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NOT ALL COUGHS ARE ASTHMA OR ALLERGIES: CHURG–STRAUSS SYNDROME

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Abstract—Background: Cardiomyopathy in patients with Churg–Strauss syndrome (CSS) carries a poor prognosis, with a high 5-year mortality rate, and requires treatment with immunosuppressive therapy. There is no single pathognomonic test or clinical finding for diagnosing CSS; instead, it is based upon meeting four of six criteria. **Case Report:** A 47-year-old woman with a 6-month medical history of “asthma” presented to our hospital with a 1-month history of dyspnea on exertion. She denied any chest pain, cough, fever, orthopnea, or leg swelling. She was afebrile and normotensive, and her physical examination was unremarkable. Her white blood cell count was 23,000/mm³ with 23% eosinophils, and her troponin T level was 1.08 Ng/ml. Extensive work-up revealed CSS. **Why Should an Emergency Physician Be Aware of This?:** Emergency physicians should be aware of unusual cases because not every patient that walks into an emergency department has a simple case of “asthma” or “allergies.” Our patient had been diagnosed with asthma for 6 months before her symptoms had progressed to a point that prompted her to seek medical attention in a hospital. Emergency physicians are in a unique position to identify patients who present with recurrent complaints of asthma—especially late-onset asthma, which gradually worsens and is refractory to usual treatment. A complete blood cell count with a differential will prove valuable. Assessments of a patient’s C-reactive protein level and erythrocyte sedimentation rate are inexpensive and check for signs of inflammation, although they are nonspecific. A chest radiograph or computed tomography scan of the chest or sinuses in some patients can also prove to be of value.

Prompt recognition and treatment with steroids is imperative to ablate vasculitis tissue damage because this can improve the outcome. © 2016 Elsevier Inc. All rights reserved.

Keywords—asthma; autoimmune; cardiomyopathy; chest pain; dyspnea; eosinophilia; troponins; vasculitis

INTRODUCTION

Churg–Strauss syndrome (CSS), also known as eosinophilic granulomatosis with polyangiitis, is a rare autoimmune disease that is highly variable with regard to signs and symptoms. Asthma is the most common sign of CSS, but it can cause a host of problems ranging from hay fever and rash to gastrointestinal symptoms to neuropathy—and the list of complaints varies according to which organs are affected. Therefore, the expansive array of signs and symptoms and their resemblance to those of other disorders makes CSS difficult to diagnose.

CASE REPORT

A 47-year-old woman with a 6-month medical history of “asthma” presented to our hospital with a 1-month history of dyspnea on exertion. She denied any chest pain, cough, fever, orthopnea, or leg swelling. She was afebrile and normotensive, and the physical examination was unremarkable. Her white blood cell count was 23,000/mm³

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with 23% eosinophils and her troponin T level was 1.08 Ng/ml. An electrocardiogram showed T wave inversion in the anterolateral leads. A chest radiograph revealed infiltrates in the left lower lobe. A computed tomography (CT) scan of the chest also revealed bilateral multilobar patchy infiltrates. An echocardiogram measured a left ventricular ejection fraction of 40% to 45% with apical and anteroseptal hypokinesis and severe mitral regurgitation. Cardiac catheterization was negative for significant coronary artery disease. A CT scan of the sinuses was consistent with bilateral sinusitis. An extensive rheumatologic work-up was negative, including antineutrophil cytoplasmic antibody levels, except for an elevated erythrocyte sedimentation rate and high levels of immunoglobulin E. A lung biopsy specimen revealed eosinophilic vasculitis and granuloma formation. The patient met criteria for CSS. To confirm this diagnosis, a cardiac magnetic resonance imaging scan was performed, which revealed a left ventricular ejection fraction of 34% with apical and anteroseptal akinesis. Patchy endomyocardial delayed enhancement was seen, which was suggestive of CSS cardiomyopathy (Figure 1).

