Lemierre's Syndrome

Yun-Chiu Yang, Kwan-Han Shian, Chi-Der Chiang

Lemierre's syndrome is a recognized but infrequently seen complication of acute oropharyngitis. It is characterized by an acute oropharyngeal infection followed by thrombophlebitis of the internal jugular vein and disseminated metastatic infections, most frequently involving the lungs with septic emboli. The main pathogen is *Fusobacterium necrophorum*, an obligate anaerobic, pleomorphic, Gram-negative rod. We report the case of a young patient with a typical presentation of Lemierre's syndrome. Prompt recognition and appropriate antibiotic treatment resulted in complete recovery. ***(Thorac Med 2003; 18: 75-79)***

Key words: Lemierre's syndrome, *Fusobacterium necrophorum*, oropharyngitis, thrombophlebitis

Introduction

Lemierre's syndrome is a rare but still life-threatening disease up to today. We describe a confirmed case of *Fusobacterium necrophorum* bacteremia with widespread pulmonary involvement. A typical image study of internal jugular vein thrombophlebitis was also observed. A high index of suspicion is most important with this disease entity.

Case Report

A previously healthy 20-year-old male presented to the emergency department with a 3-day history of sore throat, fever, and chills.

On admission, he appeared acutely unwell; his temperature was 38.0°C, respiratory rate was 28 breaths/min, heart rate was 138 beats/min, and blood pressure was 98/47 mmHg. The throat examination revealed a swollen tonsil, and decreased breathing sounds throughout the lungs, which were clear to auscultation. The results of the hematological and biochemical investigations were as follows: hemoglobin 10.1g/dl, white blood cell count 40,600/cm^3 (neutrophils 91%; lymphocytes 7%), platelet count 223,000/mm^3, C-reactive protein 28.8 mg/L, GOT 24, GPT 21, LDH 191, ALP 235, BUN 18, creatinine 0.9, direct bilirubin 1.5 mg/dl, and total bilirubin 3.3mg/dl.

A plain chest film showed multiple ill-defined patchy infiltrates in the bilateral lung fields (Figure 1); pulmonary septic embolism was the first impression. Cultures of body fluid specimens were obtained, and empiric intravenous antibiotics (piperacillin-tazobactam and amikacin) were initiated for presumed Gram-negative sepsis.

Series examinations, including echocardiography, abdominal sonography, and computed tomography (CT) of the neck, were performed in order to uncover the origin of the septic emboli.

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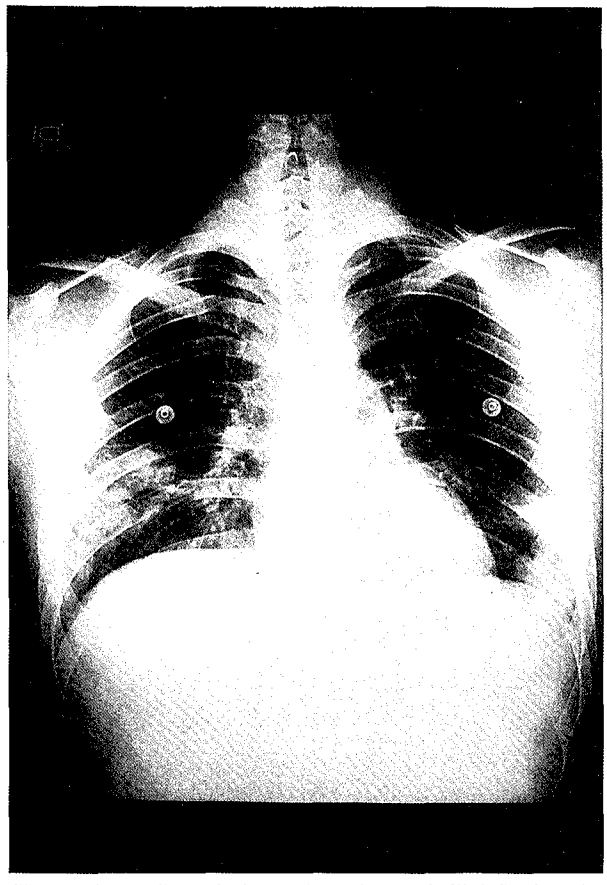

Fig. 1. Chest radiograph shows bilateral multiple ill-defined patchy infiltrates consistent with pulmonary septic emboli.

