Eosinophilic Granulomatosis With Polyangiitis and Cardiac Involvement: A Case Report

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Eosinophilic granulomatosis with polyangiitis (EGPA, Churg-Strauss syndrome) is characterized by asthma, eosinophilia and small vessel vasculitis affecting the lungs, nasal sinuses, peripheral nerves, and heart [1]. Although antineutrophil cytoplasmic antibodies (ANCAs) play an important role in the pathogenesis of EGPA, many patients present the condition without these specific antibodies, especially patients with cardiac involvement [2]. Rituximab, a monoclonal anti-CD20 antibody, was recently included in the EULAR ANCA-associated vasculitis treatment recommendations [3]. Two published trials involving patients with granulomatosis with polyangiitis and with microscopic polyangiitis, respectively, showed rituximab to be safe and effective in inducing remission [4,5]. As far as EGPA is concerned, rituximab has been reported as a treatment option in very few case reports [6]. The potential pathogenic role of ANCAs supports the use of rituximab in EGPA, as well as B cell–dependent activation of T lymphocytes with subsequent IL-5 production. We report the case of a patient affected by ANCA-negative EGPA with life-threatening heart and pulmonary involvement who was successfully treated with rituximab.

In July 2017, a 17-year-old girl attended the emergency department of University of Verona Hospital, Verona, Italy with severe dyspnea, fever, cough, and asthenia. In 2016, she was diagnosed with new-onset allergic asthma. During the first admission to hospital, she had general malaise and dyspnea. Her heart rate was 122 bpm, and her respiratory rate was 25 breaths per minute; arterial pressure was 90/60 mmHg. Cardiac examination only revealed muffled heart sounds. Pulmonary auscultation revealed diffuse expiratory rhonchi and wheezes. Chest x-ray revealed parenchymal infiltrate with peripheral distribution in the middle and lower areas of the lungs. Heart ultrasound showed circumferential pericardial effusion (maximum thickness, 8 mm) with apical and inferior wall hypokinesia. Determination of total and specific IgE revealed sensitization to animal dander and grasses. High levels of cationic eosinophilic protein were also found. A complete blood count revealed leukocytosis with an important eosinophilic component (leukocytes, 20 000/μL; eosinophils, 13 000/μL [65% on the white blood cell count differential]). C-reactive protein (CRP) and high-sensitivity troponin I were elevated (47 mg/L and 14.435 ng/L, respectively). ANCAs were within the normal range. All laboratory tests were performed at University of Verona Hospital. High-resolution computed tomography (HRCT) of the chest showed multiple ground-glass patterns in the middle and lower areas of the lungs accompanied by large confluent parenchymal consolidations. Pericardial effusion was confirmed (maximum thickness, 9 mm) (Figure). The patient was diagnosed with EGPA.

Treatment with rituximab and high-dose pulse corticosteroid therapy with methylprednisolone was started immediately. Rituximab was administered intravenously at a dose of 375 mg/m^2 at baseline and on days 7, 14, and 21, without adverse events. Methylprednisolone was administered intravenously for 3 consecutive days at a dose of 1000 mg and then continued orally at a dose of 0.75 mg/kg. The patient's clinical situation improved, and dyspnea resolved almost completely. In addition, laboratory data confirmed the response to therapy, with a significant drop in the peripheral eosinophil count (from 13 000/μL to 200/μL) and CRP (from 47 mg/L to 7 mg/L). Cardiac magnetic resonance imaging (MRI) performed 2 days after initiation of treatment showed left ventricular wall motion abnormalities and multiple foci of myocarditis with late gadolinium enhancement. The left ventricular ejection fraction was 49%, and T2-weighted sequences showed edema at the lateral wall and interventricular septum (Figure). The Birmingham Vasculitis Activity Score (BVAS) was 13 points.

