

## LETTERS TO THE EDITOR

# Eosinophilic granulomatosis with polyangiitis treated with Mepolizumab and Rituximab combination therapy – a case report

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## INTRODUCTION

Eosinophilic granulomatosis with polyangiitis (EGPA) is a multisystemic disease characterized by eosinophilic necrotizing vasculitis of small and medium sized blood vessels, primarily involving the lungs, skin, and peripheral nervous system (PNS)<sup>1</sup>. Both rituximab and mepolizumab are recommended treatments for EGPA, but there is limited evidence supporting their combined use<sup>2</sup>, with only six cases reporting this combination<sup>3-8</sup>.

## CASE REPORT

We report a case of a 46-year-old man with a history of mild asthma and chronic rhinosinusitis. He presented to the emergency department with a one-week history of worsening dyspnoea, numbness in both feet, and purpuric lesions on his lower limbs, leading to complete inability to walk. Laboratory studies revealed an eosinophil count of 1420 cells/mcL (reference range: 30-500 cells/mcL), an ESR of 58 mm/h (reference value: < 20 mm/h), and negative antineutrophil cytoplasmic antibodies (ANCA). A chest CT scan showed bilateral ground-glass opacities, and a head CT scan revealed inflammatory mucosal thickening in all perinasal sinuses. A skin punch biopsy of the purpuric lesions demonstrated a predominantly eosinophilic inflammatory infiltrate with granulomas. Electromyography revealed severe axonal polyneuropathy affecting both upper and lower limbs. Based on these findings, a diagnosis of ANCA-negative EGPA was established.

The patient was initially treated with methylprednis-

olone pulse therapy (1 g/day for five days), followed by monthly cyclophosphamide (750mg/m<sup>2</sup>) for six months, according to the National Institutes of Health (NIH) protocol. Maintenance therapy consisted of prednisolone (1 mg/kg/day with gradual tapering) and azathioprine (150 mg/day). Disease activity was assessed using the Birmingham Vasculitis Activity Score (BVAS) and peripheral blood eosinophil counts. Despite significant clinical (primarily neurological and cutaneous) and analytical improvement after two years of treatment, it was not possible to taper prednisolone below 10mg/day due to recurrent respiratory symptoms. As a complication of prolonged corticosteroid use, the patient developed osteoporosis with multiple vertebral fractures. Approximately seven years after the diagnosis, mepolizumab was approved for EGPA and it was initiated, allowing tapering of prednisolone to 5 mg/day without further respiratory exacerbations. However, the patient subsequently developed polyarthritis, which only partially responded to optimised subcutaneous methotrexate and joint synoviorthesis.

At a multidisciplinary meeting, rituximab was proposed for both articular and pulmonary involvement, but pneumonology specialists recommended maintaining mepolizumab due to its efficacy in controlling respiratory symptoms. Consequently, the patient was started on combination therapy with mepolizumab (300 mg every four weeks) and rituximab (2 infusions of 1000 mg each, 15 days apart, every 6 months). After six months, the patient experienced significant improvement in joint symptoms. No further disease exacerbations occurred, even with a gradual reduction of prednisolone to 5 mg/day. No adverse effects were reported.

## CONCLUSION

We report a case of ANCA-negative EGPA with severe respiratory, PNS and articular involvement, requiring multiple therapeutic adjustments. Mepolizumab effectively controlled respiratory symptoms but had limited impact on arthritis, prompting the addition of ritux-

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imab for joint disease. The therapeutic rationale stems from using complementary mechanisms of action, targeting different pathways in EGPA pathogenesis. Mepolizumab, an anti-IL5 monoclonal antibody, controls eosinophil-driven airway inflammation<sup>9</sup>. However, in articular involvement, dysregulated B cells play a key role. Rituximab depletes CD20+ B cells, reducing auto-antibody production, antigen presentation, and pro-inflammatory cytokine release, all contributing to arthritis. Emerging evidence suggests that B cells promote eosinophil recruitment through chemokines, supporting the potential synergy between B cell depletion and IL-5 blockade<sup>10</sup>. This combined strategy offers broader immunomodulation, particularly in refractory, multi-organ cases.

This case highlights the complexity of EGPA and the need for tailored, multi-targeted treatment strategies. It contributes to the growing body of evidence supporting the safety and efficacy of combined mepolizumab and rituximab in complex, treatment-resistant EGPA presentations.

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