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Lemierre Syndrome Secondary to Community-Acquired Methicillin-Resistant *Staphylococcus Aureus* Infection Associated with Cavernous Sinus Thromboses

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Abstract

Background—Lemierre's Syndrome (LS) is a highly aggressive rare disease process with a predilection for young, healthy adolescents. Often beginning with a primary cervicofacial infection, LS rapidly progresses to thrombophlebitis of the cerebral vasculature, metastatic infection, and septicemia. Untreated LS can be rapidly fatal. Thrombus within the cerebral vasculature can have devastating neurological effects. Advances in antibacterial therapy have resulted in a global decline in the incidence of LS, and clinicians may not consider LS early in the disease process. While the mortality of LS has declined, the morbidity associated with the disease has increased, particularly the neurological sequelae.

Objectives—This report will provide readers with a better understanding of the etiology, clinical presentation, evaluation methods, and appropriate treatment of LS.

Case Report—We present an atypical case of LS secondary to community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) infection progressing to bilateral cavernous sinus and ophthalmic vein thromboses with resultant binocular vision loss secondary to optic nerve and retinal ischemia.

Conclusion—This case highlights the importance of early recognition of LS in the setting of a community-acquired MRSA infection as the unifying condition in a young patient with multiple acute neurologic impairments.

Keywords

Lemierre's Syndrome; MRSA; cerebral venous thrombosis; cavernous sinus; blindness

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INTRODUCTION

Lemierre's syndrome (LS), also known as postanginal sepsis, is a relatively rare form of thrombophlebitis that is often missed in the early stages of infection given its predilection for previously healthy adolescents and young adults [1]. Classically, a cervicofacial infection focus with subsequent extension to the parapharyngeal space produces thrombophlebitis of the internal jugular vein, septicemia, and multiple metastatic infections, particularly involving the lungs [2, 3]. *Fusobacterium necrophorum*, a gram-negative bacterium, is isolated in 70% of Lemierre's cases, however, there have been an increasing number of reports of LS secondary to methicillin-resistant *Staphylococcus aureus* (MRSA) [4–10]. Extension of jugular thromboses to include the superior cerebral venous system has been described, although thrombosis of the cavernous sinus with ophthalmic complications are exceedingly rare [3, 11–13]. We present a unique case of Lemierre's syndrome presenting to our Emergency Department (ED) that was secondary to a community-acquired MRSA infection, with cerebral venous thrombosis progressing to bilateral ophthalmic vein occlusion and binocular vision loss secondary to optic nerve ischemia.

CASE REPORT

A previously healthy 18 year-old man presented to our Emergency Department (ED) with progressive visual loss and unilateral right-sided weakness in his upper and lower extremities. Two weeks prior, the patient had sustained a collision during football practice involving his right shoulder, although he had continued to practice up until the day of admission. One week prior to presentation, the patient had severe neck pain, nausea, vomiting, and right sided weakness so severe that he had fallen, hitting the left side of his face and causing unilateral periorbital edema. During this time, he denied any fevers, chills, rashes, a sore throat, exposure to sick contacts, sexual activity, or intravenous drug use. He did endorse a one day history of urinary frequency and hesitancy. On the day of admission, the patient was evaluated at an outpatient orthopedics clinic for his football injury occurring 2 weeks prior. Due to his clinical worsening, a traumatic progressive spinal cord injury was presumed and the patient was transferred by ambulance to our Shock Trauma Emergency Department.

Upon initial examination, the patient was afebrile (97.2°F) with a pulse rate of 105 beats/min, blood pressure of 135/75 mm Hg, respiratory rate of 16 breaths/min, and SpO₂ of >93%. Significant left periorbital edema was noted on examination with surrounding erythema and unilateral yellow discharge; however, over the course of several hours the swelling extended to include the right eye. Coarse lung sounds were appreciated bilaterally, although the rest of the pulmonary, cardiac, abdominal, and extremity examinations were within normal limits. Neurologically the patient remained cooperative, alert, and orientated to person, place, and time with clear speech and no elements of aphasia. The pupils were equally miotic and non-reactive to light; the patient could not discriminate between light and dark in either eye. The patient was unable to move his eyes in any direction and a "doll's eye" examination was deferred due to potential cervical spine instability. Cranial nerves V, VII–XII were intact. Motor examination revealed normal bulk and tone with no evidence of tremor or other non-purposeful movements. An obvious right-sided hemiparesis was noted with motor strength testing demonstrating bilateral weakness; right arm at 1/5, right leg at 1/5, left arm at 4/5, and left leg at 3/5. Reflexes were 1+ and symmetric throughout with muted Babinski reflexes bilaterally. Sensation was intact throughout and no extinction was evident. Coordination and gait were not testable secondary to weakness; however, no obvious limb ataxia was noted.

