World Journal of Clinical Cases

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World J Clin Cases 2017 March 16; 5(3): 112-118

DOI: 10.12998/wjcc.v5.i3.112

ISSN 2307-8960 (online)

CASE REPORT

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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Author contributions: All the authors contributed to the work reported in the manuscript.

Institutional review board statement: The study was reviewed and approved by the Azienda Ospedaliero-Universitaria S. Anna of Ferrara Institutional Review Board.

Informed consent statement: The patient involved in this study gave her written informed consent authorizing use and disclosure of her protected health information.

Conflict-of-interest statement: The author(s) declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Manuscript source: Invited manuscript

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Received: August 11, 2016
Peer-review started: August 11, 2016
First decision: September 12, 2016
Revised: October 11, 2016
Accepted: December 7, 2016
Article in press: December 9, 2016
Published online: March 16, 2017

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 emboli 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

Core tip: We report a case of Lemierre's syndrome (LS) complicated by pulmonary embolism (PE) that mimicked

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 Andrè Lemierre in 1936 in a personal experience describing 20 patients[1].

Primary sites of infection in these patients are the tonsils (palatine tonsils or peritonsillar tissue), pharynx and lower respiratory tract[2]. Fusobacterium represents the most common micro-organism 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[5].

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/mm^3, 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/mm^3, 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 ovular 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 emboli[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[5].

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*,

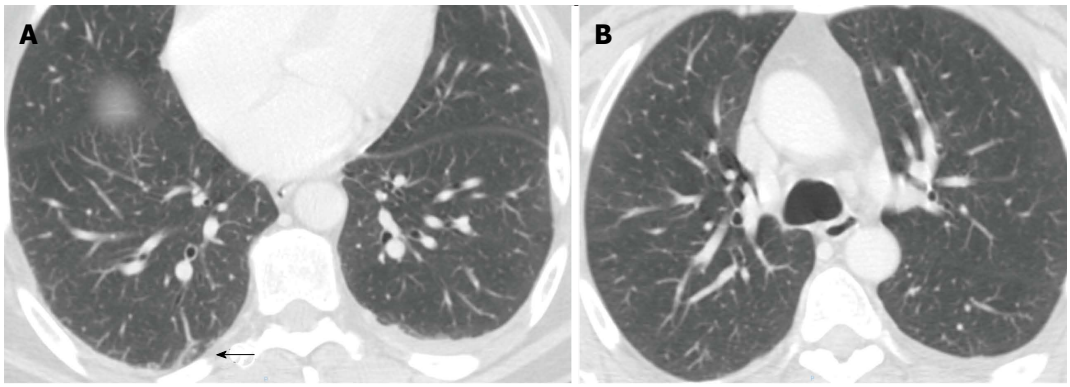

Figure 1 Chest computed tomography showing pulmonary lesions in the posterior region of the right lung (A) associated with left pulmonary embolism (B).

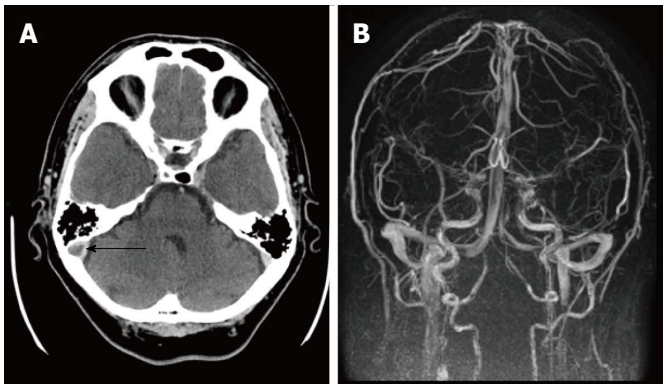

Figure 2 Internal jugular vein thrombosis (arrow) showed by brain TC (A), and further complete re-canalization demonstrated by cerebral magnetic resonance angiogram after antibiotic and anticoagulant therapy (B).

Enterococcus sp., *Proteus mirabilis*, Eubacterium sp., *Eikenella corrodens*, lactobacilli and Candida sp. On the other hand, culture results are negative in 12% of cases[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[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[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.

