Churg-Strauss Angiitis

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Abstract: Churg-Strauss angiitis is a rare vasculitic disorder affecting small- and medium-sized blood vessels. It is clinically characterized by the presence of a wide spectrum of multisystem organ involvement, with allergic rhinitis, asthma and peripheral blood eosinophilia as the most typical manifestations. The authors describe 2 cases of Churg-Strauss angiitis from an urban community of Southern Louisiana, exhibiting an atypical presentation with myocardial ischemia and cerebrovascular complications. Epidemiology, pathophysiology and clinical overview are presented. The therapeutic management is also discussed.

Key Indexing Terms: Churg-Strauss angiitis; Vasculitis; Eosinophilic granulomatosis with polyangiitis; Antinuclear cytoplasmic antibody; 5 factor score. **[Am J Med Sci 2014;348(6):522–527.]**

Churg-Strauss angiitis (CSA) is the least common of the antinuclear cytoplasmic antibody (ANCA)-associated vasculitides, affects small- and medium-sized vessels and distinguishes itself from other small vessel vasculitic processes by the presence of severe asthma and peripheral blood eosinophilia. In their original description in 1951, Churg and Strauss reported 13 cases that had been labeled as polyarteritis nodosa, and by using the histologic criteria of necrotizing vasculitis, tissue infiltration by eosinophilic leukocytes and extravascular granulomas, they reclassified these cases into what is now known as CSA.[1] Impressively, the description of this entity in the landmark article from more than 6 decades back still remains accurate. The Chapel Hill Consensus Conference on the nomenclature of systemic vasculitis defined CSA as "eosinophil-rich and granulomatous inflammation involving the respiratory tract, coupled with necrotizing vasculitis affecting small- to medium-sized vessels, and associated with asthma and eosinophilia." It is classified along with granulomatosis with polyangiitis (Wegener's granulomatosis) and microscopic polyangiitis as 1 of the ANCA-associated vasculitides.[2] The 2012 Revised International Chapel Hill Consensus Conference recommends replacing the eponym "Churg-Strauss angiitis" by "eosinophilic granulomatosis with polyangiitis (EGPA)."[3] In light of this recent recommendation, the term EGPA shall be used through the remainder of this review.

EGPA is a systemic illness that can affect virtually any organ system but often is phasic in nature, with the clinical presentation varying not only with the anatomical side affected but also with the illness phase. Classically, EGPA develops in 3 sequential phases: prodromal phase, eosinophilic phase and vasculitic phase. These phases frequently overlap and are rarely clearly distinguishable. The majority of patients report nonspecific constitutional symptoms at some stage during the course of their illness. These include fever, malaise, fatigue, arthralgia and weight loss. Most patients develop respiratory and cardiovascular involvement, followed by peripheral neurologic and skin involvement.[4] Herein, we describe 2 patients with EGPA exhibiting some unusual clinical manifestations: the 1st with peripheral neurologic involvement triggered by a leukotriene receptor antagonist (LTRA) and the 2nd presenting with cardiac system and central nervous system involvement.

Case Descriptions

Case 1

A 56-year-old man who was being treated for bronchial asthma for several years with a LTRA, montelukast, presented with pain and numbness in both feet and in the 4th and 5th digits of the left hand. Physical examination was significant for weakness in dorsiflexors of both feet, right more than left. Initial blood examination revealed anemia and an eosinophilic leukocytosis with an absolute eosinophil count of 12,300/μL. In addition, a markedly elevated erythrocyte sedimentation rate of 112 mm/hr was noted. Vasculitic workup revealed an elevated myeloperoxidase (MPO) antibody level at 90 U/mL (normal < 6 U/mL). Chest imaging revealed bilateral interstitial infiltrates. Sural nerve biopsy revealed perivascular chronic inflammation consistent with a vasculitic process. Transbronchial lung biopsy revealed marked infiltration of eosinophils with fibrinoid necrosis within the vessels, characteristic of EGPA (Figures 1

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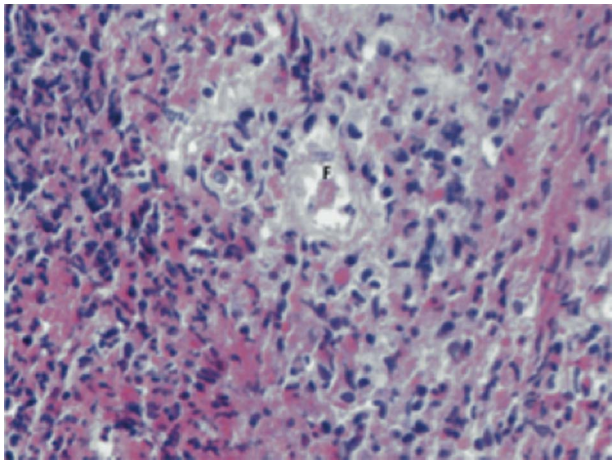

FIGURE 1. Section of lung with marked infiltration of eosinophils and fibrinoid necrosis (F) within a small vessel, characteristic of eosinophilic granulomatosis with polyangiitis (hematoxylin and eosin stain at 40×).

and 2). Montelukast was discontinued, and treatment with oral steroids was initiated. Eosinophilia resolved, and the patient experienced complete recovery.

