



Anti-interleukin (IL)-5 as a steroid-sparing agent in chronic eosinophilic pneumonia

Edmond Sarkis, Sumit Patel, Kenneth Burns, Hanan Batarseh & M. Jeffery Mador

To cite this article: Edmond Sarkis, Sumit Patel, Kenneth Burns, Hanan Batarseh & M. Jeffery Mador (2018): Anti-interleukin (IL)-5 as a steroid-sparing agent in chronic eosinophilic pneumonia, Journal of Asthma, DOI: [10.1080/02770903.2018.1543434](https://doi.org/10.1080/02770903.2018.1543434)

To link to this article: <https://doi.org/10.1080/02770903.2018.1543434>



Published online: 16 Nov 2018.



Submit your article to this journal [↗](#)



Article views: 12



View Crossmark data [↗](#)

CASE REPORT



Anti-interleukin (IL)-5 as a steroid-sparing agent in chronic eosinophilic pneumonia

Edmond Sarkis, MD^a, Sumit Patel, MD^a, Kenneth Burns, MD^a, Hanan Batarseh, MD^b, and M. Jeffery Mador, MD^{c,d} 

^aPulmonary and Critical Care, School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, New York, USA; ^bInternal Medicine, School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, New York, USA; ^cMedicine, University at Buffalo, Buffalo, New York, USA; ^dMedicine, Buffalo VAMC, Buffalo, New York, USA

ABSTRACT

Introduction: Anti-interleukin (IL)-5 therapy is a novel drug class clinically effective in patients with diverse eosinophil-related disorders such as allergic eosinophilic asthma, eosinophilic granulomatosis with polyangiitis (EGPA), nasal polyposis, eosinophilic COPD, and other non-pulmonary disorders such as eosinophilic esophagitis. Chronic eosinophilic pneumonia (CEP) is a steroid responsive disorder, however, relapses are common following corticosteroid tapering. **Case Study:** We present the case of a 42-year-old woman with steroid-dependent relapsing CEP successfully treated with anti-IL-5 antibody. **Results:** Treatment with anti-IL-5 antibody resulted in remission with the ability to taper off the steroids, and no recurrence of the disease for 6 months. **Conclusion:** Our case report supports the potential use of anti-IL-5 therapy for remission of patients with CEP with recurrent relapses. Whether, it would also be an effective initial therapy might also be an area that deserves future investigation.

Abbreviations: ANA: Antinuclear antibody; ANCA: Antineutrophil cytoplasmic antibodies; BAL: Broncho-alveolar lavage; CEP: Chronic eosinophilic pneumonia; CT: Computed tomography; EGPA: Eosinophilic granulomatosis with polyangiitis; IL-5: Interleukin-5

ARTICLE HISTORY

Received 8 August 2018
Revised 19 October 2018
Accepted 29 October 2018

KEYWORDS

Case reports;
immunopathogenesis;
therapy; treatment

Introduction

Chronic eosinophilic pneumonia (CEP) is an idiopathic pulmonary disease associated with abnormal and significant accumulation of eosinophils in the lung parenchyma [1]. Systemic corticosteroids are the mainstay of treatment in CEP. We present the case of a patient with glucocorticoid-dependent CEP who was successfully treated with anti-interleukin-5 (anti-IL-5) antibody.

Case study

A 42-year-old woman with type 2 diabetes mellitus, with a 28 pack year smoking history, actively smoking cigarettes and marijuana, presented with a 3 months' history of cough, low grade intermittent fever, dyspnea on exertion and right sided pleuritic chest pain, poorly responsive to multiple courses of antibiotics. We first met her during her admission to the intensive care unit for hypoxic respiratory failure requiring mechanical ventilation. Computed tomography (CT) of the chest

showed ground glass opacity in the left upper lobe and patchy bilateral lower lobes consolidations with small to moderate bilateral pleural effusions (Figure 1(A)). A diagnostic thoracentesis of the right pleural effusion was performed and revealed an exudative effusion with 23% eosinophils [2]. A Broncho-alveolar lavage (BAL) was also performed and the cell count contained 48% eosinophils [3] with no organisms on gram stain, silver stain, acid fast and fungal stains. Further work up was unrevealing for parasitic, fungal, mycobacterial infection, HIV, vasculitis (antinuclear antibody (ANA), antineutrophilic cytoplasmic antibodies (ANCA), rheumatoid factor, antiproteinase 3, myeloperoxidase) and hematologic causes (Janus-activated kinase (JAK-2), BCR/ABL mutation). Hence, patient was diagnosed with CEP and was started on systemic glucocorticoids at 0.5 mg/kg. Our patient had significant improvement and was subsequently liberated from mechanical ventilation within 48 h of starting the treatment. Repeat CT scan chest after 1 month of therapy revealed complete resolution of the parenchymal and pleural abnormalities (Figure 1(B)).