Table 1 Reported cases of Lemierre's syndrome with internal jugular vein documenting microbiology

Ref.	Pathogen
Vogel *et al*, *Am J Dis Child* 1980	FN
	FN
Sinave *et al*, *Medicine* (Baltimore) 1989	FN
	FN, *Staphy. epidermidis*
Jones *et al*, *Postgrad Med J* 1990	FN
Blok *et al*, *Ned Tijdschr Geneeskd* 1993	FN
	FN
	FN
Ahkee *et al*, *Ann Otol Rhinol Laryngol* 1994	FN
Bader-Meuiner *et al*, *Eur J Pediatr* 1994	FN
Dykhuizen *et al*, *Eur Respir J* 1994	FN and *Bacteroides fragilis*
Hughes *et al*, *Clin Infect Dis* 1994	Multiple microrganisms
Kubota *et al*, *Nihon Kyobu Shikkan Gakkai Zasshi* 1994	FN
Alvarez *et al*, *Pediatrics* 1995	FN
Gupta *et al*, *Clin Pediatr* (Phila) 1995	FN and *Staphy. epidermidis*
Karanas *et al*, *Ann Plast Surg* 1995	FN
Bhagat *et al*, *Infect Dis Clin Pract* (Baltim Md) 1996	*Klebsiella pneumoniae*
De Sena *et al*, *Pediatr Radiol* 1996	FN
	FN
Harar *et al*, *ORL J Otorhinolaryngol Relat Spec* 1996	FN
Lee *et al*, *South Med J* 1997	*Strepto. viridans*
Bouton *et al*, *Rev Med Brux* 1998	FN
Dhawan *et al*, *Indian J Pediatr* 1998	*Peptostrepto. anaerobius, Bacteroides fragilis, Eikenella corrodens*
Williams *et al*, *Int J Pediatr Otorhinolaryngol* 1998	*Strepto. viridians*
	Strepto. viridians
Gong *et al*, *Eur Radiol* 1999	FN
Stokroos *et al*, *Arch Otolaryngol Head Neck Surg* 1999	FN
Agarwal *et al*, *J Laryngol Otol* 2000	FN
Alifano *et al*, *Ann Thorac Surg* 2000	FS and Propionibacterium
Chemlal *et al*, *Presse Med* 2000	*Strepto. intermedius*
Edibam *et al*, *Crit Care Resusc* 2000	FN
Gowan *et al*, *Can Respir J* 2000	FN
Ockrim *et al*, *J R Soc Med* 2000	FN
Shaham *et al*, *Clin Imaging* 2000	FS
Abele-Horn *et al*, *Eur J Clin Microbiol Infect Dis* 2001	FN
De Vos *et al*, *Neth J Med* 2001	FN
Singhal *et al*, *South Med J* 2001	FN
Turay *et al*, *Respirology* 2001	FN
Chirinos *et al*, *Medicine* (Baltimore) 2002	FN
	FN
Hoehn *et al*, *Crit Care Med* 2002	FN
Hope *et al*, *J Laryngol Otol* 2002	FN
Nguyen-Dinh *et al*, *J Neuroradiol* 2002	Strepto. species
Boo *et al*, *Ir Med J* 2003	FN
Dalamaga *et al*, *Anaerobe* 2003	FN
de Lima *et al*, *Pediatr Radiol* 2003	FN
Figueras *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
	FN
	FN
	FN
	FN
Ahad *et al*, *Eye* (Lond) 2004	FN
Bentham *et al*, *Pediatr Neurol* 2004	FN
Giridharan *et al*, *J Laryngol Otol* 2004	FN
	FN
	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*, *J Vasc Surg* 2005	FN
Dool *et al*, *Eur Arch Otorhinolaryngol* 2005	FN
	FN
	FN

