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CASE REPORT

Severe idiopathic hypereosinophilic syndrome

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Summary
Hypereosinophilic syndrome (HES) is a systemic illness that usually presents with nonspecific symptoms. However, HES can be fatal, particularly when eosinophils infiltrate vital organs. We report a patient with HES who presented with a perforated viscus and sepsis-like syndrome and rapidly improved with drotrecogin-alfa and steroid therapy.

Case

A 52 yr old male with a 5-month history of fever and fatigue presented to an outside hospital (OSH) with cough and debilitating abdominal pain. He promptly underwent an exploratory laprotomy, which revealed a small colonic perforation. A portion of bowel was resected and repaired with end to end anastomosis. He was reintubated soon after surgery for increasing hypoxemia and transferred to our institution.

On transfer, the patient was afebrile with a pulse rate of 122. His oxygen saturation was 92% on FiO_2 100% and PEEP of 15 cmH_2O. His blood pressure was 96/46 while receiving norepinephrine at 10 mcg/min. His cardiac exam revealed tachycardia without murmur. Lungs demonstrated bilateral crackles. Abdomen was soft and nontender, with a clean midline scar. His skin appeared flushed. The rest of the exam was normal.

WBC count was 36.0×10^3 cells/mm^3, hemoglobin concentration was 9.4 gm/dL, and platelet count was 289,000/mm^3. WBC differential (automated) was 57% neutrophils, 27% bands, 6% eosinophils, and 10% lymphocytes. The chemistry demonstrated a sodium of 148, chloride 106, HCO_3 35, BUN 36, creatinine 1.0, and calcium of 8.0. All other chemistry values were normal. The AST was 32. Serum troponin was 25 ng/mL (normal: 0–0.5 ng/mL). The admission chest radiograph demonstrated diffuse bilateral air space disease with mild cardiomegaly.

Cultures were obtained from blood, urine, and sputum. Drotrecogin alfa (activated) and broad-spectrum antibiotics were given. Over the next 24 h, the patient's oxygen requirement decreased significantly (FiO_2 50%, PEEP 8 cm H_2O), and blood pressure was 122/70 off pressors. However, his peripheral blood smears were manually reviewed and demonstrated a peripheral eosinophil count

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of 12,000 cells/mm^3 (34% eosinophils—erroneously reported as bands initially). By 72 h, his troponin levels returned to normal. Echocardiogram at the outside institution had demonstrated regional hypokinesis, but repeat evaluation showed normal ventricular function. CT scan of the chest demonstrated extensive ground-glass opacities and bibasilar infiltrates (Figure 1). As he was unable to wean from mechanical ventilation, bronchoscopy with bronchoalveolar lavage day 3 of transfer showed a few alveolar macrophages and 94% eosinophils (Figure 2).

Records obtained revealed that the patient had eosinophilia (18% of the total WBCs) at an outpatient evaluation for fatigue 4 months earlier. Histology slides from his colon resection were obtained and showed a marked eosinophilic infiltration with evidence of eosinophilic vasculitis. Bone marrow biopsy was eventually performed to exclude eosinophilic leukemia and showed eosinophilic precursors and no blasts. Antibiotics were stopped, but eosinophilia persisted. No drug reaction, parasitic infection, or autoantibodies were detected. Genetic testing was negative. Flow cytometry was negative for hematologic malignancy.

Idiopathic hypereosinophilic syndrome (HES) with lung, colon, and cardiac involvement was diagnosed and the patient was started on methylprednisolone (60 mg IV q6) and hydroxyurea. The patient was extubated 24 h after the initiation of steroids. He did well over the next few days and was discharged home on 40 mg of prednisone. His WBC count at the time of discharge was 24,000 with 14% eosinophils.

