

CASE REPORT

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Lemierre's syndrome: The “forgotten disease” that should not be forgotten

Inês de Sousa Miranda, Marta Monteiro, Elsa Gonçalves,
Cristina Toscano, Raquel Domingos

ABSTRACT

Introduction: Lemierre's syndrome (LS) is often misdiagnosed as a common cold or viral infection. It is characterized by sepsis often evolving after a sore throat or tonsillitis and then complicated by various septic emboli and thrombosis of the internal jugular vein. *Fusobacterium necrophorum* is the most common causative organism. The recommended management is antibiotic treatment.

Case Report: We present a case of LS with positive blood cultures for *F. necrophorum* and pulmonary septic emboli without internal jugular vein thrombosis. The patient was successfully treated with prolonged antibiotic management.

Conclusion: Once observed, LS is unlikely to be forgotten by the spectator. Early antibiotic initiation of septic young patients with tonsillitis or neck infections is essential.

Keywords: *Fusobacterium necrophorum*, Lemierre's syndrome, Septic embolization, Thrombophlebitis

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INTRODUCTION

Lemierre's syndrome owes its name to Frenchman Andre Lemierre who described 20 French cases of “anaerobic septicaemias” [1]. The syndrome is defined by a pharyngeal infection, complicated by septicemia and internal jugular vein thrombosis followed by septic emboli [2, 3]. It was initially named as post-anginal septicemia, and then, “forgotten disease,” by becoming a rare condition after the advent of antibiotics, with fewer than 100 cases reported since 1974. The most commonly involved bacterium is *F. necrophorum* [4].

This clinical entity remains difficult to diagnose due to its low incidence and absence of pathognomonic symptoms.

In this case report we describe a patient who exhibited LS without internal jugular vein thrombosis.

CASE REPORT

We report the case of a 28-year-old male, born in Cabo Verde, and had been living in Portugal for 16 years. Hitherto healthy, he had performed his daily physical activities with no complaints prior to this occurrence. He presented to the emergency room with right acute odynophagia, fever, prostration, and pleuritic left chest pain with seven days of duration.

Inês de Sousa Miranda¹, Marta Monteiro¹, Elsa Gonçalves²,
Cristina Toscano³, Raquel Domingos⁴

Affiliations: ¹Internal Medicine Resident, Internal Medicine Department, Hospital Egas Moniz, Centro Hospitalar Lisboa Ocidental, Lisboa, Portugal; ²Graduate Assistant of Clinical Pathology, Clinical Microbiology and Molecular Biology Laboratory, Hospital Egas Moniz, Centro Hospitalar Lisboa Ocidental, Lisboa, Portugal; ³Graduate Senior Assistant of Clinical Pathology, Clinical Microbiology and Molecular Biology Laboratory, Hospital Egas Moniz, Centro Hospitalar Lisboa Ocidental, Lisboa, Portugal; ⁴Graduate Assistant of Internal Medicine, Internal Medicine Department, Hospital Egas Moniz, Centro Hospitalar Lisboa Ocidental, Lisboa, Portugal.

Corresponding Author: Inês de Sousa Miranda, Avenida Embaixador Augusto de Castro, N° 5, 7° Frente, 2780-199 Oeiras, Lisboa, Portugal; Email: issilva@chlo.min-saude.pt

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Physical examination showed no significant findings, namely, no oropharyngeal changes and normal cardiopulmonary auscultation.

Laboratory evaluation (Table 1) showed a clear increase in inflammatory parameters and a slight increase in liver enzymes. Chest X-ray (Figure 1) showed bilateral nodular images, predominantly on the left base, which led to the performance of a thoracic computed tomography (CT) scan. Chest CT scan (Figures 2 and 3) showed at least eight focal cavitated nodular areas, predominantly peripheral and subpleural; left pleural thickening and left pleural effusion.

Antibiotic treatment was empirically initiated with amoxicillin/clavulanic acid and azithromycin after blood culture collection (1 set).