Kuduvalli *et al*, *Acta Anaesthesiol Scand* 2005	FN
Libeer *et al*, *Acta Clin Belg* 2005	FN
	FN and *Bacteroides spp*
Masterson *et al*, *Int J Pediatr Otorhinolaryngol* 2005	FN
Min *et al*, *Angiology* 2005	*Staphy. haemolyticus* and *himinis*
Morizono *et al*, *Intern Med* 2005	*Porphyromonas asaccharolytica*
Nadkarni *et al*, *J Emerg Med* 2005	FN
Nakamura *et al*, *Angiology* 2000	FN
Ochoa *et al*, *Acad Emerg Med* 2005	FN
Peng *et al*, *J Formos Med Assoc* 2005	FN
Rivero Marcotegui *et al*, *An Med Interna* 2005	*Mycoplasma pneumoniae*
Schmid *et al*, *Pediatrics* 2005	FN
Shah *et al*, *J Ayub Med Coll Abbottabad* 2005	FN
	FN
Touitou *et al*, *Eur J Neurol* 2006	FN
Venkateswaran *et al*, *Ann Acad Med Singapore* 2005	FS and *Bacteroides fragilis*
Varkey Maramattom *et al*, *Cerebrovasc Dis* 2005	FN
Hochmair *et al*, *Wien Klin Wochenschr* 2006	FN
Fleskens *et al*, *Ned Tijdschr Geneeskd* 2006	FN
	FN
Constantin *et al*, *BMC Infect Dis* 2006	FN
Ravn *et al*, *Scand J Infect Dis* 2006	FN
Morris *et al*, *Ir Med J* 2006	FN
Olson *et al*, *Br J Ophthalmol* 2006	FN
Park *et al*, *J Bone Joint Surg Br* 2006	FN
Perović *et al*, *Acta Med Croatica* 2006	FN
Singaporewalla *et al*, *Singapore Med J* 2006	*Klebsiella pneumoniae*
Boga *et al*, *J Thromb Thrombolysis* 2007	*Staphy. aureus*
Brown *et al*, *J Laryngol Otol* 2007	FN
Chiu *et al*, *Australas Radiol* 2007	FN
Cholette *et al*, *Pediatr Pulmonol* 2007	FN
	FN
Juárez Escalona *et al*, *Med Oral Patol Oral Cir Bucal* 2007	*Strepto. intermedius* and *Bacteroides fragilis*
Thompson *et al*, *Infect Dis Obstet Gynecol* 2007	*Peptostrepto. anaerobius*, *Bacteroides fragilis*, and *Eikenella corrodens*
Wang *et al*, *Anaesth Intensive Care* 2007	FN
Westhout *et al*, *J Neurosurg* 2007	FN
Garimorth *et al*, *Wien Klin Wochenschr* 2008	FN
Georgopoulos *et al*, *J Laryngol Otol* 2008	FN
Kadhiravan *et al*, *J Med Case Rep* 2008	*Staphy. aureus*
Bentley *et al*, *J Emerg Med* 2009	*Staphy. aureus*
Goyal *et al*, *Neurol Sci* 2009	FN
Lee *et al*, *J AAPOS* 2009	*Strepto. viridans and salivarius*
Lu *et al*, *J Am Board Fam Med* 2009	FN
	FS
	FS
Takazono *et al*, *Jpn J Infect Dis* 2009	FN
van Wissen *et al*, *Blood Coagul Fibrinolysis* 2009	FN
	FN
Castro-Marín *et al*, *J Emerg Med* 2010	FN
Chacko *et al*, *J Laryngol Otol* 2010	FN
Herek *et al*, *J Emerg Med* 2010	*Staphy. aureus*
Courtin *et al*, *Ann Fr Anesth Reanim* 2010	FN
Bonhoeffer *et al*, *Klin Padiatr* 2010	FN
Lim et al, *Auris Nasus Larynx* 2010	*Staphy. aureus*
Nakayama *et al*, *Auris Nasus Larynx* 2010	FN
Ridgway *et al*, *Am J Otolaryngol* 2010	FN
Vargiami *et al*, *Eur J Pediatr* 2010	*Abiotrophia defective*
Vincent *et al*, *J Pediatr* 2010	FN
Gülmez *et al*, *Mikrobiyol Bul* 2011	FN
Huynh-Moynot *et al*, *Ann Biol Clin* (Paris) 2011	FN
Maalikjy Akkawi *et al*, *Neurol Sci* 2001	*Klebsiella pneumoniae*
Naito *et al*, *Nihon Kokyuki Gakkai Zasshi* 2011	FN
O'Dwyer *et al*, *Ir J Med Sci* 2011	FN
Yamamoto *et al*, *Nihon Rinsho Meneki Gakkai Kaishi* 2011	FN
Garbati *et al*, *J Med Case Rep* 2012	*Klebsiella pneumoniae*
Hile *et al*, *J Emerg Med* 2012	*Peptococcus anaerobius*
Kuppalli *et al*, *Lancet Infect Dis* 2012	FN
Lee *et al*, *J Microbiol Immunol Infect* 2012	*Klebsiella pneumoniae*
Lim *et al*, *Med J Malaysia* 2012	*Klebsiella pneumoniae*
Teai *et al*, *J Formos Med Assoc* 2012	*Klebsiella pneumoniae*

