



## Early Diagnosis and Treatment of Lemierre Syndrome in a Neutropenic Cancer Patient

Ko-Chiang Hsu, Shih-Hung Tsai, Shi-Jye Chu, and Chin-Wang Hsu\*

*Department of Emergency Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, Republic of China.*

Lemierre syndrome (LS) is a rare but potentially life-threatening disease. It originates from an oropharyngeal infection of the internal jugular vein (IJV) leading to thrombophlebitis and metastatic infection. We report a 42-year-old woman with gastric adenocarcinoma presenting with febrile neutropenia, sore throat, and a tender induration in the left neck. Early LS was diagnosed by finding thrombophlebitis of the IJV following oropharyngeal infection but without bacteremia. Antibiotic treatment led to freedom from metastatic infection. Physicians should suspect LS after identifying the “red-flag” signs, i.e., tender induration of the unilateral neck following an oropharyngeal infection. A prompt diagnosis can be made by finding thrombophlebitis of the IJV. Early antibiotic therapy may lead to favorable clinical outcomes.

**Key words:** Lemierre syndrome; Oropharyngeal infection; Thrombophlebitis

### INTRODUCTION

Lemierre syndrome (LS) is thrombophlebitis of the internal jugular vein (IJV) following an oropharyngeal infection. If left untreated, complications such as disseminated metastatic infections of the lung or liver can develop. The most common cause is *Fusobacterium necrophorum*, an anaerobic Gram-negative bacillus that often leads to septic emboli. Morbidity and mortality often occur because of the lack of familiarity with this syndrome<sup>1</sup>. Here we present a neutropenic woman who developed a painful induration on the neck following an oropharyngeal infection. Thrombophlebitis of the IJV with inflammatory changes of the adjacent soft tissue was demonstrated by contrast-enhanced computed tomography (CECT). She had a favorable clinical outcome because of early recognition and prompt antibiotic therapy.

### CASE REPORT

A 42-year-old woman underwent chemotherapy with tegafur and uracil for adenocarcinoma of the stomach 10 days before coming to our attention. She reported a sore throat 3 days after the chemotherapy. Acute pharyngotonsillitis was diagnosed. She visited the emergency department (ED) because of fever, progressive worsening of odynophagia, and pain in the left neck for 2 days. On presentation, she was alert, with a blood pressure of 99/72 mmHg, a pulse of 112 beats per minute, and a body temperature of 38.6 °C. She had an inflamed left tonsil and a severe tender induration on the left side of her neck (Figure 1). Otherwise, the examination was normal. Laboratory tests revealed an absolute neutrophil count of 990/mm<sup>3</sup> and an elevated C-reactive protein up to 4.16 mg/dL (< 0.5 mg/dL). The chest radiography was normal. CECT of the neck disclosed fat stranding over the left carotid space and the adjacent soft tissue and a filling defect in the left IJV, indicating thrombophlebitis (Figure 2). CECT of the chest and upper abdomen showed no pulmonary or liver septic emboli.

Early-stage LS was tentatively diagnosed from the oropharyngeal infection complicated by IJV thrombophlebitis in the absence of metastatic septic emboli. We began piperacillin/tazobactam treatment. The patient was admitted to the hospital, and subsequent blood cultures yielded no microorganisms. We administered intravenous ampicillin/sulbactam for 4 weeks during her recovery from the neutropenia. Subsequent ultrasounds of the neck showed no thrombus in the IJV. She completed an additional 1-

Received: November 29, 2007; Revised: February 4, 2008;  
Accepted: March 11, 2008

\*Corresponding author: Chin-Wang Hsu, Department of Emergency Medicine, Tri-Service General Hospital, National Defense Medical Center, 325, Sec. 2, Cheng-gong Rd., Taipei 114, Taiwan, Republic of China. Tel: 886-2-8792-7018; Fax: 886-2-8792-7034; E-mail: wan11119@gmail.com (C.-W. Hsu)

The authors declare no conflict of interests.



