASL Latina, Latina, Italy

^bAllergy Unit, Fondazione Policlinico Universitario A. Gemelli, IRCCS, Rome, Italy

^cIRCCS Oasi Maria S.S., Troina, Italy & Fondazione Mediterranea G.B. Morgagni, Catania, Italy

No funding was received for this work

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication March 18, 2020; revised June 18, 2020; accepted for publication June 19, 2020.

Available online July 13, 2020.

Corresponding author: Cristiano Caruso, MD, c/o Policlinico Gemelli, Largo Gemelli, 1, Rome, Italy. E-mail: cristiano.caruso@policlinicogemelli.it.

2213-2198

© 2020 American Academy of Allergy, Asthma & Immunology

<https://doi.org/10.1016/j.jaip.2020.06.053>

REFERENCES

1. Allen J, Wert M. Eosinophilic pneumonias. *J Allergy Clin Immunol Pract* 2018;6:1455-61.
2. Crowe M, Robinson D, Sagar M, Chen L, Ghamande S. Chronic eosinophilic pneumonia: clinical perspectives. *Ther Clin Risk Manag* 2019;15:397-403.
3. Shimizu Y, Kurosawa M, Sutoh Y, Sutoh E. Long-term treatment with anti-interleukin 5 antibodies in a patient with chronic eosinophilic pneumonia. *J Investig Allergol Clin Immunol* 2020;30:154-5.
4. To M, Kono Y, Yamawaki S, Soeda S, Katsube O, Kishi H, et al. A case of chronic eosinophilic pneumonia successfully treated with mepolizumab. *J Allergy Clin Immunol Pract* 2018;6:1746-1748.e1.
5. Cogen FC, Mayock RL, Zweiman B. Chronic eosinophilic pneumonia followed by polyarteritis nodosa complicating the course of bronchial asthma. *J Allergy Clin Immunol* 1977;60:377-82.
6. Lanham JG, Elkon KB, Pusey CD, Hughes GR. Systemic vasculitis with asthma and eosinophilia: a clinical approach to the Churg-Strauss syndrome. *Medicine (Baltimore)* 1984;63:65-81.
7. Steinfeld S, Golstein M, De Vuyst P. Chronic eosinophilic pneumonia (CEP) as a presenting feature of Churg-Strauss syndrome (CSS). *Eur Resp J* 1994;7:2098.