The 2-dimensional echocardiography showed mild to moderate aortic regurgitation and mild tricuspid regurgitation with a pressure gradient of 36.5 mmHg; there was no valvular vegetation. Abdominal sonography showed no evidence of abscess or any abnormality of the solid organs. A contrast-enhanced CT of the neck demonstrated a filling defect in the left internal jugular vein (Figure 2), consistent with thrombophlebitis.

Three days later, an anaerobic organism was isolated from the blood and identified as *Fusobacterium necrophorum*. The drug sensitivity test disclosed that the pathogen was sensitive to penicillin, clindamycin, ampicillin-salbactam, metronidazole, cefmetazone, piperacillin-tazobactm, and imipenem. The intravenous antibiotic therapy was continued to a total course of 3 weeks, and the patient was discharged home. He recovered well and had no complications.

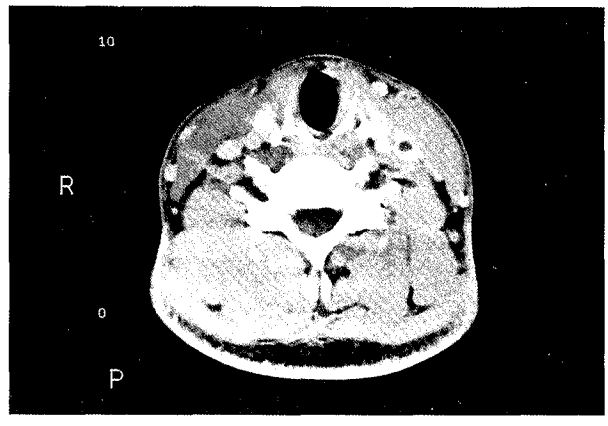

Fig. 2. Contrast-enhanced computed tomography of the neck demonstrates a filling defect of the left internal jugular vein, consistent with thrombophlebitis.

Discussion

In 1936, Lemierre reviewed and analyzed the common findings among 20 cases with similar presentations and disease course, and described a constellation of symptoms and signs, which he called "postanginal septicemia" [1].

Lemierre's syndrome is a rare infection, and is referred to as "the forgotten disease" [2-3]. The diagnosis was often made late because most physicians did not know the characteristic syndrome, and because there was poor communication between the microbiologists and the clinicians [2]. In a recent retrospective study in Denmark [4], an incidence of only 0.8 case per million per year was found, but there was also an increased tendency during the 6 years they studied. The study proposed that the increased incidence may have been due to improved anaerobic blood culture techniques and better final identifications of *Fusobacterium spp.* during the study period [4]. Investigators have also suggested that the "reappearance" of Lemierre's syndrome during the last few decades is due to a more restricted use of penicillin in the treatment of tonsillitis [5]. However, the incidence is certainly higher because there were suspected cases of *Fusobacterium spp,* that were never fully identified, and mild cases may have been treated successfully without hospitalization [4, 6].

In its clinical aspect, the disease primarily affects healthy teenagers and young adults, the oropharynx is often the primary site of infection, and the interval between the oropharyngeal infection and the onset of septicemia is usually less than a week. The laboratory data disclose leukocytosis and a raised C-reactive protein level; subclinical hyperbilirubinemia and a slight elevation of liver enzyme levels are also found, and have been hypothesized to be the toxic effect to the hepatobiliary system of the circulating bacterial endotoxins. However, Lemierre's syndrome is primarily a clinical diagnosis, with clinical symptoms including fever, oropharyngeal pain, neck swelling, arthralgia, and pulmonary symptoms.

