

Hemorrhagic Tracheobronchitis with Streptococcal Toxic Shock Syndrome

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Streptococcal infections have reemerged in the last two decades. Elderly persons, children, immunocompromised patients, and menstruating women are particularly susceptible to such infections. Other young adults have also become infected. Streptococcal toxic shock syndrome (STSS), caused by group A β -hemolytic streptococci, was first identified in the 1980s.¹ STSS is characterized by shock, skin rash, and multisystem organ failure. This article describes a patient with hemorrhagic tracheobronchitis associated with STSS. This association has not been previously reported in the literature.

CASE PRESENTATION

Initial Presentation and History

A 30-year-old man with no other significant medical history reported a 2-day history of fever, chills, sore throat, generalized weakness, headache, dry cough with pleuritic chest pain, dyspnea, and profuse watery diarrhea (10 times per day). The patient was taking no medications. He had no history of trauma or exposure to insect bites, had no allergies, and did not smoke. He denied inhaling any fumes or dust or ever abusing drugs or alcoholic beverages. The patient was a construction worker, was single, and denied sexual promiscuity.

Physical Examination

On physical examination, the patient was toxic and in mild respiratory distress. He had hypotension (blood pressure, 75/52 mm Hg), tachycardia (pulse, 126 bpm), tachypnea (respiratory rate, 22 breaths/min), a fever (temperature, 40.5°C [104.9°F]), diffusely erythematous skin (with 2 discrete crops of papulovesicular lesions measuring 2 cm in diameter each on the left flank), an erythematous pharynx (with enlarged tonsils covered with a purulent exudate), clear lungs, a benign abdomen, and no signs of heart failure.

Laboratory and Imaging Studies

The patient's laboratory results are listed in [Table 1](#). The patient had an increased leukocyte count, hyponatremia, hypokalemia, non-anion gap metabolic acidosis, renal failure, hypomagnesemia, hypocalcemia, hyperglycemia, an increased creatinine phosphokinase level, abnormal liver enzyme levels, and coagulopathy. There were protein, erythrocytes, and granular casts in his urine. An electrocardiogram showed sinus tachycardia. Ileus was evident on an abdominal radiograph. The findings on a chest radiograph were normal.

Continued Clinical Course

The patient was admitted to the medical intensive care unit and treated with broad-spectrum antibiotics and intravenous hydration. Two days later, the patient's dyspnea worsened and bronchospasm developed. Pulmonary function tests revealed a moderate-to-severe obstructive ventilatory defect at the level of the small airways. Despite the addition of intravenous corticosteroids and bronchodilators, the patient developed hypoxemic respiratory failure with bilateral pulmonary infiltrates ([Figure 1](#)) requiring intubation (PO₂ = 56 mm Hg, respiratory rate = 45 breaths/min).

Bronchoscopic inspection of the airways revealed an edematous and hemorrhagic tracheobronchial mucosa ([Figure 2](#)), indicative of hemorrhagic tracheobronchitis. Bronchoalveolar lavage did not reveal any infectious cause of the patient's respiratory failure; it

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Table 1. Laboratory Results of Case Patient

Component Measured	Value
Complete leukocyte count	19.1 × 10 ³ /mm ³
Prothrombin time	15.3 s
Partial thromboplastin time	53.1 s
Blood urea nitrogen	47 mg/dL
Serum levels	
Sodium	128 mEq/L
Potassium	3.3 mEq/L
Magnesium	0.9 mg/dL
Total calcium	7.3 mg/dL
Bicarbonate	19.5 mEq/L
Creatinine	4.8 mg/dL
Creatine kinase	312 U/L
Glucose	161 mg/dL
Aspartate aminotransferase	66 U/L

was negative for *Pneumocystis carinii*, acid-fast bacilli, viruses, and fungi. A collagen vascular evaluation, to detect pulmonary and renal syndromes, yielded negative results. Anti-neutrophil cytoplasm antibody and anti-glomerular basement membrane antibody titers were negative. The results of a cold agglutination test, tests for the presence of *Mycoplasma pneumoniae* and *Legionella* urinary antigen, and a test for HIV infection yielded negative results as well.

