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Case Report

Lemierre's Syndrome Caused by *Streptococcus anginosus* Presenting as Postseptal Cellulitis in a Pediatric Patient

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Lemierre's syndrome · *Streptococcus anginosus* · Internal jugular vein · Lung abscess · Orbital cellulitis · Septic thrombophlebitis · Pediatrics

Abstract
Lemierre's syndrome is an infrequent disease characterized by septic thrombosis of the internal jugular vein followed by pulmonary embolism generally occurring after upper respiratory and gastrointestinal tract infections. We present the case of a 15-year-old female patient with postseptal cellulitis and cervical abscess who developed pulmonary embolism and pleural effusion secondary to internal jugular vein thrombosis. Cultures were positive for *Streptococcus anginosus*, antibiotic treatment was established with satisfactory clinical outcome. High clinical suspicion is required for a diagnosis. The mainstay of treatment is a multidisciplinary approach based on two essential pillars: antibiotic therapy and surgical drainage. This is an important case because of the unusual presentation, the isolation of an infrequent pathogen, and the primary infection site (postseptal cellulitis), which are rare characteristics of this condition in the pediatric population.

Clinical Case

A 15-year-old female patient complained of a left frontal headache, 10 out of 10 on the pain scale, associated with vertigo, tinnitus, and left orbital edema. On admission, the patient had an edema of the left side of her face, palpebral emphysema extending to the malar and retroauricular region, and proptosis in her left eye with normal pupils, but no other relevant findings on physical examination. Axial computed tomography (CT) of the face performed in another institution showed left maxillary sinusitis, proptosis with postseptal collection, and soft-tissue edema, consistent with left periorbital cellulitis Chandler grade IV, prompting

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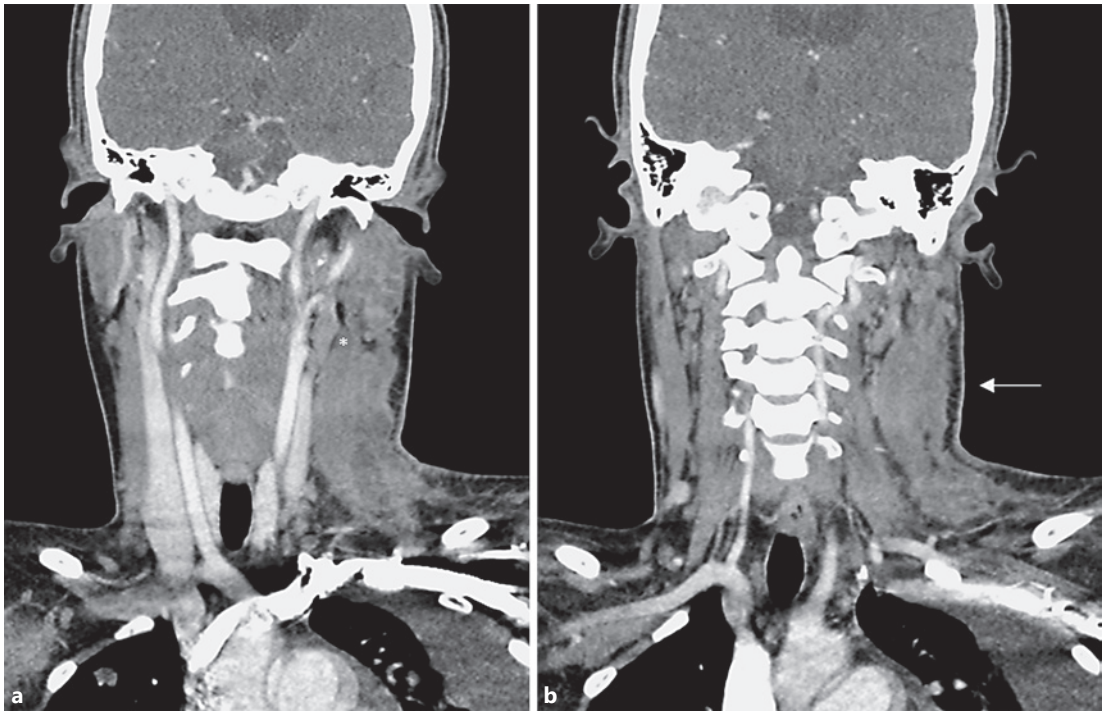

Fig. 1. a Neck CT. Coronal reconstruction. Opacification defect of the left internal jugular vein (white asterisk), consistent with the presence of a thrombus. **b** Neck CT. Coronal reconstruction. Enlargement and hypodense collection in the thickness of the left sternocleidomastoid muscle (white arrow), consistent with myositis.

treatment with vancomycin and ceftriaxone. Contrast-enhanced magnetic resonance imaging of the brain ruled out cavernous sinus thrombosis. The patient underwent surgical management by drainage of the orbital collection, frontal sinusotomy, maxillary antrostomy, and anterior and posterior ethmoidectomy. Orbital cultures were obtained in the operating room under sterile conditions.