Fig. 1 Photograph of the left neck. There is a swollen induration in the left neck from the left mandible angle to the supra-clavicle region (*Asterisk*).

week course of oral amoxicillin/clavulanic acid. The patient had no disseminated metastatic infections and recovered completely after 6 weeks of antibiotic therapy.

## DISCUSSION

We report a febrile neutropenic cancer patient who had early-stage LS. She had no bacteremia and was free of disseminated metastatic infections. Despite the neutropenia, the patient had a similar indolent clinical course to immunocompetent individuals with LS. ED physicians should be mindful of any tender induration of the neck following an oropharyngeal infection for potential LS. A timely administration of antibiotics may prevent ominous outcomes from disseminated metastatic infections.

In 1936, Lemierre wrote a comprehensive article about a postanginal sepsis that had a three-stage clinical course<sup>2</sup>. The first stage depends on the primary site of infection, usually the pharynx, tonsils, ears, or other sites on the face. A sore throat and fever are the most common initial symptoms. The second stage is the invasion of the lateral pharyngeal space and thrombophlebitis of the IJV through the lymphatic vessels or peritonsillar veins. The final stage is the propagation into metastatic infections, mainly in the lungs. Morbidity or mortality can occur if accurate diagnosis and prompt management are delayed.

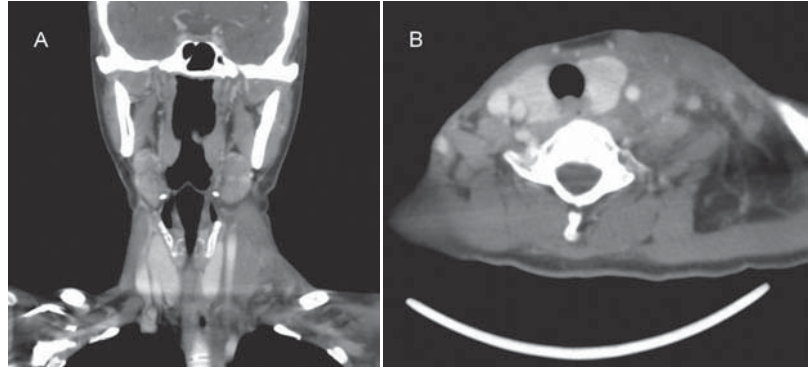


Fig. 2 Contrast-enhanced computed tomography of the neck with coronal multiplanar reformation (A), axial view (B). There is a central low density (non-enhanced filling defect of the internal jugular vein) which indicating thrombophlebitis of the internal jugular vein (*Asterisk*) and marked swelling with fat stranding over the adjacent left neck. (*T*: thyroid tissue, *A*: the right internal carotid artery, *V*: the right internal jugular vein).

The only treatment for LS before the advent of antibiotics was ligation of the IJV on the affected side to prevent septicemic spread. The case-mortality rate was 32-90% at that time<sup>2</sup>. Today, this procedure is rarely necessary except for patients with uncontrolled sepsis and repeated septic pulmonary emboli<sup>3</sup>. Surgical drainage of purulent collection (empyema, septic arthritis, soft-tissue abscess) may be needed along with antibiotic therapy in these cases. Some authors have suggested the use of intravenous heparin for treating thrombophlebitis<sup>4</sup>, but in one review, the outcome was unchanged by anticoagulants in most LS patients studied<sup>5</sup>. Currently, the ideal treatment is beta-lactam/beta-lactamase inhibitors for up to 6 weeks<sup>6</sup>. Even with antibiotic therapy and early recognition, recent literature still suggests that LS is a potentially life-threatening disease but with a decreased mortality rate of 5-10%<sup>7</sup>. There are still many reports of cases that lacked prompt diagnosis because of unusual presentations of LS, resulting in cavernous sinus thrombosis, carotid thrombosis, cerebral abscess, abdomen pain with septic shock, and multiple sites of metastatic infections<sup>8-10</sup>. The diagnosis of late-stage LS was based on thrombophlebitis of the IJV by CECT or the presence of *F. necrophorum* in blood cultures. Most patients died of sepsis or metastatic complications of LS if not diagnosed early and treated promptly.

