

Letters

Atypical eosinophilic granulomatosis with polyangiitis with spontaneous aspirin reactivity and immunoglobulin E–mediated anaphylaxis

Eosinophilic granulomatosis with polyangiitis (EGPA) and aspirin-exacerbated respiratory disease (AERD) share overlapping pathophysiology characterized by peripheral eosinophilia, nasal polyps, and asthma.^{1,2} The overlapping nature of the symptoms and etiologies of these 2 diseases emerged recently in a series of case reports reporting additional potential comorbidities.^{3,4}

Here, we describe a previously healthy woman in her mid-twenties, initially presenting with severe shortness of breath with a history of subacute nocturnal cough unresponsive to antibiotics and no signs of environmental allergies. She had no history of asthma, allergies, or aspirin sensitivity. Blood-based immunoglobulin E testing of common environmental allergens before admission was negative. At admission, she had peripheral eosinophilia (up to 1.85 K/uL) and elevated C-reactive protein (17.4 mg/L). Chest computerized tomography findings revealed changes consistent with atypical pneumonia or interstitial lung disease with overt interstitial thickening of the pulmonary vasculature (Fig 1).

She was admitted and treated with oxygen and antibiotics for atypical pneumonia. During admission, she continued to have eosinophilia and cough. Bronchoscopy with lavage was performed, which revealed 85% eosinophils. Infectious, allergic, and rheumatologic testing did not explain the cause of eosinophilia. At the time, the patient had no upper respiratory tract signs or symptoms, including nasal polyps. Vasculitis was initially ruled out on the basis of the negative results of antinuclear antibodies and antineutrophil cytoplasmic antibodies (ANCA) testing and clinical history. She was discharged and started on a course of 60 mg prednisone and planned tapering.

After 8 weeks from the initial hospitalization, the patient experienced severe epigastric pain, nausea, and diarrhea, which prompted her to visit the emergency department. Imaging was performed, which revealed nonspecific duodenitis. The pain was managed with intramuscular dosing of dicyclomine and ketorolac. Within minutes, the patient experienced respiratory failure and required extensive resuscitative efforts. There was no urticaria, angioedema, or wheezing.

Because of this crisis, the patient was admitted to the hospital and peripheral eosinophilia (up to 1.78 K/uL), epigastric pain, and nocturnal cough were noted for the duration of her admission. A chest computed tomography scan was again performed, which revealed

interstitial thickening and edema. An endoscopy and biopsy of the duodenum were performed 3 days after her admission while on high-dose corticosteroids, which did not exhibit eosinophilic infiltration. A repeat bronchoscopy and lavage were done and revealed cytologic eosinophilia (49%).

Extensive testing was completed to rule out mastocytosis, eosinophilic pneumonia, other hypereosinophilia syndromes, and infectious causes. A head computed tomography scan was performed 6 weeks after the second hospitalization, which revealed sinusitis with nasal polyps. At this point, the patient was unable to taper prednisone below 40 mg orally without asthmatic symptoms or eosinophilia. However, AERD alone failed to explain the multiorgan involvement or lower respiratory findings. The cumulative laboratory findings and presentation led to a diagnosis of EGPA, and the patient was started on 300 mg of mepolizumab every 28 days.

An aspirin challenge was planned to explore the patient's reported respiratory failure. While the patient was on prednisone, montelukast, and mepolizumab, a clinical aspirin challenge up to 325 mg had negative results, and AERD was excluded at that time. While continuing mepolizumab therapy and prednisone taper, the patient underwent a polypectomy, which improved the upper respiratory symptoms. Microscopic exam of resected polyps revealed severe eosinophilic and lymphocytic tissue infiltration and edema.

After the patient completed the prednisone taper, she reported nasal congestion, sinus headache, and mild asthmatic symptoms after naproxen (200 mg orally), which aligned with AERD symptoms. A repeated clinical aspirin challenge evoked a nasal-ocular reaction at 81 mg orally, confirming sensitivity to nonsteroidal anti-inflammatory drugs. During this last clinical challenge, the patient was on mepolizumab alone—in contrast with the triple therapy she was on during the first clinical challenge.

Finally, approximately a year after initial hospitalization, the patient reported an anaphylactoid reaction to a potential bee sting. Her reported symptoms included urticaria, angioedema, and syncope from presumed hypotension. Blood and intradermal testing confirmed immunoglobulin E–mediated reaction to honeybee venom. She had never reacted to a bee sting in the past.

This patient had an atypical presentation of EGPA. There were no prodromal symptoms including asthma, rhinitis, sinusitis, or nasal polyps. Rather, she first presented with the disease in the prevasculitic or eosinophilic phase with peripheral eosinophilia above 1.5 K/uL, a multiorgan involvement, asthma, and interstitial thickening and pulmonary opacities on imaging.^{1,5} This extraordinarily acute presentation with negative vasculitic and ANCA tests may initially rule out EGPA as a differential diagnosis. However, ANCA status is not

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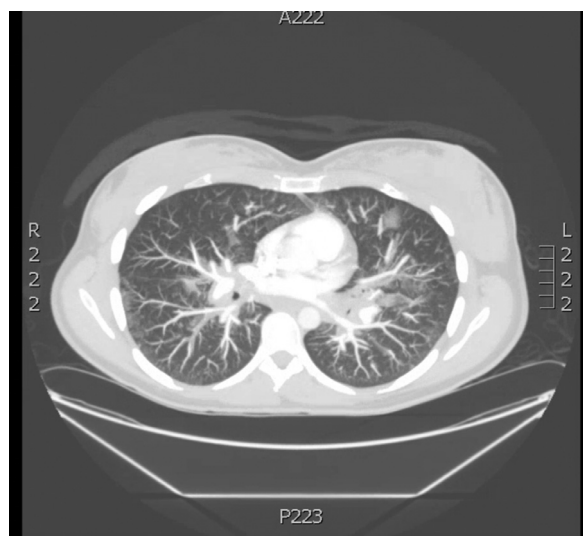


Figure 1. Computed tomography of the chest at the time of initial presentation in the emergency department, which revealed interstitial thickening, interlobular thickening, pulmonary edema, and nodules.

a sensitive test for EGPA.^{5,6} Although EGPA and AERD have overlapping clinical findings, they have only been reported in the literature once before.⁴ This patient had variable reactions to nonsteroidal anti-inflammatory drugs depending on the medical therapies she was receiving, illustrating the need for cognizance around potential false negatives in clinical aspirin challenges. The progression and development of AERD and anaphylaxis within EGPA indicate dysregulation in the intersecting and overlapping pathways of T_H2 lymphocytes and eosinophils. Given the duality of the effector functions of T_H2 cells and eosinophils in peripheral blood and tissue, these results reveal overlapping physiological pathways in the conditions this patient developed.^{7,8} This fascinating case illustrates the overlap of unique allergic disorders that may co-exist in the same individual and merit careful attention during the workup of complex cases.

Laurel L. Ball, BSc*
Stephanie A. Velasquez, BSc*
Omar M. Al Jammal, BSc*
Andrew A. White, MD†
Praveen Akuthota, MD‡

* School of Medicine
University of California
San Diego, La Jolla, California

† Division of Allergy, Asthma, and Immunology
Scripps Clinic
San Diego, California

‡ Division of Pulmonary, Critical Care and Sleep Medicine
Department of Medicine
University of California
San Diego, La Jolla, California
llball@health.ucsd.edu

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