Mepolizumab for the Treatment of Eosinophilic Granulomatosis With Polyangiitis: Our Experience

Díaz-Campos RM[1,*], Prudencio-Ribera VC[1,*], García-Moguel I[2], Fernández-Rodríguez C[2], Corral-Blanco M[1], Jarrin-Estupiñan ME[1], Melero-Moreno C[3]

[1]*Severe Asthma Unit. Pneumology Service, Hospital Universitario 12 de Octubre, Madrid, Spain*

[2]*Severe Asthma Unit. Allergology Service, Hospital Universitario 12 de Octubre, Madrid, Spain*

[3]*Institute for Health Research (i+12), Hospital Universitario 12 de Octubre, Madrid, Spain*

[*]*These authors contributed equally to this manuscript.*

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Eosinophilic granulomatosis with polyangiitis (EGPA) is considered a hybrid condition comprising a hypereosinophilic disorder and systemic antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis. It is characterized by the presence of asthma, eosinophilia, multiorgan involvement, and, sometimes, serum ANCA [1]. Its incidence has been reported to be 0.5 to 6.8 new cases per million habitants in the asthmatic population [2].

Systemic corticosteroids are the first-line treatment for EGPA. As their short- and long-term consequences are well-known, therapy is generally with corticosteroid-sparing immunomodulators, such as methotrexate or azathioprine [3].

Advances in knowledge of the pathophysiology of EGPA have led to a range of new treatments, such as omalizumab, which enables corticosteroids to be spared. However, reducing the dose of corticosteroids can increase the risk of severe EGPA flares [4]. Mepolizumab is an anti–interleukin-5 (IL-5) monoclonal antibody that reduces the absolute eosinophil count with clinical improvement in patients with other eosinophilic disorders, such as severe eosinophilic asthma [5].

Since the serum IL-5 level is increased in EGPA, targeted therapy against this cytokine has proven to be an effective alternative.

Mepolizumab has been used successfully in patients with relapsing or refractory EGPA at an intravenous dose of 750 mg once every 4 to 6 weeks [6,7]. In a multicenter phase 3 study, Wechsler et al [8] administered mepolizumab subcutaneously at 300 mg every 4 weeks and compared it with placebo in 126 patients [8]. Since mepolizumab led to more accrued weeks of remission than placebo, corticosteroid use could thus be reduced. Furthermore, the time to first relapse was longer with mepolizumab, and the exacerbation rate was significantly lower during the treatment period than during the nontreatment period. However, manifestations of EGPA recurred on discontinuation [6-8]. A systematic review of the results of these 3 studies was published in 2019 [9].

A recent post hoc analysis investigated the clinical benefit of mepolizumab in patients with relapsing or refractory EGPA and found that compared with the previous trial [8], significantly more patients experienced remission or a ≥50% reduction in corticosteroid dose or were relapse-free with mepolizumab, mainly in specific subgroups (blood eosinophil count <150/μL and weight >85 kg) [10].

We report 2 patients with corticosteroid-refractory EGPA treated successfully with 300 mg of subcutaneous mepolizumab every 4 weeks, according to the 2017 United States Food and Drug Administration recommendation for adult EGPA treatment.

A 43-year-old nonsmoking woman with a history of allergic asthma, positive prick test results for dog epithelium and house dust mite (*Dermatophagoides pteronyssinus, Dermatophagoides farinae, Lepidoglyphus destructor, Blomia tropicalis*), rhinosinusitis, and chronic suppurative otitis media presented multiple mononeuritis, erythematous skin lesions compatible with biopsy-proven vasculitis, and bilateral, patchy, ground glass opacities with an upper lung distribution in a chest computed tomography (CT) scan. Blood tests revealed a positive ANCA titer, eosinophilia (37%), increased IgE level (234 IU/mL), and a normal C-reactive protein level (CRP, 0.76 mg/dL). The patient was initially treated with prednisone 0.5 mg/kg/d, followed by 6 cyclophosphamide pulses (750 mg each) and azathioprine in order to spare treatment with corticosteroids. The lowest dose reached was 10 mg/d of prednisone, because symptoms recurred when the dose was reduced. Omalizumab was subsequently administered for 1 year, although it was discontinued because of lack of efficacy (frequent asthma exacerbations and episodes of suppurative otitis media). Subcutaneous mepolizumab was tried at 300 mg every 4 weeks. Before starting mepolizumab (while the patient was receiving 10 mg/d of prednisone), the laboratory values were as follows: eosinophil blood count, 13%; serum IgE level, 234 IU/mL; and CRP, 2.07 mg/dL. The Birmingham Vasculitis Activity Score (BVAS) was >3, and FEV_1 was 103% of predicted. Six months later, the asthma and otic symptoms had improved significantly, the Asthma Control Test (ACT) score had increased 3 points (22 to 25), blood eosinophilia and CRP had decreased (1.1% and 0.26 mg/dL, respectively),

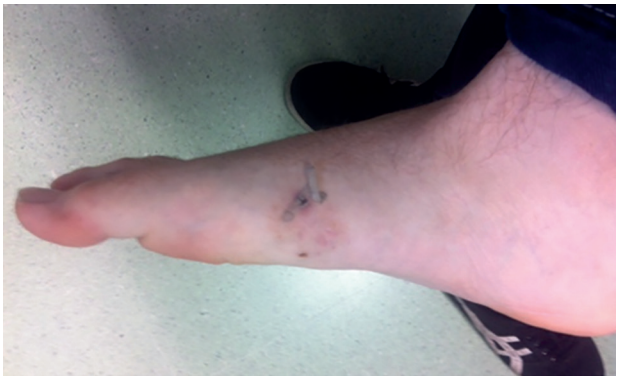

Figure. Erythematous skin lesions in a patient with eosinophilic granulomatosis with polyangiitis.

the BVAS was 0, and FEV_1 was 92% of predicted. There were no exacerbations, and we were able to reduce prednisone to 2.5 mg/d.

