Mepolizumab as an Effective Alternative to Immunosuppressive and Teratogenic Therapies for the Early Treatment of EGPA: A Case Report

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Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare systemic inflammatory disease characterized by vasculitis of the small- and medium-sized blood vessels and multisystemic manifestations. The most common characteristics include impaired lung function (mainly worsening asthma despite high doses of inhaled corticosteroids), peripheral blood eosinophilia, chronic sinonasal involvement with polyposis and peripheral mononeuropathy [1]. Some symptoms can persist for years before other features become clinically relevant, and vasculitis is often absent on biopsy. EGPA mainly affects women aged 40-60 years, and approximately 30%-40% of patients present with positive antineutrophil cytoplasmic antibody (anti-myeloperoxidase [ANCA]) titers. The scales applied to assess the activity and prognosis of relapsing disease are the Birmingham Vasculitis Activity Score and the Five Factor Score (FFS), respectively [2]. According to recent guidelines, the use of immunosuppressive therapies to treat EGPA with vital organ involvement is mandatory [1]. However, new treatments targeting eosinophils could be an effective alternative option, especially in young patients [3].

A 22-year-old woman diagnosed with asthma and chronic rhinosinusitis without nasal polyps was referred to our clinic in January 2021 with worsening dyspnea, persistent nasal congestion, and hyposmia. She also reported asthenia, chest tightness, and hypoesthesia in the inner region of her right leg, which progressively worsened. She was taking fluticasone furoate/vilanterol 184/22 µg, montelukast 10 mg, fluticasone/azelastine nasal spray, and bilastine 20 mg.

The patient had been diagnosed with asthma 2 years earlier. Control was intermittent despite high-dose inhaled corticosteroids combined with long-acting ß-agonists. One year earlier, she had also received systemic corticosteroids and antibiotics to treat her rhinosinusitis symptoms. She was sensitized to cat dander, although avoidance of exposure did not improve her symptoms.

A multidisciplinary approach was taken when she arrived at our center. Blood testing revealed 3170 eosinophils/mm^3 and total IgE 1239 kU/L. Testing for immunoglobulins, rheumatoid factor, ANCA, antinuclear antibodies, parasite/virus serology, and FIP1L1/PDGFRA revealed normal and negative results. The allergy work-up showed sensitization to olive tree pollen, serum albumins, and lipocalins, although this was not clinically relevant. Evaluation of respiratory function revealed 70% eosinophils in sputum with normal spirometry values and FeNO 108 ppb.

The patient complained of chest pain. Auscultation revealed cardiac rub. An ECG showed negative T waves in V3-V6; this was suggestive of myopericarditis, which was confirmed by cardiac magnetic resonance imaging (Figure, C). Troponins were 59.4 ng/L (normal <14 ng/L), and B-type natriuretic peptide was 1807 pg/mL (normal 68-112 pg/mL).

Computed tomography of the paranasal sinuses and chest revealed inflammation of the paranasal sinuses with ethmoidal polyps, mild pleural effusion, and ground glass opacities. Smooth thickening of the interlobular septa of the lower lobes and the base of the middle lobe and lingula was also observed (Figure, A). Nasal biopsy did not show vasculitis. An electromyogram revealed mild mononeuropathy of the saphenous nerve, thus confirming neurologic involvement. The patient gave her written informed consent for her medical data to be published.

Based on the clinical and diagnostic test findings, we suspected EGPA despite the absence of demonstrated vasculitis. Methylprednisolone 1 mg/kg boluses were administered for 3 days, with clinical and serologic improvement (the eosinophil count decreased from 9430 to 340/mm^3, initial eosinophil cationic protein [ECP] was >200 µg/L). Oral prednisone 1 mg/kg was subsequently initiated for 2 weeks. When prednisone was tapered to 30 mg/d, the eosinophil count increased (1250/mm^3), and the patient reported asthenia, dyspnea, and nasal congestion again. Mepolizumab was initiated at 300 mg/4 wk. Prednisolone was maintained at 30 mg/d but was decreased progressively over 6 months. The patient developed adrenal insufficiency due to systemic corticosteroids; prednisone was maintained at 5 mg/d until this resolved. After 24 months without systemic corticosteroids and treatment with mepolizumab 300 mg/4 wk, the patient remains asymptomatic clinically, analytically (eosinophils,