DISCUSSION

CSS was first described in 1951 as an autoimmune disorder that affected small- and medium-sized vessels (1). The annual incidence of CSS is 1 to 3 cases per 100,000 adults in the United States. The age at onset ranges from 15 to 70 years. The mean age at diagnosis is around 50 years (2). A diagnosis is based on the presence of four of six criteria, with a sensitivity of 85% and specificity of 99.7%: 1) asthma; 2) sinusitis; 3) pulmonary infiltrates; 4) eosinophils >10% in peripheral blood; 5) histologic proof of vasculitis with extravascular eosinophils (Figure 2); and 6) evidence of neuropathy (3). Our patient met five of these six criteria. The three stages of progression are allergic, eosinophilic, and vasculitis. Progression between stages may span from a few months

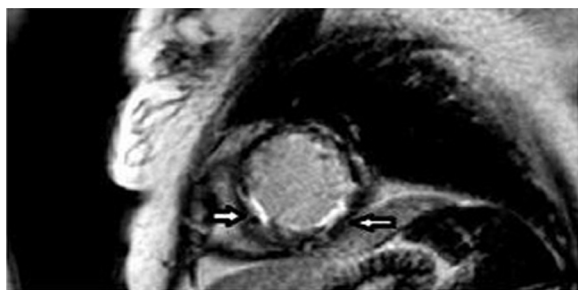


Figure 1. A cardiac magnetic resonance imaging scan with an arrow showing delayed enhancement of the endocardium, which is indicative of inflammation and suggestive of Churg-Strauss syndrome.

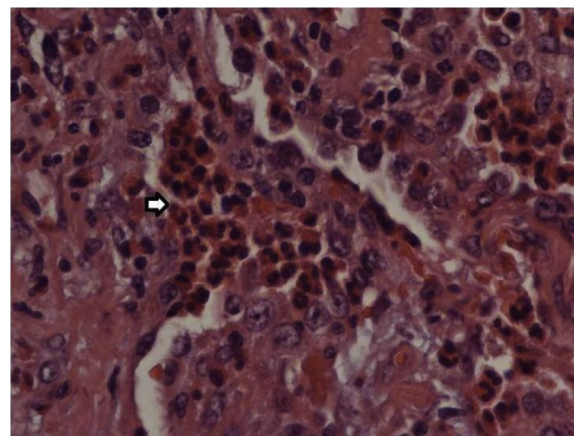


Figure 2. A biopsy specimen of tissue from the small artery in a patient with marked inflammatory infiltrates consisting of many eosinophils (arrows) admixed with lymphocytes.

to years. There are five known risk factors to predict the risk of death: 1) presence of cardiomyopathy; 2) gastrointestinal bleed or pancreatitis; 3) central nervous system involvement; 4) proteinuria >1 g/day; and 5) a creatinine level >1.58. The presence of these factors was shown to increase 5-year mortality (patients with 0 factors have a 5-year mortality rate of 11.9%; with 1 factor, this increased to 26%, and with ≥ 2 factors this increased to 46%) (4).

In the early stages of CSS, the common symptoms mimic those of upper airway bronchospastic disease, allergic/viral rhinorrhea, and sinusitis. Although some of these symptoms may resemble those of patients with Kartagener syndrome, there are distinct differences of chest radiography findings of dextrocardia, peribronchial infiltrates, overinflation of the lung, an impaired sense of smell, and recurrent otitis media in Kartagener syndrome (5).

In CSS, elevated serum levels of eosinophils should alert physicians to give consideration to the differential diagnosis of parasites, eosinophilic granulomatous polyangiitis (CSS), or bronchopulmonary aspergillosis (6). Immediate treatment and prompt referral to the appropriate specialists based upon test results and patient condition would further mitigate medical demise.

Cardiac manifestations include pericarditis, cardiomyopathy, myocarditis, dysrhythmias, and sudden death. Cardiac morbidities account for nearly 50% of deaths. A study has shown a 78-month survival rate of 90% vs. 30% in presence or absence of cardiac manifestations, respectively. Cardiomyopathy is more common in antineutrophil cytoplasmic antibody-negative patients, as was noted in our patient.