Initial laboratory findings were significant for a white blood cell (WBC) count of 23.9 with a 53% bandemia; the patient remained afebrile throughout the ED course. Urinalysis showed leukocyte esterase and nitrites, large bacteria and 10–25 WBCs. Computed tomography (CT) imaging of the head (Figure 1) was performed. This showed left orbital proptosis with associated fat stranding in the preseptal region of the left orbit (arrow), suggestive of an infectious or inflammatory process. There were no intracranial abnormalities. No pathology was noted in the cervical spine or surrounding areas at that time. The patient was placed on Ciprofloxacin for a presumed urinary tract infection and on Azithromycin for presumed community acquired pneumonia.

While in the ED, the patient developed an acute change in mental status that necessitated intubation. Worsening bilateral periorbital edema also became evident; however, a repeat head CT scan was unchanged from the initial study. Given the leukocytosis and acute change in mental status, a lumbar puncture was performed, revealing an elevated opening pressure of 47 cm H₂O; the cerebral spinal fluid was free of organisms upon cytological examination, with 3 white blood cells. Immediately following lumbar puncture, the patient developed anisocoria, prompting a third head CT scan that was again unchanged.

Cerebral venous thrombosis (CVT) was suspected; cerebral magnetic resonance venography (MRV) imaging (Figure 2) demonstrated thromboses of the right internal jugular (arrows) with extension into the right sigmoid and transverse sinuses. Bilateral cavernous sinus thromboses were also noted with potential extension into the ophthalmic veins. Cervical spine magnetic resonance imaging (Figure 3) demonstrated a large retropharyngeal abscess extending from C2 to C6 with corresponding vertebral changes suggestive of osteomyelitis; a corresponding epidural fluid collection without cord compression also could be seen. Also of note, a signal abnormality was noted in the spinal cord at the C6 level. The right internal carotid artery (ICA) was narrowed as it coursed through the retropharyngeal fluid collection. Multiple bilateral pulmonary nodules with cavitations were found on chest CT imaging (Figure 4) suggestive of septic emboli. A bedside transesophageal echocardiogram was performed, demonstrating no valvular vegetation. Neurosurgery was consulted regarding the epidural fluid collection, however, the patient was not deemed a surgical candidate at that time.

Given the significant central venous thromboses seen on radiographic studies, intravenous heparin was administered with a target aPTT of 100–120 seconds to prevent further extension of the thrombus. Surgical incision and drainage of the retropharyngeal phlegmon was attempted by otorhinolaryngology but was unsuccessful due to the location of the abscess and concern for carotid artery injury, although a small amount of aspirate was attained. Per Infectious Disease consultation, broad-spectrum antibacterial therapy with central nervous system coverage was initiated including clindamycin, vancomycin, piperacillin-tazobactam, and acyclovir. Blood and urine cultures subsequently demonstrated a MRSA bacteremia, with cultures of the sputum, eye discharge, and the retropharyngeal phlegmon aspirate also demonstrating MRSA infection. Upon the results of organism antibacterial sensitivity testing, the patient was placed on vancomycin, rifampin, metronidazole, and gentamicin; acyclovir was discontinued after spinal fluid Herpes Simplex Virus polymerase chain reaction returned negative.

The patient was admitted to the Intensive Care Unit for several weeks. A short course of steroids given early in the admission for concern of cervical cord edema resulted in a mild improvement in right-sided motor strength, but no improvement in infection status. Follow-up magnetic resonance imaging (MRI) demonstrated ischemic infarcts of the bilateral optic nerves and continued CVT of the bilateral cavernous sinuses despite improving infection status. Ophthalmologic assessment attributed the binocular blindness to progressive retinal

ischemia secondary to retinal vein thrombosis. Over the course of hospitalization, the patient reported sporadic occasions when he was able to perceive light. Electroretinogram and visual evoked potentials findings were consistent with injury to the retinas and optic nerves bilaterally; the possibility of the patient regaining sight was felt to be negligible. The patient was eventually transferred to an acute rehabilitation facility for further rehabilitation.

Approximately two months post-hospital discharge the patient was seen at outpatient follow-up. He was in good spirits, although unfortunately he had not regained visual function on examination, with no pupillary reaction to light, no light perception, or perception of motion as tested by hand waving. The patient reported some subjective accounts of a transient ability to see out a window, and at times, the television. Extraocular movements were full with some bilateral ptosis persisting. The remainder of the cranial nerves were normal. He continued to have right-sided weakness with 4/5 strength in the upper extremity with the wrist flexors and extensors most significantly affected; the right lower extremity had 4/5 strength. No follow-up imaging was obtained.