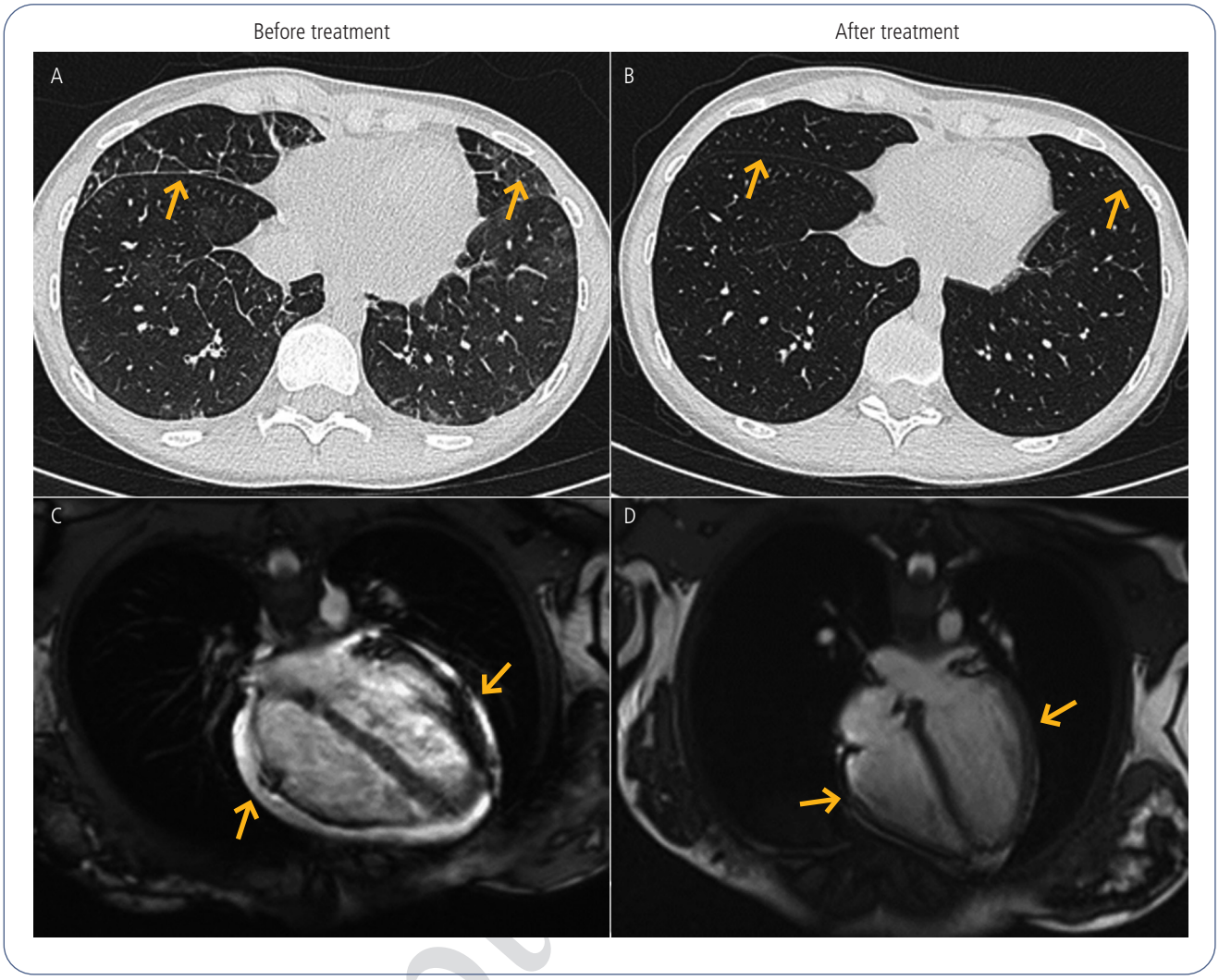

Figure. A, Computed tomography scan showing smooth thickening of interlobular septa and patchy ground glass opacities. B, The alterations of the previous study have been resolved. No thickening of intra- or interlobular septa, honeycombing, nodules, consolidations, or bronchiectasis or significant alterations in the attenuation of the lung parenchyma. C, Cardiac magnetic resonance image with fuzzy patched enhancement and myocardial inflammation associated with acute myocarditis. D, Slight residual alterations are observed, albeit without inflammation. The figure shows the improvement compared with the acute phase.

30/mm^3; ECP 4.2 µg/L; FeNO, 25 ppb), and radiologically. The alterations seen in the previous study resolved as observed in the chest computed tomography scan, with no thickening of interlobular septa, honeycombing, nodules, consolidations, or bronchiectasis in the lung parenchyma. Cardiac magnetic resonance imaging revealed slight residual alterations without cardiomegaly or pericardial effusion (Figure, B and D). A recent electromyogram revealed that the neuropathy had resolved.

We report a case of ANCA-negative EGPA in a young patient with cardiopulmonary, sinonasal, and neurological involvement controlled with mepolizumab 300 mg/4 wk. Biological antieosinophil therapy enabled complete withdrawal of systemic corticosteroids and resolution of their adverse effects (adrenal insufficiency), with no relapses over 2 years of follow-up. We discontinued montelukast to avoid potential confounders because of reports of EGPA [4].

Current guidelines differentiate new-onset, active EGPA from relapsing disease [5]. For new-onset cases, the therapeutic decision is based on prognosis, as assessed using the FFS. In the case we report, the patient presented with vital organ involvement (FFS >1), in which high doses of systemic corticosteroids and cyclophosphamide or rituximab are recommended.

Systemic corticosteroids are the mainstay of EGPA treatment, although high doses can cause significant long-term adverse effects, such as adrenal insufficiency, fractures, and infections. Cyclophosphamide is not recommended in young patients owing to its teratogenic effect and may not always fully control symptoms. The introduction of biological drugs, including the anti–CD-20 agent rituximab and the anti–IL-5 agent mepolizumab, has changed the treatment paradigm for EGPA, reducing adverse effects [6,7]. Rituximab has proven efficient with respect to cardiac symptoms [8]. However, the

associated susceptibility to infection was a handicap, since the patient had experienced recurrent airway infections. Consequently, mepolizumab was the best option to prevent an increased risk of infections and negative effects on her fertility.

Mepolizumab is the only antieosinophilic therapy approved for EGPA in clinical guidelines. It is indicated for relapses or flare-ups and is administered alone or in combination with systemic corticosteroids [9]. Recent clinical trials have shown relevant data regarding the use of benralizumab as a new therapeutic option, demonstrating that it is not inferior to mepolizumab [10].

We emphasize the importance of multidisciplinary management. Treatment should be prompt and appropriate to prevent adverse effects and sequelae of EGPA. This is particularly important in younger patients to preserve fertility. Despite traditional treatments with immunosuppressants and systemic corticosteroids, the use of targeted therapies against eosinophils reduces adverse effects while maintaining effectiveness.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Previous Presentation

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