Case 2

A 58-year-old man was admitted with intermittent substernal chest pain of 4 days duration. The patient also reported sporadic dry cough and shortness of breath for the preceding 3 months and was being treated with inhaled short acting bronchodilators. Physical examination revealed expiratory wheezes in both lung fields. Laboratory data revealed an eosinophilic leukocytosis with an absolute eosinophil count of 2959/μL. Chest imaging revealed multiple patchy areas of ground glass attenuation bilaterally (Figure 3). Serial electrocardiograms showed dynamic ST-T changes, and cardiac biomarkers were positive. Cardiac catheterization was scheduled for the following day, but the patient developed right upper extremity weakness on the morning of the procedure. Angiography revealed normal coronary arteries with normal ascending and transverse aorta

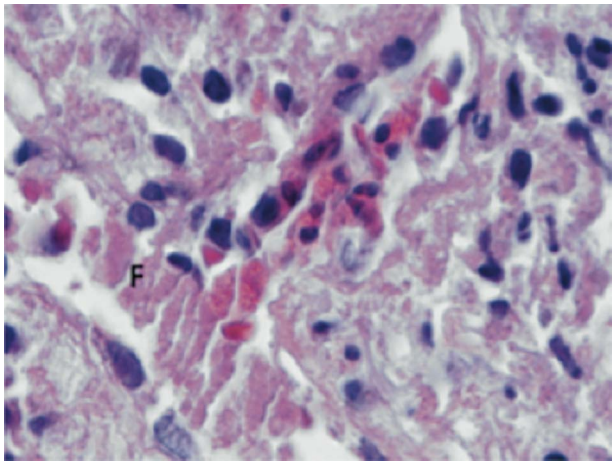

FIGURE 2. Section of lung with infiltration of eosinophils and fibrinoid necrosis (F) within a small vessel, characteristic of eosinophilic granulomatosis with polyangiitis (hematoxylin and eosin stain at 100×).

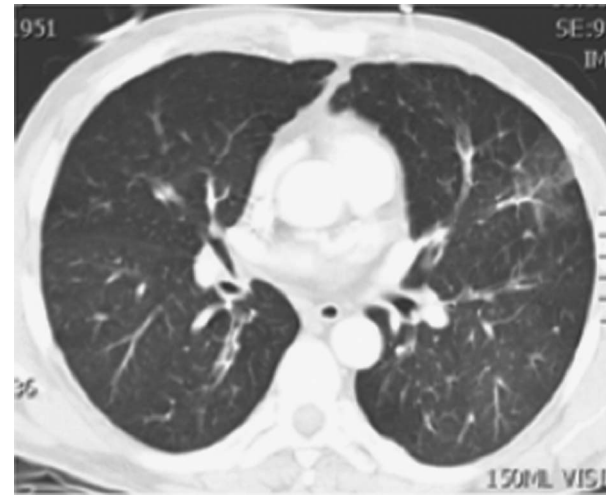

FIGURE 3. Representative section from computed tomography scan of the chest showing an area of ground glass attenuation in the left upper lobe.

without obvious embolic source. Transthoracic echocardiogram imaging was normal. Neurologic deficits progressed to involve right upper motor neuron facial paralysis. Brain magnetic resonance imaging (MRI) revealed multiple areas of acute ischemia bilaterally (Figure 4). Additional diagnostic workup showed a positive perinuclear-ANCA (p-ANCA). A diagnosis of EGPA was made, and the patient was treated with pulse methylprednisolone (500 mg intravenously) for 2 days, followed by oral prednisone. Treatment was followed by complete resolution of neurologic deficits and peripheral eosinophilia and negativization of p-ANCA. Patient remains asymptomatic 2 years later with repeat high-resolution computed tomography of the chest and MRI of the brain being normal to date.

DISCUSSION

Epidemiology and Etiopathogenesis

EGPA is the least common of the ANCA-associated vasculitides, with an incidence ranging between 0.5 and 6.8 new cases per 1,000,000 patients per year and with a prevalence ranging from 10.7 to 13 per 1,000,000 adults, depending on the geographical location and the classification criteria applied.[5–7] The mean age at diagnosis is 48 years, although cases at extremes of age are well documented.[8,9] There is no clear sex predominance, and there are scarce data on ethnic differences in the occurrence of EGPA.[10]

The pathogenesis of EGPA is not fully elucidated. It seems to be complex, multifactorial and the result of interplay between environmental factors and genetic and immune-mediated mechanisms (Table 1). Although most cases of EGPA are idiopathic, certain triggering factors have been incriminated. These include infectious agents (eg, *Actinomyces*), drugs (eg, sulfonamides and carbamazepine) and vaccinations.[10,11] The onset of EGPA has also been associated with the use of anti-asthmatic drugs, particularly the LTRAs montelukast and zafirlukast, and more recently with the anti-IgE monoclonal antibody, omalizumab.[12,13] However, it is now increasingly accepted that it is the corticosteroid tapering allowed by these drugs and not the drugs themselves that might result in unmasking a previously undiagnosed EGPA.[14]

HLA-DRB4 has been suggested to be a genetic risk factor for EGPA, but several other predisposing genetic factors