In the face of a healthy young man with no signs of previous disease presenting with pulmonary cavitated nodular lesions, infectious and inflammatory causes were investigated. Blood cultures showed the growth of Penicillin-sensitive *F. necrophorum* (Figures 4 and 5). From the remaining study, direct and cultural examination of mycobacteria, RT-PCR SARS-CoV-2, anti-Epstein-Barr virus capsid antigen IgM (IgM anti-VCA) antibody were negative. Human immunodeficiency virus (HIV) serologies and anti-hepatitis C virus (HCV) antibody were negative. However, hepatitis B virus (HBV) serology revealed active chronic hepatitis B. Upper abdominal ultrasonography showed no foci of intra-abdominal septic embolization, nor alterations in hepatic structure. The patient didn't have stigmas of chronic liver disease, nor any portal hypertension signs. The levels of albumin and international normalized ratio (INR) were normal. The immunological study, namely antinuclear antibodies (ANAs), antineutrophil cytoplasmic antibodies (ANCA), rheumatoid factor, anti-citrullinated protein antibodies (ACPAs), was negative.

Lemierre's syndrome was assumed and antimicrobial therapy with clindamycin and ceftriaxone was started.

Doppler echo and CT angiography of neck vessels (Figure 6) were performed at three days of directed treatment and internal jugular vein thrombophlebitis was excluded. Transthoracic echocardiogram showed no vegetations. To evaluate embolic foci and complications

Table 1: Laboratory evaluation

Hemoglobin (g/dL)	13.6
Leucocyte count (cells/mL)	25,000
CRP (mg/dL), SR (mm/h), Procalcitonin (ng/mL)	26.6, 42, >100
AST and ALT (U/L)	86 and 82
RT-PCR SARS-CoV-2	Negative
Urinary antigen <i>Streptococcus pneumoniae</i> and <i>Legionella pneumophila</i>	Negative

CRP: C-reactive protein; SR: sedimentation rate; AST: aspartate aminotransferase; ALT: alanine aminotransferase; RT-PCR: reverse transcription-polymerase chain reaction

of the infectious process total body positron emission tomography (PET)-scan (Figure 7) was performed at 14 days of antibiotic treatment which revealed inflammatory signal on lungs, left pleura, and right amygdala. The evaluation by otorhinolaryngology and stomatology showed no alterations.

The patient evolved with clinical and imaging improvement. Negative blood cultures (a total of three sets separated from 48 hours from different peripheral venous punctures) were confirmed. He was discharged for home hospitalization to complete four weeks of intravenous antibiotic treatment.

He was seen in consultation two weeks after completing the therapy, with clinical and imaging recovery (Figures 8 and 9).



Figure 1: Chest X-ray (postero-anterior view).



Figure 2: Thoracic CT-scan (transversal view)—cavitated lesion (arrow).

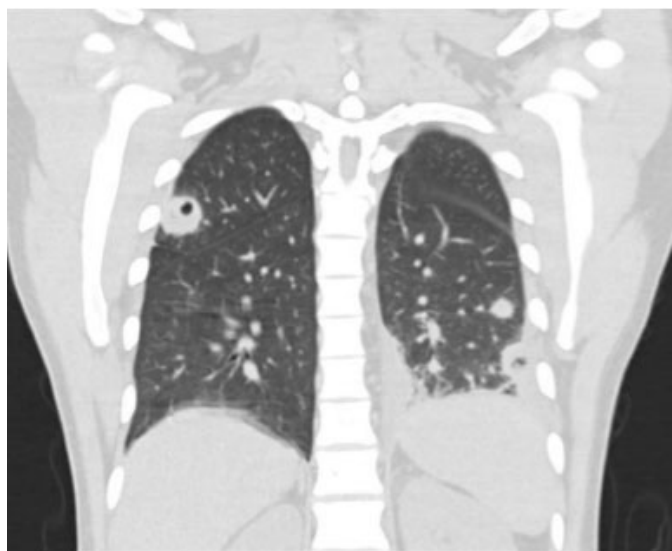


Figure 3: Thoracic CT-scan (coronal view)—cavitated lesions and left pleural effusion.

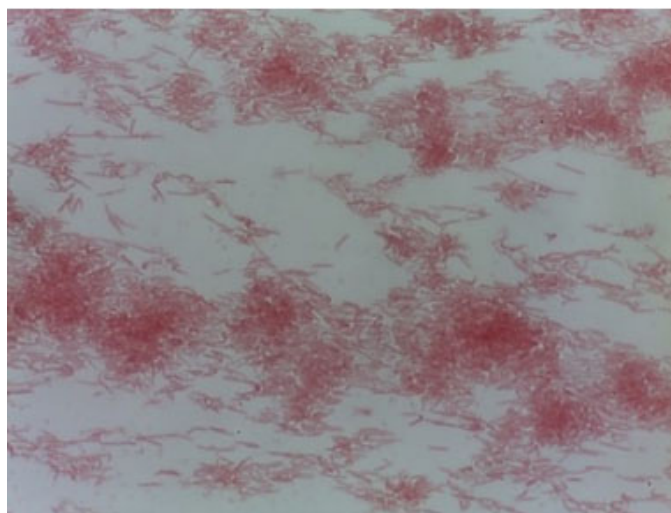


Figure 5: Gram stain—*Fusobacterium necrophorum*.

