Eosinophilic granulomatosis with polyangiitis (Churg-Strauss vasculitis) presenting as Samter’s triad

Rohan Ameratunga, MBChB, PhD, FRACP, FRCPath, ABMLI, FFSc, FRCP, FRCPA, and Richard Steele, MBChB, FRACP, FRCPA

Clinical Implications

- Eosinophilic granulomatosis with polyangiitis (Churg-Strauss vasculitis) has overlapping features of Samter’s triad/aspirin-exacerbated respiratory disease. Both can present with nasal polyposis, aspirin sensitivity, and asthma. Failure to diagnose eosinophilic granulomatosis with polyangiitis can have potentially catastrophic consequences.

TO THE EDITOR:

Eosinophilic granulomatosis with polyangiitis (EGPA, Churg-Strauss vasculitis) is a rare life-threatening multisystem vasculitis. The disorder often develops in 3 phases. In the initial prodromal phase, patients have typical allergic symptoms including asthma, allergic rhinitis, and eczema. In the second prevasculitic phase, progressive tissue and blood eosinophilia occurs. In the third and final phase, an eosinophilic vasculitis ensues, which can lead to life-threatening complications including myocarditis, nephritis, bowel perforation, and mononeuritis multiplex.1

Here, we describe a patient with EGPA who presented with eosinophilic nasal polyposis with aspirin-exacerbated asthma, features that are diagnostic of Samter’s triad (nasal polyposis, asthma, and aspirin sensitivity: aspirin-exacerbated respiratory disease [AERD]). This case highlights the overlapping features of Samter’s triad/AERD and the prevasculitis phase of EGPA. Physicians should actively exclude EGPA in patients diagnosed with Samter’s triad/AERD.

The patient, in her early thirties, presented for evaluation of unexplained eosinophilia. She had previously suffered from chronic sinus disease and had nasal polyps removed (Figure 1). Histology had shown eosinophilic infiltration (Figure 2). She gave a history of mild eczema but no other skin rashes. She developed asthma in her late twenties and had a severe reaction to aspirin, requiring urgent nebulizer treatment. She was on inhaled steroid prophylaxis. This history was diagnostic of Samter’s triad/AERD.

On further questioning, she had suffered from postpartum acute cholecystitis and had undergone a laparoscopic cholecystectomy. Review of the histology showed intense eosinophilic infiltrates and a diagnosis of acalculous eosinophilic cholecystitis had been made (Figure 2). Before review, she had a gastroscopy and a gastric biopsy had shown the presence of eosinophils (Figure 2). She did not complain of neurological or gastrointestinal symptoms. Her blood cell count showed eosinophilia (1.19 cells/L; 16.5% of white blood cells). Specific IgE tests were negative for common inhalant allergens in New Zealand including those from dust mites, grass, cats, dogs, grass, and English plantain. There was no evidence of cardiac or pulmonary involvement (apart from asthma). An echocardiogram and a magnetic resonance imaging scan of the heart were both normal. She had normal troponins. A high-resolution computed tomography of the thorax was normal. She had transient elevation in liver enzymes, which normalized before a liver biopsy was undertaken. Laboratory testing showed absence of ANCA antibodies and normal urine sediment. The ANCA antibodies have remained negative.

Given the presence of eosinophilic gastritis and acalculous eosinophilic cholecystitis, a diagnosis of stage 2 EGPA was made. Careful review of her histopathological specimens did not show evidence of eosinophilic vasculitis (Figure 2). In our experience, the intensity of the initial remission induction regimen influences the durability of the remission and therefore the long-term prognosis in EGPA. Our practice is to undertake intense remission induction treatment with pulsed methylprednisolone and continue maintenance therapy for 18 to 24 months with...
low-dose oral prednisone and a steroid-sparing drug. She received 6 cycles of pulsed intravenous methylprednisolone (1 g per month) as well as low-dose oral steroids and mycophenolate 1 g twice a day.

She was placed on a bone mineral density protection program as well as Pneumocystis jiroveci prophylaxis. She tolerated the treatment well and after 18 months of mycophenolate, her dose is being slowly tapered. She has not suffered significant adverse effects from the treatment. Her inflammatory markers have remained within the normal range. The asthma has been well controlled. She has mild eczema of the hands.

The five factor score and its revision is a frequently used prognostic marker in EGPA. These consist of cardiac, renal, neurological, gut, and renal involvement. Because our patient was identified in stage 2 of the disease, she had not developed any of these vasculitic complications. Given her good prognosis, she was not treated with cyclophosphamide or rituximab. Long-term monitoring will be needed given the risk of relapse.

