A 37-Year-Old Man With Severe COPD, Rash, and Conjunctivitis*

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A 37-year-old Hispanic man with a 20-pack-year smoking history presented with a 4-day history of worsening shortness of breath (SOB). The patient reported that he has had SOB for several years but has noticed a significant increase over the last 1.5 years. Due to the severity of his symptoms, he had to quit his job as a commercial fisherman.

The patient had several hospitalizations for presumed asthma exacerbations. The patient never required intubation. During these hospitalizations, he was treated with IV steroids and β-agonists with good responses.

The patient reported intermittent episodes of conjunctivitis involving one or both eyes and an intermittent rash that he described as “hives.” Both symptoms predated his pulmonary problems. The eye symptoms started 4 years ago, and the findings of the cultures of the discharge from the patient’s eyes were negative. He also experienced intermittent photophobia. The rash began on his back but spread to his torso and extremities. It has resolved in the past when he has been given steroids for his pulmonary symptoms, but it recurs intermittently when he is weaned from the steroids.

Physical Examination

A physical examination revealed the following data: no fever; pulse, 113 beats/min; BP, 125/87 mm Hg; and respiratory rate, 32 breaths/min. An examination of his eyes showed bilateral conjunctivitis. Auscultation of his lungs revealed diminished breath sounds bilaterally. His cardiac examination revealed tachycardia with a regular rhythm. His extremities did not show clubbing or edema. His skin examination showed diffuse urticarial, mildly erythematous plaques scattered over his back, arms, hands, lower extremities, and neck.

His chest radiograph showed marked hyperinflation that was consistent with bullous lung disease (Fig 1).

Laboratory Findings

The patient’s α1-antitrypsin level was in the normal range (139 mg/dL). C3 and C4 complement levels also were normal, but the result of his C1q precipitin test was positive. Urinalysis showed 169 RBCs per high-power field, a large amount of hemoglobin, and positive result for protein. A 24-h urine collection had 210 mg/dL protein. The result of a skin biopsy of an urticarial lesion was consistent with leukocytoclastic vasculitis.

Pulmonary Function Tests

Spirometry demonstrated the following: FVC, 1.18 (22% of predicted); FEV1, 0.62 (15% of predicted); FEV1/FVC ratio, 53 (predicted ratio, 76); and bronchodilator response, negative. The measurement of lung volumes demonstrated the following: functional residual capacity, 8.05 (221% of predicted); total lung capacity, 9.75 (131% of predicted); and residual volume, 7.83 (399% of predicted). The diffusing capacity corrected for hemoglobin was 30% of predicted. The patient’s arterial blood gas levels on room air were the following: pH, 7.43; Pco2, 41 mm Hg; and Po2, 59 mm Hg.

What was the cause of this patient’s rapid respiratory failure?

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Diagnosis: Hypocomplementemic urticarial vasculitis

This patient had hypocomplementemic urticarial vasculitis syndrome (HUVS). HUVS is an uncommon disorder that may be confused with systemic lupus erythematosus (SLE). HUVS was originally reported in 1973. Patients with HUVS present with urticarial vasculitis in association with pulmonary symptoms, arthritis or arthralgias, renal disease, angioedema, and eye involvement. Most patients with HUVS are white, and women are affected more frequently than men. The onset of disease is usually between 20 and 65 years of age.

The cause of HUVS is unknown, however, HUVS has been described in identical twins, which suggests that genetic background may be an important causative factor. Patients with HUVS have serologic evidence of complement activation, with low serum C4, C2, and C1q levels. Patients with HUVS have been found to have a positive result of serum C1q precipitin test. The C1q precipitin level represents a diagnostic marker for HUVS. C1q is the recognition molecule of the classic complement activation pathway and leads to the first component of the complement. The C1q precipitin in HUVS is a polyclonal IgG antibody to the collagen-like region of C1q and has been implicated in the pathogenesis of HUVS. Autoimmune responses to the C1q collagen-like region are found in patients with SLE and HUVS. Unlike patients with SLE, those with HUVS lack the anti-double-stranded DNA antibody. The autoantibody to the C1q collagen-like region is present in all patients with HUVS and in 35% of those with SLE.

