Pulmonary embolism and internal jugular vein thrombosis as evocative clues of Lemierre’s syndrome: A case report and review of the literature

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**Abstract**
Lemierre’s syndrome (LS) is an uncommon condition with oropharyngeal infections, internal jugular vein thrombosis, and systemic metastatic septic embolization as the main features. Fusobacterium species, a group of strictly anaerobic Gram negative rod shaped bacteria, are advocated to be the main pathogen involved. We report a case of LS complicated by pulmonary embolism and pulmonary septic embolism that mimicked a neoplastic lung condition. A Medline search revealed 173 case reports of LS associated with internal jugular vein thrombosis that documented the type of microorganism. Data confirmed high prevalence in young males with Gram negative infections (83.2%). Pulmonary embolism was reported in 8.7% of cases mainly described in subjects with Gram positive infections (OR = 9.786; 95%CI: 2.577-37.168, \( P = 0.001 \)), independently of age and gender. Only four fatal cases were reported. LS is an uncommon condition that could be complicated by pulmonary embolism, especially in subjects with Gram positive infections.

**Key words:** Lemierre’s syndrome; Pulmonary embolism; Fusobacterium species; Internal jugular vein thrombosis; Systemic septic embolization

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a neoplastic lung condition. The case was related to previously reported cases in Medline that documented the type of microorganism. We associated PE with LS due to Gram positive infections.

De Giorgi A, Fabbian F, Molino C, Misurati E, Tiseo R, Parisi C, Boari B, Manfredini R. Pulmonary embolism and internal jugular vein thrombosis as evocative clues of Lemierre’s syndrome: A case report and review of the literature. World J Clin Cases 2017; 5(3): 112-118 Available from: URL: http://www.wjgnet.com/2307-8960/full/v5/i3/112.htm DOI: http://dx.doi.org/10.12998/wjcc.v5.i3.112

INTRODUCTION

Lemierre’s syndrome (LS) is an uncommon condition characterized mainly by oropharyngeal infections complicated with internal jugular vein (IJV) thrombosis and subsequently metastatic infections secondary to septic emboli. This syndrome was first reported by André Lemierre in 1936 in a personal experience describing 20 patients[3].

Primary sites of infection in these patients are the tonsils (palatine tonsils or peritonsillar tissue), pharynx and lower respiratory tract[5]. Fusobacterium represents the most common microorganism related to this syndrome (about 90% of cases). Fusobacterium spp. are strictly anaerobic Gram-negative rod shaped bacteria, mainly isolated from the oral cavity[3]. The mechanisms underlying virulent clinical conditions are not known, and Fusobacterium is considered a rare cause of head and neck infections[4].

After local proliferation, neck infection is associated with IJV thrombosis and then hematogenous spread to other peripheral organs could happen such as the lung, joints, soft tissue, abdominal parenchyma, and central nervous system[6].

We report a case of LS complicated by pulmonary embolism and pulmonary septic emboli after IJV thrombosis.

CASE REPORT

A 53-year-old man presented to emergency department because of a history of occipital headache, malaise, hacking cough, chest pain exacerbated by inspiration, and fever for one month. He had a history of smoking, hypertension, hyperuricemia, and gastro-esophageal reflux. His general practitioner treated him unsuccessfully with clarithromycin and ceftriaxone. Blood chemistry panel showed increasing inflammatory indexes, such as white blood cells (WBC) 16.560/mm³, C-reactive protein (CRP) 13.60 mg/dL, and erythrocyte sedimentation rate (ESR) 70 mm. Chest X-ray did not show parenchymal lesions, and either spinal column X-ray or encephalic nuclear magnetic resonance (NMR) was unremarkable.

On admission, the physical examination was unremarkable except that pharyngeal and tonsil hyperemia was detected. He was diagnosed with chronic tonsillitis by an otorhinolaryngologist. Pharyngeal packing with cultural exam identified saprophytic flora. Levofloxacin and nebulizer therapies were prescribed.

Further laboratory tests showed WBC = 11.070/mm³, CRP = 3.70 mg/dL, ESR = 53 mm, fibrinogen = 706 mg/dL, and D-dimer = 773 ng/mL. Immunoglobulin-A was 559 mg/dL. Chest X-ray showed parenchymal and pulmonary consolidation associated with pleural effusion. Bronchoscopy with broncho-alveolar lavage (BAL) including microbiology and cytology was negative.

