A previously healthy 17-year-old boy was transferred to our institution from a referring hospital. The child was in respiratory distress and required oxygen support. He was febrile to 40°C and complained of neck stiffness and pain, and body aches. Almost immediately upon arrival to the General Pediatrics floor, the patient showed signs of increased respiratory distress, requiring transfer to the pediatric intensive care unit (PICU) for bi-level positive airway pressure (BiPAP) support.

The patient’s symptoms began 5 days prior to admission (PTA) with an extremely severe (10/10 on verbal analogue scale) frontal headache. The headache persisted the next day (4 days PTA) when he also developed body aches, which were most prominent in his neck and back. At home that day he was febrile to 38°C. Three days PTA, the patient was seen by his primary care physician, who diagnosed him with a viral syndrome and advised ibuprofen for control of pain and fever. The following morning, the patient awoke with non-bilious, non-bloody emesis and diarrhea. This continued, along with headache, body aches, with notable neck pain, into the following morning.

One day PTA, the patient was taken to the referring hospital (RH) emergency department. There, he was judged to be dehydrated and ill appearing. The patient had no complaints of sore throat, chest pain, or abdominal pain. He had not traveled; however, he had been exposed to an uncle the week prior who had been sick for 6 months with body aches and fever. The patient had also been exposed to the family dog that had recently been started on medication for pneumonia. In the emergency room, his chest radiograph was concerning for bilateral lower lobe pneumonia, although he had no hypoxia noted at that time. A blood culture was drawn that was subsequently negative. A lumbar puncture was performed that yielded cerebrospinal fluid (CSF) with 1 white blood cell, 16 red blood cells, glucose of 69 mg/dL, and protein of 34 mg/dL. The patient was treated empirically with ceftriaxone, vancomycin, and azithromycin.

Overnight at the RH, the patient received three intravenous bolus

Case Challenge

An Unusual Cause of Respiratory Distress in a 17-Year-Old Boy

Crystal Duke, MD; Kenneth Alexander, MD; and Joseph R. Hageman, MD

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Overnight at the RH, the patient received three intravenous bolus
doses of normal saline, with resultant improvement in his hydration status. However, the following morning he developed hypoxia, for which he was given oxygen support by nasal cannula. He was also found to be febrile to 40°C. Given his escalating need for oxygen support and his continued fevers, the patient was transferred to a children’s hospital for further care and management.

Hospital Day 1: Upon arrival, the patient’s physical examination was significant for nasal flaring, retractions, and inability to speak in full sentences on 10 liters per minute of a non-rebreather oxygen mask. He had decreased breath sounds at bases bilaterally of the lungs and coarse breath sounds in remaining lung fields with intermittent crackles. Transverse leukonychia was noted. He appeared uncomfortable and diaphoretic and was transferred to the PICU. Upon arrival to the PICU, the patient was stabilized on BiPAP. A chest radiograph showed bilateral lower lobe opacities that appeared worse than those seen the previous day.

Post-transfer laboratory studies showed complete blood count with a white blood cell count of 11,700 with 82% neutrophils and 3% lymphocytes, hemoglobin of 14.6 g/dL, platelet count of 101,000, and a C-reactive protein of 229 mg/L. Prothrombin time (PT) was 17.7 seconds, partial thromboplastin time (PTT) was 36.4 seconds, and International Normalized Ratio (INR) was 1.4. A basic metabolic panel was remarkable for blood urea nitrogen of 43 g/L and a serum creatinine of 1.2 mg/dL. Total protein was 5.2 g/dL, albumin was 2.2 g/dL, and total bilirubin was 3.3 mg/dL (conjugated was 0.7 mg/dL). Complement levels for C3 were 30 mg/dL (low) and for C4 were 5 mg/dL (low).

A respiratory viral panel was negative for influenza A, influenza B, respiratory syncytial virus, human metapneumovirus, parainfluenza, rhinovirus/enterovirus, and adenovirus. Additional laboratory studies included tuberculosis (TB) interferon release test, cytomegalovirus polymerase chain reaction (CMV PCR), Epstein-Barr virus (EBV) capsid antibody, HIV antibody, Histoplasma serum/urinary antigen, Bartonella antibody, and pneumococcal urinary antigen.

The patient was diagnosed with pneumonia with moderate respiratory distress with risk of TB exposure from his uncle and concern for possible underlying illness with transverse leukonychia. He was continued on ceftriaxone and vancomycin and was started on isoniazid and rifampin. Rheumatology service and Infectious Disease service were consulted.