The urticarial vasculitis is the most frequent presenting manifestation of HUVS. The urticarial lesions can vary in diameter from a few millimeters to several centimeters and can vary in color from pale pink to erythematous. Palpable purpura also has been reported. Lesions can vary in quality, and different types include painful, burning, stinging, pruritic, or asymptomatic lesions. A biopsy of urticarial lesions shows findings that are consistent with leukocytoclastic vasculitis. Other systemic manifestations include eye and articular involvement. The eye involvement can include uveitis, episcleritis, conjunctivitis, and photophobia. HUVS can be associated with arthritis/arthralgias, including severe polyarthritis. The ocular, cutaneous, and articular manifestations frequently respond to treatment. Renal involvement in HUVS-associated renal disease is immune mediated. Mesangial proliferative glomerulonephritis is the most frequent histopathologic type of renal pathology. Although cardiac disease is rare in patients with HUVS, cardiac manifestations may occur and include pericardial effusions with cardiac tamponade. Severe cardiac valve disease also has been suggested.

COPD, typically emphysema, is a leading cause of significant morbidity and mortality. Most patients have chronic or recurrent dyspnea. Dyspnea appears within 4 years of the onset of the urticarial vasculitis. Cigarette smoking is a significant risk factor for progression of the lung disease, although nonsmokers and patients with minimal cigarette use who have HUVS have been reported to develop severe COPD. Patients with HUVS must be urged to quit smoking.

One hypothesis regarding the possible mechanisms of lung destruction in patients with HUVS includes the cross-reactive binding of anti-C1q antibodies to the collagen-like region of surfactant proteins in the pulmonary alveoli and vasculitis of pulmonary capillaries and venules. If small vessels in the lungs of patients with HUVS are involved, then this inflammation may result in the local release of elastase by neutrophils, which could induce proteolytic lung destruction. Tobacco smoking may potentiate the proposed neutrophil-derived elastase release in areas of pulmonary vasculitis.

There is no satisfactory treatment available for HUVS-related COPD, although many drugs have been tried. These include prednisone, dapsone, anti-histamines (H1- and H2-blockers), hydroxychloroquine, colchicine, indomethacin, pentoxifylline, cyclophosphamide, and azathioprine. High-dose prednisone, with or without a cytotoxic agent or dapsone, may improve the prognosis when given early in the development of airway obstruction. Based on one case report of a patient whose pulmonary disease responded to dapsone, it was suggested that dapsone should be used as a first-line drug for HUVS.
although another case report described a patient with severe COPD that progressed despite treatment with dapsone.

After HUVS was diagnosed in our patient, he was treated with high-dose corticosteroids but did not respond to therapy. A transplantation was considered, but, due to his systemic disease, he was not an ideal candidate. This patient had a rapid progression of respiratory failure and died within 1 month of presentation.

**Clinical Pearls**

1. *In young patients with emphysema, HUVS should be considered because early recognition may be beneficial to the patient’s prognosis.*

2. *Clues to the diagnosis of HUVS-associated lung disease include other systemic manifestations, such as urticarial vasculitis, eye involvement, arthritis/arthralgias, and renal disease.*

3. *The presence of serum C1q precipitin may represent a diagnostic marker for HUVS.*

4. *Although there is no satisfactory treatment for HUVS-related COPD, prednisone and dapsone have been used with erratic success.*

**Suggested Readings**


Wisnieski JJ, Jones SM. IgG autoantibody to the collagen-like region of C1q in hypocomplementemic urticarial vasculitis syndrome, systemic lupus erythematosus, and 6 other musculoskeletal or rheumatic diseases. J Rheumatol 1992; 19:854–868