A chest computed tomography (CT) scan showed left pleural effusion, contralateral sub-pleural fibrosis and, above all, an important oval lesion at the level of medial right lobe measuring 25.7 mm with central cavitation. Further three lesions of 5-6 mm at the superior right lobe, and enlargement of pulmonary hilar lymph nodes were evident (the largest was 13.4 mm). Since these images were suggestive of pulmonary neoplastic lesions (Figure 1A), a brain CT scan was planned. The latter detected a deficit of right sigmoid sinus and bulb of jugular vein filling, which were suggestive of thrombosis of the right jugular vein (Figure 2A). Doppler ultrasonography of upper and lower limbs and echocardiography were negative. A further careful re-evaluation of chest CT supported the hypothesis of septic pulmonary outbreaks, and filling defect in the upper and middle branches of the right pulmonary artery suggested pulmonary embolism (Figure 1B). A diagnosis of LS associated with IJV thrombosis secondary to tonsillitis and pulmonary emboli was made, and low molecular weight heparin (LMWH) was added to levofloxacin. Eleven days later, the patient was discharged in good general conditions. One month after discharge, a cerebral magnetic resonance angiogram (MRA) showed the complete re-canalization of the IJV (Figure 2B).

DISCUSSION

LS is an oropharyngeal infection complicated with IJV thrombosis and subsequently metastatic infections due to septic embolism[1]. LS represent an uncommon condition, and its prevalence is 0.6-2.3 cases per million population. Mortality rate is 4%-18%[6]. LS incidence is higher in people aged 14-24, and its annual rate is 14.4 cases per million people per year. Mean age of patients is reported to be 18-20 years[6,7]. Male patients seen to be at higher risk, especially in autumn and winter[8].

The most common etiology of LS is infection due to Fusobacterium necrophorum, an anaerobic, non-motile, filamentous and non-spore forming Gram negative rod, which is described in 80% of cases. Several other organisms have been reported, isolated as single pathogen (5% of cases) or in association with Fusobacterium necrophorum (10.1%), such as many bacteria of Bacteroides family, Group B and C Streptococcus, Streptococcus oralis, Staphylococcus epidermidis, Klebsiella pneumoniae,
Enterococcus sp., Proteus mirabilis, Eubacterium sp., Eikenella corrodens, lactobacilli and Candida sp. On the other hand, culture results are negative in 12% of cases\textsuperscript{[7]}.

The main site of infection is palatine tonsils (87.1% of cases) and it could lead to exudative tonsillitis and peritonsillar tissue ulcer. However, it has been reported that only hyperemia or grey pseudo-membrane could be detected. Moreover, odontogenic infections, mastoiditis, parotitis, sinusitis, otitis, and skin or subcutaneous tissue infection of the head or neck may represent the primary infection site. Finally, the disease could happen even if the appearance of the pharynx was not remarkable\textsuperscript{[5-7]}.

Pulmonary embolism is not frequently described in LS. Lesions of the lungs are due to haematogenous spread of bacteria from the IJV, and necrotic cavitary lesions, infiltrates, pleural effusions or empyema, abscesses, pneumo-thoraces, or necrotising mediastinitis have been reported\textsuperscript{[5]}.

We performed a Medline literature search to identify papers reporting cases with LS associated with IJV thrombosis. The following search terms were used: “Lemierre syndrome” in combination with “internal jugular vein thrombosis” and “vein thrombosis”. We found that isolation of microorganism was available in 173 cases (Table 1). LS was described more frequently in males (61.3%), aged 25.5 ± 14 years. Gram negative bacteria (84.3%), particularly Fusobacterium spp (76.3%), were related to it. Multiple microorganisms were reported in 8.7% of cases. Complications such as IJV thrombosis, arterial thrombosis, and pulmonary embolism were reported in 71.7%, 2.9% and 8.7% of cases, respectively. Only four fatal cases (2.3%) were described. Univariate analysis (Table 2) showed that pulmonary embolism was more frequent in patients with Gram positive bacteria. This finding was further confirmed by multivariate analysis and we calculated an odd ratio of 9.786 (95%CI: 2.577-37.168, \(P = 0.001\)). The relationship was independent from age, gender, and site of thrombosis.