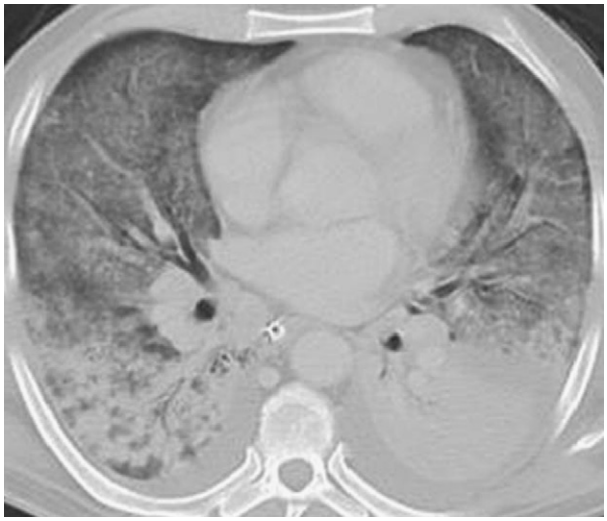

Figure 1 CT scan after drotrecogin alpha therapy. Despite rapid improvement in compliance and gas exchange, infiltrates persist and BAL is performed.

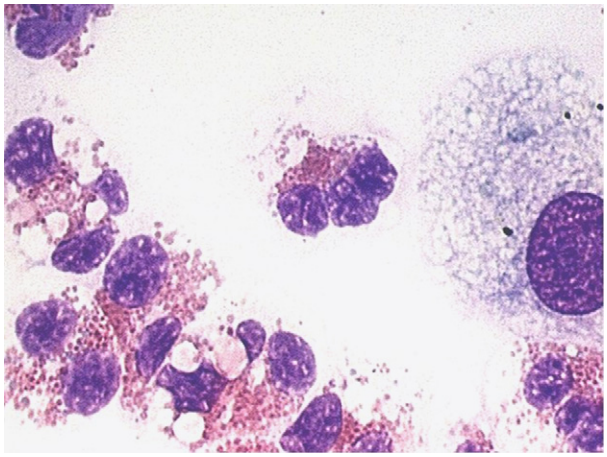

Figure 2 Cytospin of bronchoalveolar lavage shows one large alveolar macrophage with several surrounding eosinophils (Diff-Quik 400 ×).

Discussion

Idiopathic HES is a systemic illness with the pathological hallmark of eosinophil infiltration in affected organs. The classic diagnostic criteria include (1) blood eosinophilia of >1500 cells/mm^3 for 4 months, (2) no other apparent etiologies for eosinophilia, and (3) evidence of end-organ dysfunction. However, as technology now permits researchers to more rigorously define autoimmune syndromes, cellular clonality, and genetic mutations associated with HES, the number of cases defined as ''idiopathic'' is declining. Common presenting symptoms include fatigue, cough, dyspnea, fever, myalgia, and rash. HES often involves the skin, heart, lungs, nervous system, and spleen.[1,2]

Eosinophilic myocarditis is a major cause of morbidity and mortality among patients with HES. It is characterized by myocardial infiltration with eosinophils and lymphocytes followed by myocardial necrosis. Common cardiac presentations include heart failure, chest pain, arrhythmia, and cardiac thrombi. As the disease progresses, chronic manifestations of restrictive cardiac disease secondary to widespread fibrosis can occur.[2,3]

Pulmonary involvement varies significantly. Chronic, dry, insidious cough is a frequent complaint of those diagnosed with HES. However, eosinophilic infiltration into the pulmonary parenchyma may lead to focal or more widespread infiltrates. Pleural effusions can occur. Pulmonary emboli are common in HES, and result from endothelial damage secondary to local eosinophil degranulation and tissue necrosis. Because of the tendency toward thrombosis, anticoagulation is advocated by some for this disorder.[1,2]

Corticosteroids are the mainstay of treatment for acutely ill patients with HES. Most patients achieve a rapid and significant decrease in the number of circulating eosinophils and the reversible organ dysfunction usually improves quickly. Achieving long-term control of the disease has proven more difficult. As underlying etiologies of HES are discovered, targeted therapies may be beneficial. For example, those patients with a FIP1L1/PDGFRA (Fip1-like 1/platelet-derived growth factor receptor alpha) mutation have been shown to benefit from treatment with tyrosine kinase inhibitors.[4–6]

Unique to this report, our patient was given drotrecogin-alfa for his sepsis-like syndrome, which was likely to be due to HES. Other reports have documented the hypothetical use of drotrecogin alfa in other eosinophil-mediated disorders, though evidence is sparse.[7–9] This report should alert clinicians that HES can mimic sepsis and vasculitis. Prompt diagnosis and treatment with corticosteroids can result in favorable outcomes.

Conflict of interest statement

None of the authors have a conflict of interest to declare in relation to this work.

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