The treatment of CSS is similar to various other types of small-vessel vasculitis. Systemic steroids are usually the initial therapy. First, high doses of oral

steroids are given in an attempt to get the disease into remission as quickly as possible. Steroids are the mainstay of treatment and generally begin with a dose of 1 mg/kg/day (maximum 60 mg/day) of prednisolone, maintained until symptoms are controlled and then slowly tapered for 1 year. Patients with factors that have a poor prognosis (i.e., central nervous system, renal, cardiac, or gastrointestinal involvement) require a combination of steroids and cyclophosphamide, which has produced better control and sustained remission rates compared with steroids alone (7). Cyclophosphamide pulse therapy is recommended in patients with the presence of one or more high-risk markers. In non-organ-threatening or non-life-threatening disease, the use of methotrexate is a less toxic alternative to cyclophosphamide. For remission maintenance, the combination of low-dose steroids and azathioprine, leflunomide, or methotrexate is used (7). Patients not responding or those who relapse despite appropriate therapy are managed with different therapies, including mycophenolate mofetil, human intravenous immunoglobulin, and biologic agents, including rituximab, interferon-alpha, and mepolizumab (8).

WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

This case is a good example of the application of Occam's razor rule of parsimony in clinical medicine. The patient presented with shortness of breath and the initial work-up suggested nonischemic cardiomyopathy, which is presumed to be caused by viral myocarditis in most cases. Marked eosinophilia and pulmonary infiltrates in the absence of clinical findings of congestive heart failure led to the suspicion of CSS. Emergency physicians should be aware of unusual cases because not every patient that walks into the emergency department (ED) has a simple case of "asthma" or "allergies." CSS is a rare and challenging disease to diagnose given its nuances, especially in a busy ED setting. This results in patients getting diagnosed much later in the disease process, as occurred with our patient. Our patient had been diagnosed with asthma for 6 months before her symptoms

had progressed to a point that prompted her to seek medical attention in a hospital.

ED physicians are in a unique position to identify patients who present with recurrent complaints of asthma, especially late-onset asthma, that gradually worsens and is refractory to usual treatment. Patients who have recurring symptoms of bronchitis or pneumonia-like clinical presentation with increased eosinophils are also encountered. Those with recurrent, lingering, or worsening sinusitis associated with asthma and elevated eosinophil levels or patients with recurrent skin rashes with associated eosinophilia should also be considered. A complete blood cell count with a differential will prove valuable. Assessments of C-reactive protein levels and erythrocyte sedimentation rates are inexpensive and check for signs of inflammation, although they are nonspecific. In the presence of eosinophilia, urinalysis checking for microscopic hematuria may be a sign of glomerulonephritis. A chest radiograph or a CT scan of the chest or sinuses in some patients will also prove to be of value. Prompt recognition and treatment with steroids is imperative to abate vasculitis tissue damage because this can improve the outcome.

REFERENCES

1. Churg J, Strauss L. Allergic granulomatosis, allergic angiitis, and periarteritis nodosa. *Am J Pathol* 1951;27:277–301.
2. Bosch X, Guilbert A, Espinosa G, et al. Treatment of antineutrophil cytoplasmic antibody associated vasculitis: a systematic review. *JAMA* 2007;298:655–69.
3. Masi AT, Hunder GG, Lie JT, et al. The American College of Rheumatology 1990 criteria for the classification of Churg–Strauss syndrome (allergic granulomatosis and angiitis). *Arthritis Rheum* 1990;33:1094–100.
4. Guillevin L, Lhote F, Gayraud M, et al. Prognostic factors in polyarteritis nodosa and Churg–Strauss syndrome. A prospective study in 342 patients. *Medicine* 1996;75:17–28.
5. Serapinas D, Staikūnienė J, Barkauskienė D, et al. An unusual regression of the symptoms of Kartagener syndrome [in Spanish]. *Arch Bronconeumol* 2013;49:28–30.
6. Maselli DJ, Singh H, Diaz J, Peters JJ. Efficacy of omalizumab in asthmatic patients with IgE levels above 700 IU/mL: a retrospective study. *Ann Allergy Asthma Immunol* 2013;110:457–61.
7. Alfaro TM, Duarte C, Monteiro R, et al. Churg–Strauss syndrome: case series [in Spanish]. *Rev Port Pneumol* 2012;189:86–92.
8. Sinico RA, Di TL, Maggiore U, et al. Prevalence and clinical significance of antineutrophil cytoplasmic antibodies in Churg–Strauss syndrome. *Arthritis Rheum* 2005;52:2926–35.