The other patient was a 27-year-old nonsmoking man with a long history of recurrent nasal polyposis and eosinophilic asthma treated with high-dose inhaled corticosteroids and long-acting $ß_2$-agonists, antileukotrienes, and oral corticosteroids. His symptoms were uncontrolled, and he had considerable peak flow variability (>15%). He presented with erythematous skin lesions (Figure) compatible with biopsy-proven eosinophilic extravascular granuloma and bilateral, patchy, ground glass opacities, with an upper lung distribution on the chest CT scan (Supplementary Material). The blood tests revealed eosinophilia (40%), increased CRP and IgE levels (2.28 mg/dL and 2970 IU/mL, respectively), and negative ANCA titers. FEV_1 was 115% of predicted. The patient was initially treated with prednisone 60 mg/d (0.75 mg/kg/d), with 10 mg/d the lowest dose reached because of recurrent symptoms when it was reduced. Subcutaneous mepolizumab was started at 300 mg every 4 weeks. Before starting mepolizumab, the laboratory values were as follows: blood eosinophil count, 35%; serum IgE, 996 IU/mL; and CRP, 0.26 mg/dL. The BVAS was >3, and FEV_1 was 108% of predicted. Six months later, the patient was asymptomatic without exacerbations. In addition, blood eosinophilia and IgE levels decreased (1.2% and 209 IU/mL, respectively), BVAS was 0, and FEV_1 was 89% of predicted. Therefore, the dose of corticosteroid was reduced.

No allergic reactions or adverse events or relapses were associated with mepolizumab in either case.

In summary, our results are consistent with those of previous studies [6-8]. Mepolizumab may be considered a therapeutic option in patients with refractory corticosteroid EGPA in order to reduce the dose of corticosteroids and their adverse effects and thus improve quality of life.

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Conflicts of Interest

Dr. Garcia Moguel has participated in advisory boards and acted as a speaker/investigator for Novartis, AstraZeneca, Teva, GSK, Chiesi, Allergy therapeutics, Leti, Stallergenes, ALK-Abelló, Mundipharma, Pfizer, and Orion Pharma.

The remaining authors declare that they have no conflicts of interest.

References

1. Mahr A, Moosig F, Neumann T. Eosinophilic granulomatosis with polyangiitis (Churg–Strauss): evolutions in classification, etiopathogenesis, assessment and management. Curr Opin Rheumatol. 2014;26:16-23.
2. Watts RA, Lane S. What is known about the epidemiology of the vasculitides? Best Pract Res Clin Rheumatol. 2005;19:191-207.
3. Samson M, Puéchal X, Devilliers H, Ribi C, Cohen P, Stern M, et al. Long-term outcomes of 118 patients with eosinophilic granulomatosis with polyangiitis (Churg–Strauss syndrome) enrolled in two prospective trials. J Autoimmun. 2013;43:60-9.
4. Jachiet M, Samson M, Cottin V. Anti-IgE Monoclonal Antibody (Omalizumab) in Refractory and Relapsing Eosinophilic Granulomatosis With Polyangiitis (Churg-Strauss): Data on Seventeen Patients. Arthritis Rheumatol. 2016;68:2274-82.
5. Pavord ID, Korn S, Howarth P. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, doubleblind, placebo-controlled trial. Lancet. 2012;380:651-9.
6. Kim S, Marigowda G, Oren E, Israel E, Wechsler ME. Mepolizumab as a steroid sparing treatment option in patients with Churg-Strauss syndrome. J Allergy Clin Immunol. 2010;125:1336-43
7. Moosig F, Gross WL, Herrmann K, Bremer JP, Hellmich B. Targeting interleukin-5 in refractory and relapsing Churg-Strauss syndrome. Ann Intern Med. 2011;155:341-3.
8. Wechsler ME, Akuthota P, Jayne D, Khoury P, Klion A, Langford CA, et al. Mepolizumab or placebo for eosinophilic granulomatosis with polyangiitis. N Engl J Med. 2017;376:1921-32.
9. Pradhan RR, Nepal G, Mandal S. Safety and Efficacy of Mepolizumab in Patients with Eosinophilic Granulomatosis with Polyangiitis. Pulm Med. 2019;2019:4376380.
10. Steinfeld J, Bradford ES, Brown J, Mallett S, Yancey SW, Akuthota P, et al. Evaluation of clinical benefit from treatment with mepolizumab for patients with eosinophilic granulomatosis with polyangiitis. J Allergy Clin Immunol. 2019;143(6):2170-7

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Vania Cecilia Prudencio Ribera
E-mail: prudenciovania@yahoo.com