When the infection extends from the oropharynx to the lateral pharyngeal space and produces thrombophlebitis of the internal jugular vein (IJV), the clinical symptoms and signs of pain and swelling at the angle of the mandible and along the anterior border of the sternocleidomastoid muscle, trismus, and dysphagia will then appear. But, the local findings can be subtle or absent [5-7]. Moreno *et al.* found that septic thrombophlebitis was detected in 36% of patients [8]. The thrombophlebitis of the internal jugular vein can be easily diagnosed by ultrasonography, computerized tomography, or magnetic resonance angiography of the neck [9]. As a consequence of thrombophlebitis, septic embolism develops; the most common site of the embolic disease is the lung, presenting as multiple bilateral alveolar infiltrates, frequently associated with pleural effusion, empyema, and pulmonary abscesses. However, involvement of the joint, bones, meninges, and liver has also been described [5,10]. Pleuropulmonary involvement was reported in up to 85% of patients in a review by Hagelskjaer *et al* [6]; Sinave *et al* reported involvement in 97% of cases in their series [2]; and in Lemierre's original report, pulmonary septic emboli were present in all cases [1].

Fusobacterium necrophorum is the most common pathogen isolated in the majority of cases with Lemierre's syndrome. It has an unusual ability to invade as a primary pathogen in previously healthy people and cause oropharyngeal infections such as tonsillitis, pharyngitis, parotitis, otitis media and odontogenic infection. This characteristic feature of *F. necrophorum* that makes it different from other anaerobic bacteria is related to its toxins [6]. The organism can further extend to the parapharyngeal space, causing the complications of internal jugular vein thrombophlebitis, anaerobic bacteremias, multiple metastatic infections, and severe sepsis. It is not known why *F. necrophorum* becomes invasive and penetrates the mucosa. A reduced host defense in the pharyngeal mucosa due to viral or bacterial pharyngitis may play a role, with infectious mononucleosis being the most frequently suspected organism [6-7,10]. Epstein-Barr virus infection is thought to induce immunosuppression, and it may also predipose to a bacterial superinfection in Lemierre's syndrome [6].

The mainstay of treatment is intravenous antibiotics directed at anaerobic microbes. Most authors recommend a combined treatment with high-dose penicillin and metronidazole, or an alternative monotherapy with clindamycin for 2-6 weeks. *F. necrophorum* is resistant to aztreonam and trimethoprim-sulfamethoxazole and aminoglycosides [4,6,8]. Anticoagulant therapy is not advised because of the risk of extending the infection [8-9]. Surgical ligation or excision of the thrombophlebitic internal jugular vein to control sepsis and repeated septic emboli was frequently done in the pre-antibiotic era, but this procedure is rarely needed today [3,7,11].

Lemierre's syndrome was associated with a case-mortality rate of 32-90% in the pre-antibiotic era [5,8]. It is still a potentially life threatening disease, with a reported mortality rate of 4-18% nowadays [2,4,6].

Conclusion

Lemierre's syndrome is still seen today, but it is recognized infrequently at initial presentation. With a high degree of clinical suspicion, it is easy

to make an early diagnosis. Computed tomography of the neck and color doppler ultrasonography are suggested to be useful imaging modalities to detect internal jugular vein thrombophlebitis. *Fusobacterium necrophorum* is the most common anaerobe in sepsis originating from the oropharynx, so whenever an anaerobic bacterium is found in such a patient, *F. necrophorum* should immediately be suspected. Prompt use of antibiotic therapy offers a favorable outcome.

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Lemierre's 症候群

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Lemierre's 症候群是一種不常見的急性口咽炎和繼發的併發症狀。主要的特徵是急性口咽炎和伴隨發生的內頸靜脈血栓靜脈炎以及散佈的轉移性感染，通常侵犯肺部。引發此疾病的主要致病菌是壞死細梭桿菌，是一種絕對厭氧且多形性的格蘭氏陰性桿菌。本文報導一位年輕男性患者，以典型的 Lemierre's 症候表現，經早期的診斷及適當的抗生素治療後完全復原。 ***(胸腔醫學 2003; 18: 75-79)***

關鍵詞：Lemierre's 症候群，壞死細梭桿菌，口咽炎，血栓靜脈炎

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