DISCUSSION

Andre Lemierre, a French microbiologist, was not the first to describe the disease process that now bears his name. Nonetheless, he provided the definitive characterization of Lemierre's syndrome (LS) in a 1936 case series profiling 20 patients with widespread septicemia and rapidly progressive thrombophlebitis following an oropharyngeal infection [14]. Subsequent investigations identified the gram negative anaerobic bacterium *Fusobacterium necrophorum*, a part of the normal oral, gastrointestinal, and female genital tract flora, as the most common causative organism of LS [15]. Prior to the advent of antibiotics, LS was associated with frighteningly high mortality, with death quickly following diagnosis within 1–2 weeks [16]. However, what became known as a sure death sentence in the pre-antibiotic era soon became a vanishing disease with the administration of penicillin for head and neck infections [16]. Rates of LS have since remained low, so clinicians may not consider LS in the initial differential diagnosis. However, consistent with our case, reports of LS secondary to MRSA infection appear to be on the rise, and are of particular concern given the aggressive nature of such infections and the limited treatment options available [5, 7–10, 17, 18].

While the mortality of LS remains high, survival is increased when infections are recognized quickly and broad spectrum antibiotics are started early in the disease process. Recent cases have varied presentations, with some including neurological impairment, which is consistent with our case [13]. Classically, the neurological impairments associated with LS involve cranial nerve deficits associated with swallowing difficulties due to the impingement of the glossopharyngeal (CN9), vagus (CN10), and hypoglossal (CN12) nerves by the retropharyngeal abscess [15]. The abscess typically induces both a local (jugular vein) and systemic coagulopathy leading to progressive cerebral venous thrombosis, often causing impaired mentation, headaches, visual loss, and seizures [3]. Progression of the CVT, as in the present case, may cause cavernous sinus thrombosis leading to further cranial nerve impairment and presenting with eye movement abnormalities (CN 3,4,6) and visual loss (CN2).

Hudgins et al. discusses the narrowing of the ICA (as seen in our patient) ipsilateral to retropharyngeal abscess in a patient with CVT associated with LS [19]. These findings emphasize the importance of being cognizant of the location of the internal carotid arteries if a needle aspiration is being considered to drain a retropharyngeal abscess or to identify the causative bacterium. Other cases in the literature describe associated ischemic infarcts within the small branches of the anterior cerebral artery (ACA) and middle cerebral artery

(MCA), consistent with a more proximal ipsilateral embolic ICA source. A few cases of septic central nervous system (CNS) emboli also have been reported [3, 19, 20]. Such findings highlight the importance of early CNS imaging (i.e., brain, spine, neck, arterial, venous) in the course of this illness; early diagnosis of the abscess and potential sequelae, including cerebral vascular infarction, allow the patient to be treated optimally.

As survival rates of LS rise, the morbidity of the disease becomes of particular concern, particularly the neurological sequelae. As in our case, LS can be associated with significant thromboses of the cerebral venous system, which can lead to venous infarction and cerebral edema [3, 11, 12, 21]. Extension of cavernous sinus thromboses to the bilateral ophthalmic veins with ensuing compromise of the optic nerves is exceedingly rare, but can have devastating effects on the surviving individual [22].

CONCLUSION

In the antibiotic era, the incidence of LS has been so low that it has been termed the “forgotten disease” [23–25]. This appears to be changing as more cases are being reported secondary to MRSA infection [8–10, 17, 18, 26]. Regardless of the incidence of LS, the syndrome represents an extraordinarily aggressive infection in both morbidity and mortality. As described, Lemierre’s Syndrome can present as a constellation of pharyngeal, vascular, pulmonary, neurological, and ocular findings. Early recognition and aggressive treatment may not only improve survival, but also may limit the morbidity associated with this condition. This report highlights the importance of early recognition of LS and a community-acquired MRSA infection as the unifying condition in a young patient with multiple acute neurologic impairments.

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Figure 1. Non-enhanced CT scan demonstrating fat stranding on the pre-septal space of the left orbital region (arrows), suggestive of an infectious or inflammatory process. Bilateral proptosis is also evident.

Figure 2. MRV of the head, without contrast (time of flight technique). This tri-dimensional reconstruction shows a lack of venous flow within the right sigmoid (A) and part of the transverse sinuses as well as in the proximal internal jugular vein (B), as shown by the arrows.

Figure 3.

MRI of the cervical spine. “A” is T2 sagittal acquisition; “B” is T1 post-gadolinium sagittal acquisition. White open arrow in “A” shows phlegmon or abscess within the prevertebral space between C1 and C6. White long arrow in “A” shows involvement of C6 vertebral body, likely representing osteomyelitis. White short arrow in “A” shows signal abnormality in the spinal cord, representing edema. White arrows in “B” show enhancement of the posterior aspect of the cervical epidural space between C4 and T2.

Figure 4. Chest CT scan demonstrating multiple bilateral pulmonary nodules with cavitations suggestive of septic emboli.