CONTACT Edmond Sarkis, MD  edmondsarkis@gmail.com  Pulmonary and Critical Care, School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, New York 14202, USA.

Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/ijas.

© 2018 Taylor & Francis Group, LLC

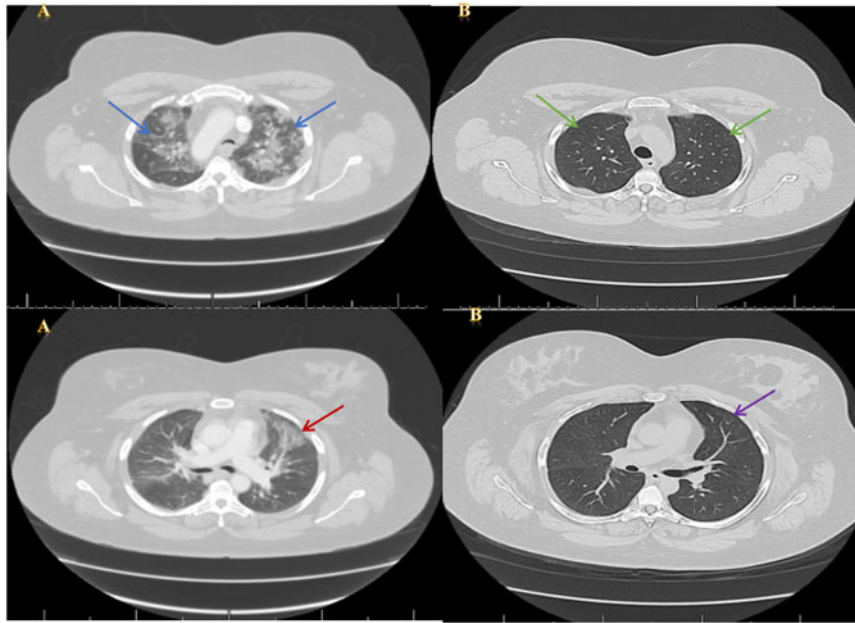


Figure 1. (A) CT chest at time of diagnosis: There was diffuse patchy areas of ground glass opacities/consolidations involving bilateral upper lobes (blue arrow). A focal consolidation in the posterior inferior portion of left lower lobe (red arrow). (B) CT chest after starting treatment with corticosteroids: Resolution of previously seen extensive multilobar ground glass opacities (green arrow). Resolution of the focal consolidation (purple arrow).

The patient was then maintained on prednisone 0.5 mg/kg and was followed regularly after hospital discharge. Attempts at tapering the glucocorticoids were met with four relapses over the course of 18 months, which were associated with worsening clinical symptoms, multiple hospital admissions and relapsing radiographic pulmonary infiltrates. She also experienced many side effects from chronic steroid use including a 40 lb. weight gain, mood swings, lingual thrush, carpal tunnel, facial acne, Cushingoid facies and muscle wasting.

Eighteen months from the initial presentation and after multiple failed attempts at tapering steroids, the decision was made to start off-label novel anti-IL5 for CEP.

Results

At the time of her last relapse, Mepolizumab at a dose of 100 mg every four weeks was started (Figure 2). Her symptoms decreased several days after the administration of Mepolizumab. About 2 weeks after the administration of Mepolizumab while tapering off the corticosteroids, her symptoms disappeared, and her peripheral blood eosinophil counts decreased to the normal range (Figure 2). However, six months into her treatment, she developed a local reaction to the injection site followed by a mild anaphylactic reaction consisting of subjective feeling of glottis closure.