Before the advent of oral and parenteral steroids, most patients succumbed to EGPA. Terminal events were typically myocarditis, nephritis, or perforation of the bowel. Therapy of the disorder is in evolution, but most patients are initially treated

FIGURE 2. A, Gallbladder (×100), showing muscularis layer with intense eosinophilic infiltrate. The eosinophils are seen as red staining cells. B, Gallbladder (×400) mucosa. The eosinophilic infiltrate can be easily seen. C, Nasal polyp (×100) subsurface showing marked eosinophilic infiltrate. D, Nasal polyp (×400) stroma showing marked eosinophilic infiltrate. E, Stomach (×100) gastric body. F, Stomach (×400) gastric body. Eosinophilic infiltrates can be seen at higher magnification. Eosinophils highlighted with arrows.
with high-dose oral or parenteral steroids to induce a rapid remission to prevent progression of the disorder. Steroids are then tapered and a steroid-sparing drug is frequently added during the maintenance phase. Most patients are treated for approximately 2 years and are monitored long-term because they are at risk of relapse in the future. Patients with life-threatening manifestations are treated with cyclophosphamide or rituximab in addition to pulsed intravenous steroids. The five factor score is often used to guide such treatment.5

There have been several attempts at developing diagnostic criteria for EGPA. The main difficulty is the rarity of eosinophilic vasculitis with concomitant granulomatous on histology. This patient did not meet the Lanham criteria6 or the Chapel Hill criteria, which require histologic evidence of eosinophilic vasculitis.7 These diagnostic criteria are therefore less useful in the prevasculitic phase of EGPA. In such patients, the diagnosis must be based on the patient’s clinical features.

She did however meet the American College of Rheumatology criteria, which require 4 or more of 6 criteria including peripheral eosinophilia (>10%), asthma, nasal symptoms, and extravascular eosinophilia. She did not have a peripheral neuropathy or nonfixed pulmonary infiltrates. We therefore suggest that the American College of Rheumatology criteria are more useful in identifying patients in the prevasculitic phase of EGPA.

The main differential diagnosis of EGPA is usually stated to be one of the variants of the hypereosinophilic syndrome. In her case, asthma, eosinophilic cholecystitis, and nasal polyps were important differentiating features. Similarly, allergic bronchopulmonary aspergillosis was excluded by the presence of nasal polyps, marked tissue eosinophilia including acalculous eosinophilic cholecystitis, and negative serology (Aspergillus precipitins and specific IgE antibodies to Aspergillus).

We believe that Samter’s triad/AERD was the most important diagnostic difference in her case.7 She had nasal polyposis and aspirin-exacerbated asthma, fulfilling criteria for Samter’s triad/AERD. The standard treatment for Samter’s triad/AERD includes confirmation of the diagnosis followed by functional endoscopic sinus surgery and long-term desensitization to aspirin. This reduces the risk of recurrence of nasal polyposis following surgery.7 Immunosuppression plays no part in the treatment of Samter’s triad.

The key findings suggestive of EGPA were a significant tissue infiltration with eosinophils as manifested by acalculous eosinophilic cholecystitis and eosinophilic gastritis. The management of EGPA is very different from Samter’s triad/AERD. Aspirin desensitization would not have prevented progression to the vasculitic phase of EGPA, with potentially lethal sequelae. Given the high frequency of aspirin sensitivity in otherwise uncomplicated asthma, it is not surprising our patient reacted to aspirin.9

Our experience should alert clinicians to the possibility of EGPA when faced with a patient with Samter’s triad/AERD, particularly with marked peripheral blood or tissue eosinophilia. Biopsy of any affected tissue and careful pathological review for evidence of eosinophilic infiltration and/or vasculitis will confirm the diagnosis of EGPA.

Acknowledgements

We thank the patient for permission to report her case for the benefit of others. This article was written in collaboration with the patient. There was no external funding for this work. We thank Dr Steve Allpress for the histology shown in this publication.

REFERENCES


Department of Virology and Immunology, Auckland Hospital, Auckland, New Zealand

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication April 29, 2017; revised June 4, 2017; accepted for publication July 10, 2017.

Available online August 30, 2017.

Corresponding author: Rohan Ameratunga, MBChB, PhD, FRACP, FRCPA, ABMLI, FFSc, FRCP, FRCPATH, Department of Virology and Immunology, Auckland Hospital, Park Rd, Grafton 1010, Auckland, New Zealand.

E-mail: rohana@adhb.govt.nz.

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http://dx.doi.org/10.1016/j.jaip.2017.07.006