An echocardiogram showed a dilated left ventricle with diffuse hypokinesia (ejection fraction of 20% to 25%) and mild mitral regurgitation. The patient remained febrile despite broad-spectrum antibiotic treatment, including levofloxacin, ceftriaxone, vancomycin, ampicillin, sulbactam, clindamycin, and acyclovir. Blood, urine, and sputum cultures (which were performed while the patient was receiving antibiotics) were sterile. A serum streptozyme assay performed on a blood sample obtained on hospital day 2 was positive (titer, 1:200). A throat culture, which was also performed while the patient was receiving antibiotics, was negative for bacteria. Multisystem organ failure developed (pulmonary, hematologic, renal, gastrointestinal, cardiac) but gradually improved over a 10-day period.

The patient was discharged home by the 11th hospital day in stable condition. One week after discharge the patient had significant desquamation of his skin, especially on the palms and soles; these findings were consistent with STSS.



Figure 1. Chest radiograph of case patient showing bilateral pulmonary infiltrates.

DISCUSSION

Definition

STSS was defined by the Working Group on Severe Group A Streptococcal Infections and the World Health Organization as the development of shock and multiorgan failure early in the course of infection (Table 2).² The clinical course of the patient presented in this report was clearly consistent with severe streptococcal infection; the case patient's negative results on cultures for group A β-hemolytic streptococci may have occurred because the patient was administered antibiotics prior to specimen collection.

Etiology

The diverse symptoms and signs of STSS are ultimately attributable to the toxins produced by the streptococci.^{1,2} Streptococcal pyrogenic exotoxins A and B induce mononuclear cells to produce tumor necrosis factor-α (TNF-α), interleukin-1β, and interleukin-6.¹ TNF-α can cause fever, shock, and other symptoms and signs of STSS.¹ Streptococcal superantigen, mitogenic factor, and other factors are also thought to play roles in the disease process.^{1,2} M proteins contribute to bacterial invasiveness by impeding leukocyte phagocytosis of streptococci. Invasive strains of group A β-hemolytic streptococci produce these toxins while noninvasive strains do not.² Bacteriophage infection of streptococci results in the lysogenic conversion of non-toxin-producing strains to invasive strains that produce the toxins.²

Diagnostic Tests

The streptozyme test is a rapid, sensitive serologic test for the detection of extracellular antigen components of