Mepolizumab was then discontinued and switched over to intravenous Reslizumab 3 mg/kg infusion every four weeks, which is another anti-IL-5 approved for severe uncontrolled asthma [4,5]. Two months later, we were able to completely taper off the steroids: She required a total of eight months' overlap of anti-IL5 and tapering doses of steroids. She had been off the steroids since with no recurrent relapses. The only medications were given through the whole course of the treatment were glucocorticoids, Mepolizumab and Reslizumab. However, in August of this year she had a relapse while on Reslizumab and steroids were restarted with resolution of her symptoms and radiologic abnormalities. She had been off steroids for 6 months. Steroids are presently being re-tapered.

Discussion

CEP is a rare disorder associated with abnormal eosinophilic lung infiltration. It is characterized by alveolar and blood eosinophilia and peripheral pulmonary infiltrates on chest imaging. All treated patients show an excellent and rapid response to systemic corticosteroid therapy and favorable prognosis. However, relapses are frequent after weaning or stopping treatment. To date, treatment options are almost nonexistent in patients with steroid dependent disease and in those with glucocorticoids side effects.

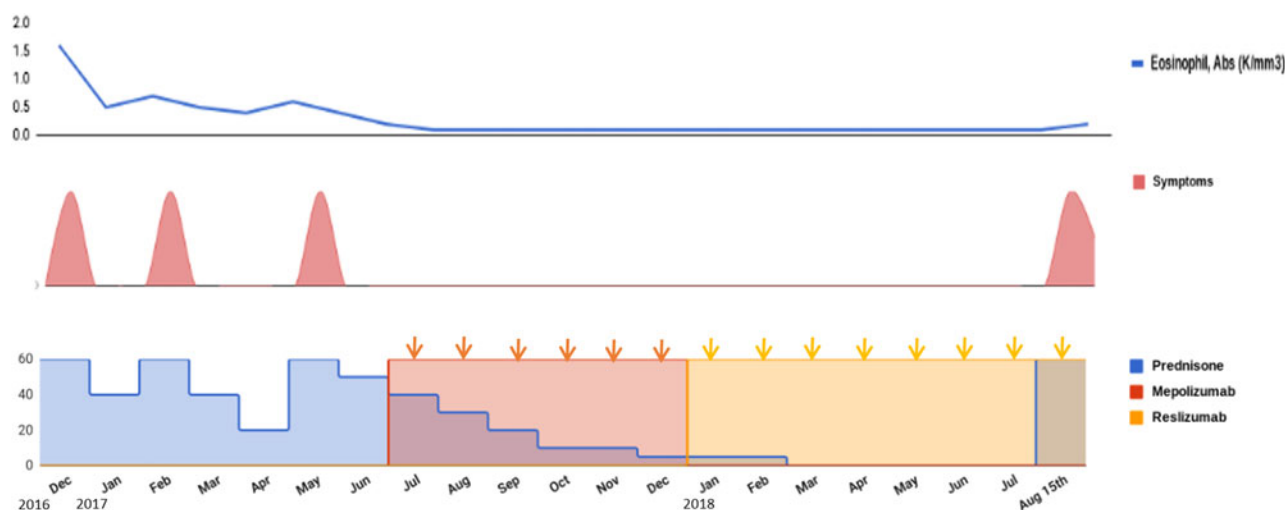


Figure 2. Treatment course. The patient responded to prednisone treatment, but relapsed each time we tapered it down to 20 mg/day. For easier illustration, we included only her last three relapses with tapering of corticosteroids before starting the IL-5 therapy. Patient had initial decrease in blood eosinophil counts consistent with the remission while on steroids, but her levels elevated again every time she relapsed. After starting IL-5 antagonist, the patient was tapered off steroids completely with no relapses. The patient had also consistent decrease in eosinophil count in the blood to normal levels. The patient got total of 13 doses of IL-5 antagonist. Mepolizumab (100 mg q 4weeks) was started in July 2017, six doses were total were given. It was stopped after the sixth dose for possible anaphylactic reaction, and Reslizumab (3 mg/kg q 4 weeks intravenous) was started, total 7 doses were given before she relapsed again in Aug 2018. She is now on Reslizumab, and started Prednisone with tapering.

Interleukin-5 is a pro-eosinophilic cytokine known to play a pivotal role in eosinophilic chemotaxis, eosinophil survival activity, degranulation, proliferation and terminal differentiation to eosinophils [6]. In eosinophilic pneumonias, there is evidence that the absolute number of eosinophils is significantly correlated with the IL-5 concentration in the BAL fluid of patients [7]. It is logical to postulate that giving medication that target eosinophils by decreasing their production and survival, could help in treating CEP. One of the novel and striking new drug classes in the allergy field is anti-IL-5 antibody, which has the ability to control many diseases in which eosinophils play a major role such as eosinophilic asthma [4,5,8–10], hyper eosinophilic syndrome [11,12], eosinophilic granulomatosis with polyangiitis (EGPA) [13], eosinophilic COPD [14], and even non-pulmonary diseases such as nasal polyposis [15] and eosinophilic esophagitis [16].