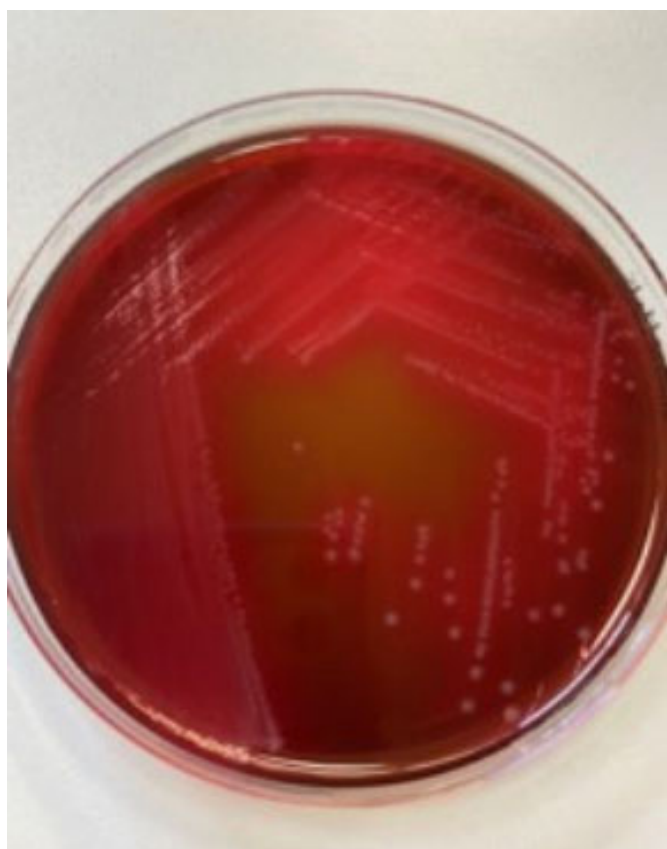


Figure 4: Petri dish showing *Fusobacterium necrophorum*.

DISCUSSION

Lemierre's syndrome is a rare disease. In a Danish study from 1998 to 2001, the annual incidence among individuals aged 14–24 was 14.4 cases per million people. The incidence in the population was 3.6 cases per million people [5]. Some studies suggest LS might occur more often in men [6, 7].



Figure 6: CT angiography of neck vessels (coronal view) without thrombosis of cervical vessels.

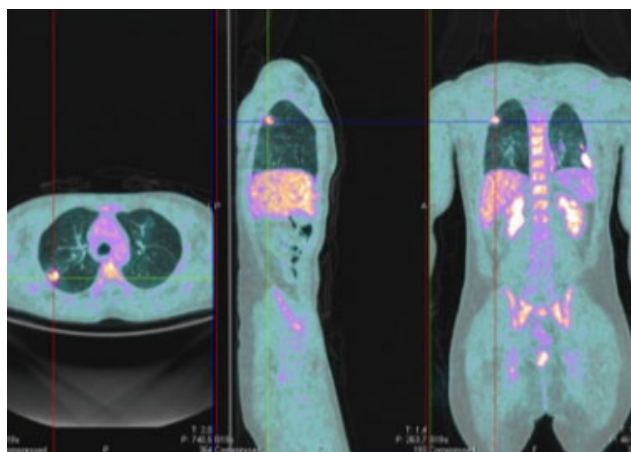


Figure 7: Total body PET-scan—inflammatory signal on lungs and left pleura.



Figure 8: Thoracic CT-scan (transversal view with intravenous contrast injection)—normal lung parenchyma.



Figure 9: Thoracic CT-scan (coronal view with intravenous contrast injection)—normal lung parenchyma.