Teng *et al*, *J Emerg Med* 2012	FN
Tsai *et al*, *J Formos Med Assoc* 2012	*Klebsiella pneumoniae*
Abhishek *et al*, *Braz J Infect Dis* 2013	*Staphy. aureus*
Blessing *et al*, *Int J Pediatr Otorhinolaryngol* 2013	FN
Khan *et al*, *Indian J Pediatr* 2013	FN
Klein *et al*, *Heart Lung* 2013	*Mycoplasma pneumoniae*
Marulasiddappa *et al*, *Indian J Crit Care Med* 2013	*Staphylococcus aureus*
Nguyen *et al*, *Malays J Med Sci* 2013	*Klebsiella pneumoniae*
Phua *et al*, *Int J Angiol* 2013	*Klebsiella pneumoniae*
Righini *et al*, *Head Neck* 2014	FN
	FN
	FN
	Strepto. costellatus
	Enterococcus faecalis
	Strepto. anginosus
	Neisseria species
	FN
	FN
Gunatilake *et al*, *Int J Emerg Med* 2014	*Staphy. aureus*
Asnani *et al*, *J Fam Pract* 2014	FN
Galyfos *et al*, *Scand J Infect Dis* 2014	FN
Aslanidis *et al*, *Pan Afr Med J* 2014	*Candida albicans*, *Staphy. epidermidis*, and *Klebsiella pneumonia*
Karnov *et al*, *Open Forum Infect Dis* 2014	FN
Choi *et al*, *Tuberc Respir Dis* (Seoul) 2015	*Staphy. epidermidis*
Chuncharunee *et al*, *Hawaii J Med Public Health* 2015	*Klebsiella pneumoniae*
Croft *et al*, *Respir Med Case Rep* 2015	FN
Fischer *et al*, *Infect Dis Rep* 2015	FN
He *et al*, *BMJ Case Rep* 2015	FN
Kempen *et al*, *Eur Spine J* 2015	*Strepto. milleri* and FS
Prakashchandra *et al*, *J Clin Diagn Res* 2015	FN
Oya *et al*, *Intern Med* 2015	FS
Takano *et al*, *BMC Res Notes* 2015	FN
Wong *et al*, *J Am Board Fam Med* 2015	FN
Habert *et al*, *Rev Mal Respir* 2016	FN

FN: *Fusobacterium necrophorum*; FS: Fusobacterium species; Strepto: Streptococcus; Staphy: Staphylococcus.

Table 2 Univariate analysis comparing cases of Lemierre's syndrome with and without pulmonary embolism

	No pulmonary embolism (n = 158)	Pulmonary embolism (n = 15)	P
Female, n (%)	61 (38.8)	6 (38.5)	NS
Male, n (%)	97 (61.2)	9 (61.5)	
Age, (yr)	25.5 ± 14.1	26.2 ± 13.6	NS
Gram positive bacteria, n (%)	21 (13.3)	6 (40)	0.006
Gram negative bacteria, n (%)	137 (86.7)	9 (60)	
Multiple microrganisms, n (%)	14 (8.9)	1 (6.7)	NS
Only jugular vein thrombosis, n (%)	113 (71.5)	11 (73.3)	NS
Arterial thrombosis, n (%)	5 (3.2)	0	NS
Fatal cases, n (%)	4 (2.5)	0	NS

NS: Not significant.

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

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