A 63-year-old white man presented with severe dyspnea requiring intubation in the Emergency Department. He responded rapidly to bronchodilators and steroids and was transferred from the medical ICU to a room within 24 h. Further medical history revealed that he had been hospitalized about 20 times over a period of the previous 5 years for exacerbations of COPD or asthma, requiring intubation on three occasions. All of the episodes had responded well to treatment, and the next attack would invariably occur shortly after tapering off the steroid dosage. Malaise, fatigue, dull epigastric pain, and nausea often preceded the asthmatic attack. For 2 days prior to the current admission and with recent episodes, he had noted a transient nonpruritic rash. He was a 50 pack-year cigarette smoker, had frequent attacks of sinusitis for the past 8 years, and had four “sinus surgeries.”

Physical Examination


Laboratory Findings

WBC count, 9,600/µL with 65% neutrophils, 11% lymphocytes, 17% eosinophils; hematocrit, 46%. Review of the hospital computer revealed intermittent eosinophilia during a period of the last 18 months which averaged around 1,000/µL, with the highest noted being 2,300/µL. BUN value, 28; creatinine 1.0.

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Arterial blood gas values (radial artery): pH, 7.37; PaCO₂, 48 mm Hg; PaO₂, 59 mm Hg. Sputum culture: normal flora. Chest radiograph (Fig 1): patchy infiltration, lower lobe of right lung. Stool examination: negative for ova or parasites.

What diagnostic entities should be considered; and, which diagnostic test would you perform next?
**Answers: Churg-Strauss syndrome. The diagnostic procedure was a skin biopsy.**

Asthma, peripheral eosinophilia, and eosinophilic vasculitis are several of the characteristics of Churg-Strauss syndrome (CSS). However, the rash often is not apparent; and episodic dyspnea and eosinophilia can be associated with a variety of other conditions. These include simple atopic asthma, adverse drug effects, parasitic infections, allergic bronchopulmonary aspergillosis, and chronic eosinophilic pneumonia. It is important to establish the correct diagnosis because the management of these conditions differs.

In 1951, Churg and Strauss described 13 patients with asthma, eosinophilia, and systemic vasculitis. They documented the pathologic hallmarks of the disease, which are tissue infiltration by eosinophils, necrotizing vasculitis of small arteries and veins, and necrotizing extravascular granulomas. They termed this syndrome “allergic granulomatosis and allergic angiitis.” Granulomas are no longer considered essential; however, asthma is fundamental to the diagnosis. The age of onset is usually 40 to 50 years old, and females and males are affected equally. Asthma usually precedes the onset of systemic vasculitis with a variable latency. The mean latency period is 8 years, with the longest being 30 years.

Three phases of CSS have been postulated. The first is a prodromal “allergic” phase, which may persist for years and consists of allergic rhinitis and asthma arising in a middle-aged individual without a past medical history or family history of atopy. The second phase is characterized by peripheral blood and tissue eosinophilia, often producing a picture resembling Löffler’s syndrome or chronic eosinophilic pneumonia. This phase may relapse and recur over a period of years before the third phase of systemic vasculitis occurs.

Fever, malaise, weight loss, myalgia, and arthralgia are common in the vasculitic phase. Upper respiratory tract involvement, as evidenced by nasal polyps or abnormalities shown on radiographs of the sinuses can be seen in the majority of patients with CSS. Skin rash occurs in up to 70% of patients and consists of purpura, erythema, urticaria, papules, or nodules. Neurologic involvement occurs in 75% of patients during the course of the disease and is usually manifested as mononeuropathy multiplex. Eosinophil infiltration of the gastrointestinal tract may result in abdominal pain, diarrhea, and bleeding. Cardiac manifestations include acute pericarditis, constrictive pericarditis, myocardial infarction, and heart failure. In one series, cardiac disease accounted for nearly 50% of the deaths. Renal involvement is rare.

Chest radiographic abnormalities can be detected in two thirds of patients. The infiltrates may be diffuse, patchy, or nodular and are generally transient. Pleural effusions are seen in one third of patients. Peripheral blood eosinophilia is a hallmark of CSS; however, it may be overlooked because the eosinophil counts fluctuate widely and rapidly. Corticosteroid therapy for asthma may contribute to the transience of eosinophilia.

The American College of Rheumatology has established six criteria for the diagnosis of CSS in a patient with documented vasculitis: (1) asthma; (2) eosinophilia of more than 1% on differential WBC count; (3) mononeuropathy (including multiplex) or polynuropathy; (4) transient radiographically evidenced pulmonary infiltrates; (5) paranasal abnormality; and (6) a biopsy containing a blood vessel with extravascular eosinophils. The presence of 4 or more of these criteria yields a sensitivity of 85% and a specificity of 99.7% in recognizing CSS.

Mortality from CSS was high in the predicorticosteroid era, with a median survival of 3 months. With corticosteroids, the median survival is 9 years, and the 5-year survival is 62%. Refractory cases may be treated with the addition of cyclophosphamide.

The patient whose case is reported herein experienced the onset of asthma in his 50s and experienced frequent episodes of sinusitis requiring multiple surgical operations. Asthma preceded the onset of eosinophilia by 6 years, and intermittent and fluctuating eosinophilia was present for nearly 18 months before a skin rash was noted. Biopsy of the rash, which showed leukocytoclastic angiitis and perivascular eosinophilic infiltration, was consistent with CSS (Fig 2), and an evanescent infiltrate was noted on a chest radiograph on two separate occasions. In addition, the patient reported gastrointestinal symptoms that may have been secondary to CSS. The skin rash resolved within 72 h, and the patient has been receiving a maintenance course of corticosteroids for 5 months without further

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**Figure 2. Photomicrograph of the 3-mm skin punch biopsy demonstrating intimal thickening of a small vessel, and an extensive inflammatory infiltrate of the muscular wall composed predominantly of eosinophils which extends to perivascular connective tissue (hematoxylin-eosin, original magnification ×400).**
exacerbations of asthma or vasculitis.

**Clinical Pearls**

1. **Asthma, rhinitis or sinusitis, and eosinophilia, with the presence of a skin rash or neuropathy, should suggest the diagnosis of CSS.**

2. **Asthma in CSS may precede eosinophilia by years and even decades; asthma with eosinophilia may be present for years before the onset of vasculitic symptoms.**

3. **Eosinophilia in CSS can be intermittent and fluctuate widely and therefore can be overlooked unless repeated blood cell counts are obtained.**

4. **The diagnosis of CSS can be missed because of the tendency to ascribe recurrent respiratory failure in elderly smokers to exacerbations of COPD.**

5. **It is important to establish the diagnosis of CSS because response to corticosteroid therapy is good and remission can be maintained by prescribing low doses.**

**Suggested Readings**