Some patients with LS may ignore the oropharyngeal symptoms until the tender induration of the unilateral neck begin. Misinterpretation of these “red-flag” signs as a lymphadenopathy or soft tissue infection can lead to

progression and dissemination of the infection. Imaging studies including ultrasonography, magnetic resonance imaging, or CECT of the neck should be performed when the neck symptoms appear in order to find thrombophlebitis of the IJV. Imaging findings often precede blood culture results; therefore, ED physicians and radiologists play a crucial role in early recognition and diagnosis. In addition, a thorough evaluation should be performed to detect the distant metastatic infectious foci.

Although *F. necrophorum*, an anaerobic Gram-negative bacillus, is the most common organism implicated in LS, Hagelskjaer et al. reported that 67% of patients yielded no growth in blood cultures<sup>3,11</sup>. In addition, Sherer et al. reported two cases of “nonsepticemic” LS with thrombophlebitis of the IJV secondary to an oropharyngeal infection without any pathogen in the blood culture<sup>12</sup>. We have established the diagnosis of LS before the development of bacteremia and subsequent metastatic infection. However, with the concern of intravascular bacterial infection, we believe that an adequate time course of antibiotic treatment is still warranted even in the absence of a microbiologic diagnosis. Moreover, complications of metastatic infections such as pulmonary emboli were not found after prompt antibiotic therapy. We concluded that our case was either “nonsepticemic” LS or was successfully prevented from metastatic infections by timely antibiotic administration.

In conclusion, patients presenting with “red-flag” signs, including tender induration of the unilateral neck and thrombophlebitis of the IJV, should be considered as potential LS cases. Early investigation with CECT and prompt antibiotic treatment is necessary to prevent disseminated metastatic infections.

## REFERENCES

1. Screaton NJ, Ravenel JG, Lehner PJ, Heitzman ER, Flower CD. Lemierre syndrome: forgotten but not extinct--report of four cases. *Radiology* 1999;213:369-74.
2. Lemierre A. On certain septicemias due to anaerobic organisms. *Lancet* 1936;2:701-3.
3. Sinave CP, Hardy GJ, Fardy PW. The Lemierre syndrome: suppurative thrombophlebitis of the internal jugular vein secondary to oropharyngeal infection. *Medicine (Baltimore)* 1989;68:85-94.
4. Moore-Gillon J, Lee TH, Eykyn SJ, Phillips I. Necrobacillosis: a forgotten disease. *British medical journal (Clinical research ed)* 1984;288:1526-7.
5. Williams A, Nagy M, Wingate J, Bailey L, Wax M. Lemierre syndrome: a complication of acute pharyngitis. *International journal of pediatric otorhinolaryngology* 1998;45:51-7.
6. Lin CH, Chiu MH, Huang CH. Lemierre's Syndrome with *Fusobacterium Necrophorum* Bacteremia: A Report of Two Cases in Taiwan. *Journal of Internal Medicine of Taiwan* 2007;18:365-70.
7. Hagelskjaer Kristensen L, Prag J. Human necrobacillosis, with emphasis on Lemierre's syndrome. *Clin Infect Dis* 2000;31:524-32.
8. Brown LM, Wallwork B. Lemierre's - the sinister sore throat. *J Laryngol Otol* 2007;1-3.
9. Maalikjy Akkawi N, Borroni B, Magoni M, Vignolo LA, Padovani A. Lemierre's syndrome complicated by carotid thrombosis. *Neurol Sci* 2001;22:403-4.
10. Zapor M, Fraser SL. A 47-year-old man with a sore throat. *Cleve Clin J Med* 2001;68:605-6.
11. Hagelskjaer LH, Prag J, Malczynski J, Kristensen JH. Incidence and clinical epidemiology of necrobacillosis, including Lemierre's syndrome, in Denmark 1990-1995. *Eur J Clin Microbiol Infect Dis* 1998;17:561-5.
12. Sherer Y, Mishal J, Leibovici O. Early antibiotic treatment may prevent complete development of Lemierre's syndrome: experience from 2 cases. *Scandinavian journal of infectious diseases* 2000;32:706-7.