Hospital Day 2: Overnight, the patient’s respiratory status worsened and he required increased respiratory support; neck pain also persisted. The patient was sent for head, neck, and chest computed tomography (CT) scans to rule out lesions in head and neck and to assess his lungs. Upon return to the PICU, he was found to have increased difficulty breathing and difficulty maintaining adequate oxygen saturation values, so the decision was
made to intubate the patient. The results of the CT scans (Figures 1-3) included 1) no lymphadenopathy appreciated in the soft tissue of the neck; 2) bilateral partial thrombosis of the internal jugular veins, more extensive on the right than the left; 3) opacification of the right ethmoid air cells and sphenoid sinus (air fluid level in the maxillary sinus was consistent with acute sinusitis); 4) adjacent broken molar with a periodontal abscess; and 5) images of the lung apices showed bilateral multifocal air space opacities and mediastinal lymph nodes.

In consultation with the Infectious Diseases service, the patient began therapy with flagyl; ceftriaxone and vancomycin were continued. In consultation with the Rheumatology service, additional laboratory work, including several autoantibody studies, was done.

Hospital Day 3: The patient remained intubated with a clinical course and radiographic findings consistent with adult respiratory distress syndrome. Physical examination continued to demonstrate poor aeration in lungs. Infectious disease laboratory studies (TB interferon release test, CMV PCR, EBV capsid antibody, HIV AB, Histoplasma serum/urine antigen, Bartonella antibody, pneumococcal urine antigen) all returned negative. Laboratory studies recommended by Rheumatology service returned negative, including anti-cardiolipin, anti-extractable nuclear antigens (ENA), anti-SSA or B antibodies, vascular anti-neutrophil cytoplasmic antibodies (ANCA), anti-nuclear antibodies (ANA), and anti-DNA native double-stranded antibodies. Blood cultures from the referring hospital and from day of admission remained negative. CSF culture from the referring hospital had no growth. The patient was given anticoagulant therapy with enoxaparin to treat the internal jugular venous thromboses. The Hematology service was consulted to assess the patient for hypercoagulability. Their recommendations included laboratory studies of antithrombin III, lupus anticoagulant (double-Russell’s Viper venom time), activated protein C resistance, factor V Leiden, protein C, protein S, and homocysteine. All values returned within normal limits. Prior to starting enoxaparin, the PT and PTT had decreased to normal values.

Diagnosis:
Atypical Lemierre Syndrome

The patient described in this case study was diagnosed with atypical Lemierre syndrome (LS) based on CT findings of right periodontal abscess and right internal jugular venous thrombosis, bilateral nodular pneumonia in distribution of possible hematologic dissemination with bilateral pleural effusion, lack of other identified source of symptoms, and young adult age; however, an organism was not isolated from the blood culture and the periodontal abscess was the most likely source of infection.

DISCUSSION
Case reports and small case series of LS have appeared in the literature more frequently in the past decade; most describe preceding antecedent pharyngitis. Of note, this patient had no symptoms of pain from this abscess in the time prior to admission. His blood cultures were not positive for any pathogen, including anaerobes. Nonetheless, it has been reported that although approximately 80% of cultures grow Fusobacterium necrophorum in LS, 12.8% of reported cases are associated with sterile blood cultures.2

LS was described by Lemierre3 in 1936, and the description was based on a series of 20 patients. Lemierre asserted that the syndrome begins as an oropharyngeal infection that results in a septic thrombophlebitis. This septic thrombophlebitis then spreads via draining veins to the internal jugular vein. Given the inflammatory nature of the infection, a thrombus may form that becomes infected, and that subsequently becomes an intravascular source for the rest of the body by releasing septic emboli. The most common infected organ systems in LS are the lungs (79.8%), the liver (49%), and bones and joints (16.5%). Goldenberg et al4 also reported a thrombophilia in seven children with LS that was marked by the presence of antiphospholipid antibodies and elevations of factor VIII activity.

Our patient’s lungs were the only major organ affected. His renal function improved after hydration; his liver enzymes remained within normal range; his mild coagulopathy resolved; and he did not develop signs of bone or joint involvement. He was hospitalized for 42 days, requiring intubation for the first 16 days. Of note, he did develop pancreatitis after extubation, which resolved after he was maintained NPO and was given parenteral nutrition. The patient received 2 weeks of ceftriaxone and 4 weeks of metronidazole and vancomycin. The patient was followed by Hematology service and remained on enoxaparin for 3 months.

CONCLUSION
Lemierre syndrome is rare in the general population, with an incidence of 0.6 to 2.3 cases per million people. More than 70% of LS patients are
young adults aged 16 to 25 years. LS carries a mortality rate of 4% to 18%. LS became a “forgotten disease” from the 1950s to 1980s, probably because of the widespread use of antibiotics (penicillin) to treat pharyngitis. The apparent re-emergence of LS in the past two decades might be explained by the more restricted use of antibiotics stemming from the recognition that most cases of pharyngitis are viral in origin. Nonetheless, it is imperative for the clinician to maintain suspicion for LS if pharyngitis is associated with high fever, rigors, severe neck tenderness or pain, or persistence of sore throat for more than 3 days. In such cases, patients should be treated with a non-macrolide, beta-lactamase–resistant antibiotic with anaerobic activity while further diagnostic evaluations are undertaken. 

REFERENCES