The classic clinical presentation of LS is a young and otherwise healthy patient with a prolonged sore throat, neck pain, and often with fever [3, 7, 8]. Laboratory findings typically show leukocytosis and elevated C-reactive protein (CRP) as well as signs of organ failure, such as elevated liver enzymes [9, 10]. The patient's hepatitis B status (active hepatitis B) may indicate a

compromised immune status predisposing the patient to develop an invasive infection with *F. necrophorum*.

Complications to this severe syndrome include a mortality rate as high as 10%, especially when antibiotic treatment is delayed. Other complications include embolic infections in internal organs (often lungs), joints, and/or the brain [11].

A definite diagnosis of LS should be made based on the following findings [12, 13]: (1) a recent pharyngeal illness, (2) complicated by septic emboli, and (3) either thrombosis of the internal jugular vein or findings of *F. necrophorum* in blood cultures. One of the most indicative, although not obligatory as stated by the diagnosis criteria, sign of LS is the development of an internal jugular venous thrombophlebitis [14, 15], which in this case report was absent. One may argue that the examination of the neck vessels was performed under a few days of directed antibiotic treatment, which could have solved the thrombophlebitis process. However, according to the literature, the treatment of septic thrombophlebitis is often difficult and requires prolonged therapy, because the fibrin clots protect the *F. necrophorum* from aerobiosis and make it difficult for antibiotics to penetrate [16]. Based on the current evidence, it is still unknown whether anticoagulation therapy is mandatory in cases of jugular thrombosis [17, 18].

The recommended treatment for LS would be a beta-lactam antibiotic plus metronidazole for 2–6 weeks due to the increase in resistance against penicillin [19]. In this case report the choice of clindamycin and ceftriaxone was based on the inflammatory intensity of the condition and the organized pleural effusion was a cause for concern.

CONCLUSION

Clinicians' awareness of this clinical entity for early diagnosis and timely and appropriate treatment is essential, thus reducing the risk of complications and mortality.

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Author Contributions

Inês de Sousa Miranda – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be

accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Marta Monteiro – Acquisition of data, Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Elsa Gonçalves – Acquisition of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Cristina Toscano – Acquisition of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Raquel Domingos – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

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Consent Statement

Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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ABOUT THE AUTHORS

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Inês de Sousa Miranda is an Internal Medicine resident at Internal Medicine Department, Hospital Egas Moniz, Centro Hospitalar Lisboa Ocidental, Lisboa, Portugal. She is also an invited Professor of Católica Medical School, Lisboa, Portugal. She earned the undergraduate and postgraduate degrees from Faculdade de Medicina, Universidade de Lisboa. She earned a merit scholarship in 2018/2019 academic year, as a recognition of excellent academic performance. Her research interests include heart failure, hepatology, and biochemistry. She intends to pursue PhD on heart failure field in the future.

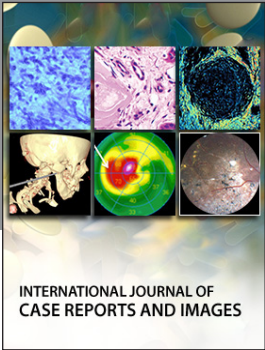
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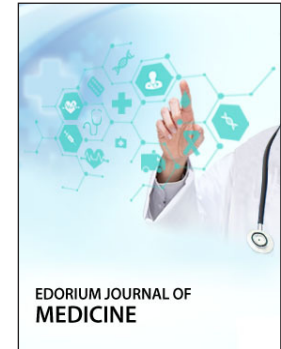
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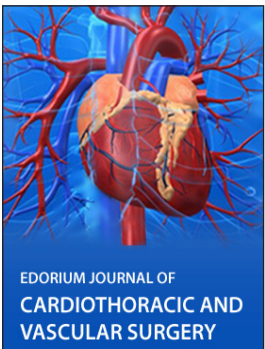
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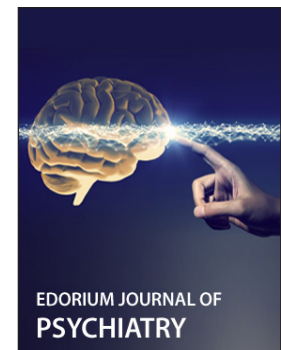
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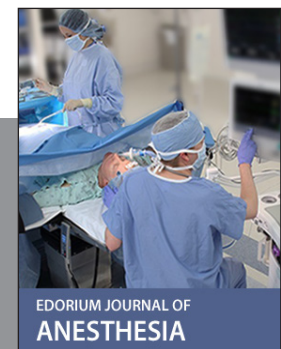
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