There have been a few case reports of Omalizumab anti-IgE treatment for refractory CEP [17–19]. However, all these patients had coexisting allergic asthma which our patient did not have. To our knowledge, targeting IL-5 cytokines has never been done in patients with CEP. We started Mepolizumab at a dose of 100 mg every 4 weeks which is the dosage used to treat eosinophilic asthma. We then switched over to Reslizumab infusion 3 mg/kg every 4 weeks due to a possible anaphylactic reaction.

While it could be argued that perhaps the patient's eventual remission was due to her prolonged steroid

course, this seems unlikely. She had multiple remissions whenever we tried to get her glucocorticoid below 15–20 mg. In contrast, once we started anti-IL-5 therapy, the patient had no relapse of CEP for 6 months off steroids. No adverse events were noted with using Reslizumab. We are planning to continue Reslizumab with careful observation of the patient.

Although long-term safety of Mepolizumab and Reslizumab treatment is demonstrated in multiple studies, there is no clear evidence to suggest the recommended duration of these agents for either CEP or asthma. In asthma it is hard to predict in the short term who will have long term benefits from these agents. Conversely, in those who appear to benefit from the drug there is no clear consensus on when it would be reasonable to consider stopping the medication to see if it is still needed. In a recent study in asthma the authors could not find a clear clinical marker at 16 weeks that would predict who would and wouldn't have long term benefit from Mepolizumab to help the decision of determining the duration of treatment [20]. Fortunately, intravenous Reslizumab 3.0 mg/kg displays favorable long-term safety and sustained long-term efficacy in treating moderate-to-severe eosinophilic asthma. These findings were maintained for up to 2 years [21]. Despite the patient's relapse on therapy with Reslizumab, we are planning to continue therapy with Reslizumab as the patient on balance appeared better on this agent as she was off steroids for a considerable time before relapsing

compared with recurrent exacerbations prior to its institution when steroids were lowered below 20 mg.

Conclusion

To date, the only treatment modality for recurrent or relapsing CEP is systemic steroids. While this therapy is extremely effective, chronic steroid usage due to relapses can be associated with many serious side effects. Thus, there is the need for alternative therapies that could be used in patients with recurrent relapses. Our case report supports the potential use of anti-IL-5 therapy for remission of patients with CEP with recurrent relapses. Furthermore, IL-5 inhibitors have much fewer side effects than chronic systemic glucocorticoids, and it can be used safely in the long term. IL-5 inhibitors might be a good treatment option for CEP with recurrent relapses or serious side effects of steroid therapy with the goal to reduce steroid dosage and reduce exacerbation rate similar to its use in asthma. Whether, it might also be an effective initial or adjunctive therapy in patients with milder disease might also be an area that deserves future investigation. We utilized the asthma dosage in our patient. Mepolizumab has been used at a higher dosage 300 mg for eosinophilic granulomatosis with polyangiitis (EGPA). The optimal dosage for CEP would also be an area for future investigation.

Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

M. Jeffery Mador  <http://orcid.org/0000-0003-2381-6339>

References

1. Marchand E, Reynaud-Gaubert M, Lauque D, Durieu J, Tonnel A-B, Cordier J-F. AB Idiopathic chronic eosinophilic pneumonia. A clinical and follow-up study of 62 cases. *Medicine (Baltimore)* 1998;77:299–312.
2. Krenke R, Nasilowski J, Korczynski P, Gorska K, Przybylowski T, Chazan R, Light RW. Incidence and aetiology of eosinophilic pleural effusion. *Eur Respir J* 2009;34:1111–1117.
3. Allen J, Wert M. Eosinophilic Pneumonias. *J Allergy Clin Immunol Pract* 2018;6(5):1455–1461.
4. Castro M, Mathur S, Hargreave F, Boulet L-P, Xie F, Young J, Wilkins HJ, et al. Reslizumab for poorly controlled, eosinophilic asthma: a randomized, placebo-controlled study. *Am J Respir Crit Care Med* 2011;184:1125–1132.
5. Castro M, Zangrilli J, Wechsler ME, Bateman ED, Brusselle GG, Bardin P, Murphy K, et al. Reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: results from two multicentre, parallel, double-blind, randomised, placebo-controlled, phase 3 trials. *Lancet Respir Med* 2015;3:355–366.
6. Okubo Y, Horie S, Hachiya T, Momose T, Tsukadaira A, Takashi S, Suzuki J-i, et al. Predominant implication of IL-5 in acute eosinophilic pneumonia: comparison with chronic eosinophilic pneumonia. *Int Arch Allergy Immunol* 1998;116:76–80.
7. Katoh S, Ikeda M, Matsumoto N, Shimizu H, Abe M, Ohue Y, Mouri K, et al. Possible role of IL-25 in eosinophilic lung inflammation in patients with chronic eosinophilic pneumonia. *Lung* 2017;195:707–712.
8. Bel EH, Wenzel SE, Thompson PJ, Prazma CM, Keene ON, Yancey SW, Ortega HG, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. *N Engl J Med* 2014;371:1189–1197.
9. Ortega HG, Liu MC, Pavord ID, Brusselle GG, FitzGerald JM, Chetta A, Humbert M, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. *N Engl J Med* 2014;371:1198–1207.
10. Pavord ID, Korn S, Howarth P, Bleecker ER, Buhl R, Keene ON, Ortega H, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. *The Lancet* 2012;380:651–659.
11. Marc ER, et al. Treatment of patients with the hyper-eosinophilic syndrome with mepolizumab. *N Engl J Med* 2008;358:1215–1228.
12. FitzGerald JM, Bleecker ER, Nair P, Korn S, Ohta K, Lommatzsch M, Ferguson GT, et al. Benralizumab, an anti-interleukin-5 receptor α monoclonal antibody, as add-on treatment for patients with severe, uncontrolled, eosinophilic asthma (CALIMA): a randomised, double-blind, placebo-controlled phase 3 trial. *The Lancet* 2016;388:2128–2141.
13. Wechsler ME, Akuthota P, Jayne D, Khoury P, Klion A, Langford CA, Merkel PA, et al. Mepolizumab or placebo for eosinophilic granulomatosis with polyangiitis. *N Engl J Med* 2017;376:1921–1932.
14. Pavord ID, Chanez P, Criner GJ, Kerstjens HAM, Korn S, Lugogo N, Martinot J-B, et al. Mepolizumab for eosinophilic chronic obstructive pulmonary disease. *N Engl J Med* 2017;377:1613–1629.
15. Gevaert P, Van Bruaene N, Cattaert T, Van Steen K, Van Zele T, Acke F, De Ruyck N, et al. Mepolizumab, a humanized anti-IL-5 mAb, as a treatment option for severe nasal polyposis. *J Allergy Clin Immunol* 2011;128:989–995. e1–8.
16. Stein M, Collins M, Villanueva J, Kushner J, Putnam P, Buckmeier B, Filipovich A, et al. Anti-IL-5 (mepolizumab) therapy for eosinophilic esophagitis. *J Allergy Clin Immunol* 2006;118:1312–1319.
17. Kaya H, Gümüş S, Uçar E, Aydoğan M, Muşabak U, Tozkoparan E, Bilgiç H, et al. Omalizumab as a

- steroid-sparing agent in chronic eosinophilic pneumonia. *Chest* 2012;142:513–516.
18. Shin YS, Jin HJ, Yoo H-S, Hwang E-k, Nam YH, Ye Y-M, Park H-S, et al. Successful treatment of chronic eosinophilic pneumonia with anti-IgE therapy. *J Korean Med Sci* 2012;27:1261–1264.
 19. Domingo C, Pomares X. Can omalizumab be effective in chronic eosinophilic pneumonia. *Chest* 2013;143:274.
 20. Gunsoy NB, Cockle SM, Yancey SW, Keene ON, Bradford ES, Albers FC, Pavord ID, et al. Evaluation of potential continuation rules for mepolizumab treatment of severe eosinophilic asthma. *J Allergy Clin Immuno* 2018; 6:874–882.e4.
 21. Murphy K, et al. Long-term Safety and Efficacy of reslizumab in Patients with eosinophilic asthma. *J Allergy Clin Immunol* 2017;5:1572–1581.e3.