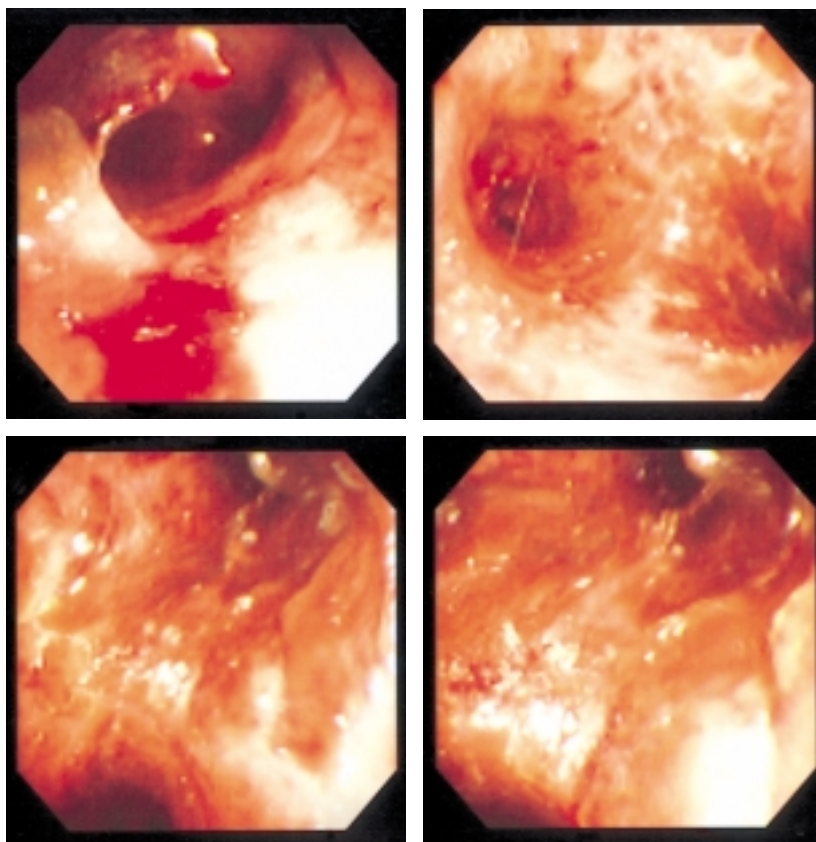


Figure 2. Images of the case patient's inner tracheobronchial tree, showing edematous and hemorrhagic tracheobronchial mucosa, indicative of hemorrhagic tracheobronchitis.

group A β -hemolytic streptococci. Its sensitivity correlates well with that of the antistreptolysin-O antibody assay. As a single test, it is superior to other single serologic tests.^{3,4} A titer of 1:100 is diagnostic of group A β -hemolytic streptococcal infection.

Clinical Associations

STSS can be associated with pharyngotonsillitis without evidence of soft-tissue involvement or skin breaks. Although purulent tracheitis has been described in association with this syndrome,⁵ an association between STSS and hemorrhagic tracheobronchitis has not been previously reported. Hemorrhagic tracheobronchitis is a serious condition owing to impairment of ventilation that might result in severe hypoxemia and respiratory failure if not promptly treated. In general, pulmonary hemorrhage may be secondary to infectious disorders (eg, viral,^{6,7} bacterial,⁸ leptospiral,^{9,10} or fungal infections^{11,12}) or may be caused by a traumatic insult.¹³ This disorder also can occur in the setting of an autoimmune disorder.¹⁴⁻¹⁶

With regard to the case patient, the hemorrhagic tracheobronchitis developed rapidly and led to hypoxemic respiratory failure requiring mechanical ventilation. Other unusual features of the case patient's clinical

Table 2. Necessary Criteria for Identifying Streptococcal Toxic Shock Syndrome

Isolation of group A β -hemolytic streptococci from either a normally sterile body site* or a nonsterile body site [†]
Evidence of severe disease, including hypotension and the presence of 2 or more clinical and/or laboratory criteria indicative of multisystem organ failure (eg, renal, pulmonary, hepatic); or hypotension and 1 such criterion together with skin erythema

*Definite case of streptococcal toxic shock syndrome.

[†]Probable case of streptococcal toxic shock syndrome.

Adapted with permission from Stevens DL. The toxic shock syndromes. *Infect Dis Clin North Am* 1996;10:727-46.

course included the moderate-to-severe obstructive ventilatory defect found on pulmonary function tests and the occurrence of left ventricular failure.¹⁷ With early administration of antibiotic agents, prompt recognition of his worsening state, and prompt administration of supportive measures, the patient recovered and was discharged home in stable condition.

CONCLUSION

Clinicians should have a high index of suspicion for STSS in febrile, hypotensive patients with early cardiopulmonary failure and hemorrhagic tracheobronchitis; they should obtain serologic and culture specimens early in the patient's clinical course. Because disease manifestations are attributable to streptococcal toxins rather than the multiplication of the microorganisms, immunomodulation by using intravenously administered immunoglobulins has been attempted with varying success.¹⁸ However, aside from antibiotic therapy, the treatment of STSS is largely supportive. HP

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