In conclusion, LS is a rare condition that can mimic a neoplastic disease. However, the careful evaluation of clinical evolution should suggest a correct diagnosis. Moreover, the presence of pulmonary embolism represents a serious complication, and should be suspected when infection is due to Gram positive bacteria.

**ACKNOWLEDGMENTS**

We are indebted to Mrs. Francesca Molinari and Mrs. Cristina Rinaldi, from the University of Ferrara Library Staff, and to Dr. Donato Bragatto, Dr. Claudia Righini, Mrs. Manuela Zappaterra, from the Health Science Library of the Azienda Ospedaliera-Universitaria of Ferrara, for their valuable and precious collaboration.

**COMMENTS**

**Case characteristics**

A 53-year-old man with a history of smoking, hypertension, hyperuricemia, and gastro-esophageal reflux presented with occipital headache, malaise, hacking cough, chest pain exacerbated by inspiration, and fever.
| Ref. | Pathogen |
|------|----------|
| Vogel et al, Am J Dis Child 1980 | FN |
| Sinave et al, Medicine (Baltimore) 1989 | FN |
| Jones et al, Postgrad Med J 1990 | FN |
| Blok et al, Ned Tijdschr Geneeskvl 1993 | FN |
| Ahkee et al, Ann Otol Rhinol Laryngol 1994 | FN |
| Bader-Meunier et al, Eur J Pediatr 1994 | FN and Bacteroides fragilis |
| Hughes et al, Clin Infect Dis 1994 | FN and Staphy. epidermidis |
| Kubota et al, Nihon Kyobu Shikkan Gakkai Zasshi 1994 | FN |
| Blok et al, Ned Tijdschr Geneeskvl 1993 | FN |
| Bader-Meunier et al, Eur J Pediatr 1994 | FN |
| Dykhuizen et al, Eur Respir J 1994 | FN |
| Sinave et al, Medicine (Baltimore) 1989 | FN |
| Kubota et al, Nihon Kyobu Shikkan Gakkai Zasshi 1994 | FN |
| Alam et al, Int J Pediatr Otorhinolaryngol 1998 | FN |
| Gowan et al, Can Respir J 2000 | FN |
| Okhrim et al, J R Soc Med 2000 | FN |
| Shaham et al, Clin Imaging 2000 | FN |
| Abele-Horn et al, Eur J Clin Microbiol Infect Dis 2001 | FN |
| De Vos et al, Neth J Med 2001 | FN |
| Sinha et al, Eur Arch Otorhinolaryngol 2002 | FN |
| Hoehn et al, Crit Care Med 2002 | FN |
| Hope et al, J Laryngol Otol 2002 | FN |
| Nguyen-Dinh et al, J Neurosurg 2002 | FN |
| Boo et al, Laryngoscope 2003 | FN |
| Dalamaga et al, Anaerobe 2003 | FN |
| de Lima et al, Pediatr Radiol 2003 | FN |
| Figuerras et al, Acta Paediatr 2003 | FN |
| Hodgson et al, Undersea Hyperb Med 2003 | FN |
| Jarmeko et al, CMAJ 2003 | FN |
| Velez et al, J Oral Maxillofac Surg 2003 | FN |
| Williams et al, J Clin Microbiol 2003 | FN |
| Ramirez et al, Pediatrics 2003 | FN |
| Lai et al, N Engl J Med 2004 | FN |
| Litterio et al, Anaerobe 2004 | FN |
| Ritter et al, Ultraschall Med 2004 | FN |
| Aliyu et al, Eur J Clin Microbiol Infect Dis 2005 | FN |
| Charles et al, Eur J Vasc Surg 2005 | FN |
| Dool et al, Eur Arch Otorhinolaryngol 2005 | FN |