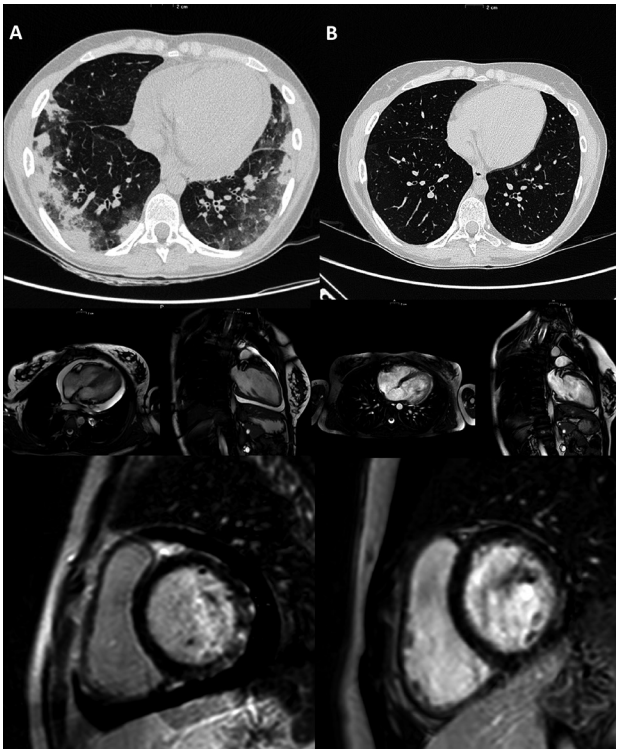

Figure. Chest high-resolution computed tomography and cardiac magnetic resonance imaging before (A) and after (B) therapy with rituximab.

After 3 months, the BVAS had fallen to 0 points, CRP was 1 mg/L, and the eosinophil count remained under 600/μL in multiple analyses. HRCT showed complete resolution of all the ground-glass patterns and consolidations. Resolution of pericardial effusion was confirmed. The enlarged lymph nodes also resolved. Heart ultrasound, chest HRCT, and cardiac MRI were repeated after 6 months with almost total recovery (Figure). Cardiac MRI showed no wall motion abnormalities and an improvement in foci of myocarditis with late gadolinium enhancement. The left ventricular ejection fraction was 50%, and T2-weighted sequences showed almost complete recovery from edema and pericardial effusion (Figure).

Reporting of this case was authorized by the Verona Medical School Institutional Review Board (IRB), and the patient provided her written consent and assent for the publication of this report.

We report on a young individual affected by EGPA and successfully treated with rituximab. The present case highlights the possibility of heart involvement in EGPA, even at early stages of the disease, in a young woman. Although the patient presented with myocarditis and pericarditis, interestingly, she did not experience coronary damage. Moreover, ANCAs were absent. EPGA rarely presents with both pulmonary and cardiac involvement. Patients with myocarditis due to EGPA usually present without ANCAs. While the prognosis of EGPA is good, cardiac involvement is the most important predictor of a negative outcome. In their study of 96 patients, Guillevin et al [7] found that 39% died of cardiac complications at early stages of the disease [7]. A recent analysis found that myocardial involvement in EGPA is strictly associated with frequent relapse [8]. Corticosteroids are the mainstay of treatment, although in the case of myocarditis, concomitant immunosuppressive therapy is recommended [3]. In the case we report, rituximab was preferred to cyclophosphamide in order to preserve the patient's reproductive potential. We also considered omalizumab (monoclonal anti-IgE antibody). However, there is some concern over vascular involvement with this drug [9].

Rituximab is a chimeric anti-CD20 monoclonal antibody that depletes B cells. The rationale for using this antibody in ANCA-associated vasculitis comes from the pathogenic role of ANCA in this disease. Indeed, binding of ANCAs to their antigens results in full neutrophil activation and eventually leads to the release of toxic granule proteins [10]. Another interesting and emerging hypothesis is that, in EGPA, B cells activate IL-5–producing T lymphocytes. Unfortunately, the largest randomized controlled trial of rituximab in vasculitis excluded patients with EGPA and patients who were ANCA-negative. A recent study confirmed the efficacy of rituximab in 41 patients with EGPA [6]. Heart involvement was recorded in 9 of these patients. In the case we report, a significant improvement was observed after the first infusion of the drug, with no adverse events in the short and medium terms.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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