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Libeer et al., Acta Clin Belg 2005
Masterson et al., Int J Pediatr Otorhinolaryngol 2005
Min et al., Angiology 2005
Morizono et al., Intern Med 2005
Nadkarni et al., J Emerg Med 2005
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Ochoa et al., Acad Emerg Med 2005
Peng et al., J Formos Med Assoc 2005
Rivero Marrotegui et al., An Med Interna 2005
Schmid et al., Pediatrics 2005
Shah et al., J Ayub Med Coll Abbottabad 2005
Touitou et al., Eur J Neurol 2006
Venkateswaran et al., Ann Acad Med Singapore 2005
Varkey Maramattom et al., Cerebrovasc Dis 2005
Hochmair et al., Wien Klin Wochenschr 2006
Fleskens et al., Ned Tijdschr Geneeskd 2006
Constantin et al., BMC Infect Dis 2006
Ravni et al., Scand J Infect Dis 2006
Morris et al., J Int Med J 2006
Olson et al., Br J Ophthalmo 2006
Park et al., J Bone Joint Surg Br 2006
Perovic et al., Acta Med Cracoviak 2006
Singapurewalla et al., Singapore Med J 2006
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Chacko et al., J Laryngol Otol 2010
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Courtin et al., Ann Fr Anesth Reanim 2010
Bonhoeffer et al., Klin Padiatr 2010
Lim et al., Auris Nasus Larynx 2010
Nakayama et al., Auris Nasus Larynx 2010
Ridgway et al., Ann Otolaryngol 2010
Vargiama et al., Eur J Pediatr 2010
Vincent et al., J Pediatr 2010
Gülmez et al., Mikrobiyol Bul 2011
Huynh-Moynot et al., Ann Biol Clin (Paris) 2011
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Naito et al., Nihon Kekkaku Gakkai Zasshi 2011
O'Dwyer et al., J Med Sci 2011
Yamamoto et al., Nihon Rinsho Meneki Gakkai Kaishi 2011
Garbati et al., J Med Case Rep 2012
Hile et al., J Emerg Med 2012
Kuppalli et al., Lancet Infect Dis 2012
Lee et al., J Microbiol Immunol Infect 2012
Lim et al., Med J Malaysia 2012
Teai et al., J Formos Med Assoc 2012

Klebsiella pneumoniae
FN
Staphylococcus aureus
FN and Bacteroides spp
Staphy. haemolyticus and hinitis
Porphyromonas asaccharolytica
Mycoplasma pneumoniae
Strept. intermedia and Bacteroides fragilis
Peptostrepto. anaerobius, Bacteroides fragilis, and Eikenella corrodens
Klebsiella pneumoniae
Staphy. aureus
Staphy. aureus
Staphy. viridans and salivarius
Staphy. aureus

FN and Bacteroides fragilis
Peptostrepto. anaerobius, Bacteroides fragilis, and Eikenella corrodens
Staphy. aureus
Staphy. aureus
Staphy. aureus
Staphy. aureus
Staphy. aureus
Klebsiella pneumoniae
Pseudomonas aeruginosa
Klebsiella pneumoniae
Klebsiella pneumoniae
Klebsiella pneumoniae
Klebsiella pneumoniae
Clinical diagnosis
Physical examination showed only pharyngeal and tonsil hyperemia related to chronic tonsillitis in the patient with a history of gastro-esophageal reflux.

Differential diagnosis
Pulmonary infection with slow resolution, pulmonary abscess, and pulmonary neoplasia.

Laboratory diagnosis
Laboratory work-up showed increased white blood cells, C-reactive protein, and erythrocyte sedimentation rate.

Imaging diagnosis
Chest X-ray was negative for parenchymal lesions at first, but then it showed parenchymal and pulmonary consolidation associated with pleural effusion confirmed by a computed tomography scan. Moreover, filling defect in the upper and middle branches of the right pulmonary artery suggestive of pulmonary embolism was detected. A brain computed tomography scan excluded parenchymal lesions, but a deficit of the right sigmoid sinus and bulb of jugular vein filling suggestive of thrombosis of right jugular vein were shown.

Pathological diagnosis
Tonsillitis related to Fusobacterium infection complicated with internal jugular vein thrombosis and pulmonary embolism.

Treatment
The patient was treated with levofloxacin and low molecular weight heparin.

Related reports
Lemierre’s syndrome is a rare condition characterized by oropharyngeal infection...
complicated by internal jugular vein thrombosis and pulmonary embolism.

**Experiences and lessons**
Lemierre's syndrome could mimic a neoplastic process. A careful follow-up of this condition is necessary.

**Peer-review**
The paper is well written.

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P- Reviewer: Grignola JC, Lazo-Langner A, Pereira-Vega A, Tarazov PG, Turner AM, Wang HY  S- Editor: Qiu S  L- Editor: Wang TQ  E- Editor: Lu YJ