Six days after the initiation of antibiotic treatment, the patient developed neck pain, headache, and cervical adenopathy. A CT scan of the neck showed a 10- to 20-mL septate collection in the left part of the neck, involving the superficial region of the ipsilateral sternocleidomastoid muscle, and a thrombus at the level of the internal jugular vein (Fig. 1). This cervical abscess was also drained in the surgery room under sterile conditions, and cultures were obtained.

The patient continued to have fever. The preliminary culture of the ocular discharge and of the neck abscess found gram-positive cocci, sensitive to oxacillin, clindamycin, linezolid, trimethoprim sulfamethoxazole and sensitive for vancomycin. The minimum inhibitory concentration for vancomycin was (<0.5) measured based on the MicroScan® parameters from Microbiology in the Hospital de San José. Twelve days after admission, the patient developed respiratory distress and hypoxemia along with abolished respiratory murmurs in the right lower lobe; she was diagnosed with pneumonia, complicated by left septate pleural effusion, based on ultrasound findings. The recovery of the patient was not adequate, she persisted to have fever, respiratory difficulty, and systemic inflammatory response for which the Infectious Diseases Department recommended adding linezolid and discontinuing vancomycin. New blood cultures were obtained. The CT of the chest showed soft-tissue dense nodules of multilobular distribution, the largest being 15 mm in diameter, and some cavitated nodules; a left pleural collection with collapse of the adjacent lung; trachea and main bronchus of normal caliber and course (Fig. 2). The findings described in the lung parenchyma suggested septic embolism. The patient underwent thoracoscopy, decortication, and closed thoracostomy. The septate effusion was collected intraoperatively; pleural fluid testing ruled out tuberculosis, and the cultures were negative.

Two cultures from the eye and two from the neck abscess were positive. The cultures were positive for *Streptococcus anginosus.* The patient completed a regimen of 14 days of linezolid and 21 days of ceftriaxone and had an adequate clinical course, after which she was discharged.

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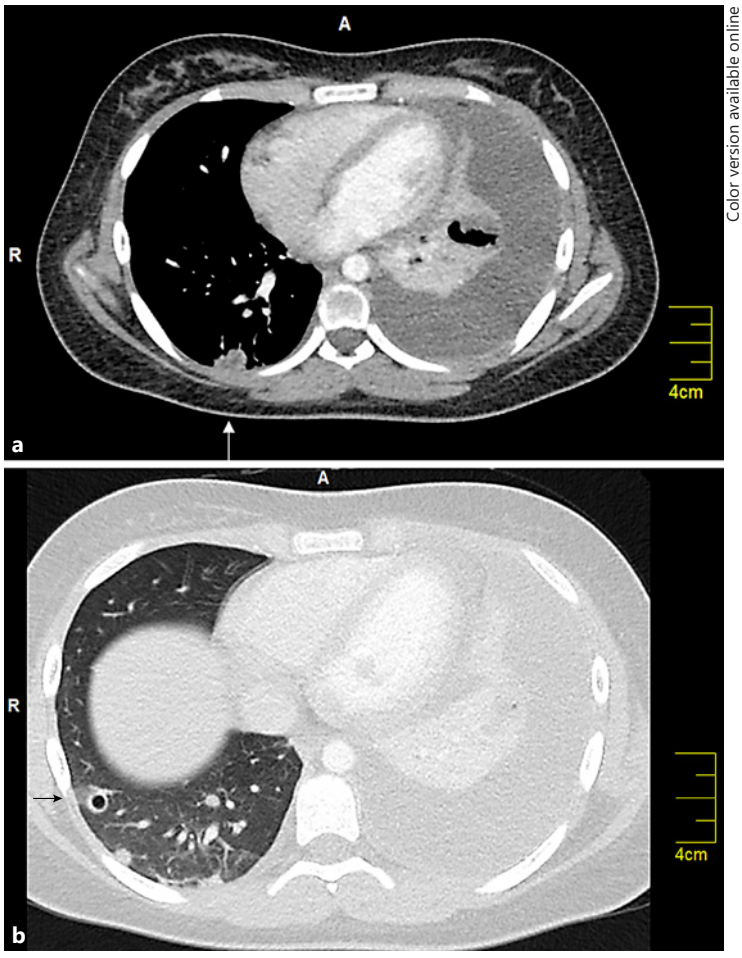

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Fig. 2. a Chest CT. Mediastinum window. Cavitated nodule in the collapsed left lower lobe (white arrow). Left pleural fluid. **b** Chest CT. Lung window. Two soft-tissue dense subpleural nodules in the right lower lobe. Air can be seen in one of the lesions, consistent with cavitation (black arrow).

Discussion

Lemierre's syndrome was described for the first time in 1936 in a series of 20 cases of infections with anaerobic sepsis, 18 of which resulted in death [1]. It was described as "post-anginal anaerobic sepsis" because of signs of sepsis that developed shortly after the onset of odynophagia. Lemierre argued that sepsis originated from inflammatory or suppurative lesions of the tissues or cavities where anaerobic organisms exist under physiological conditions and, after proliferating, crossed to the bloodstream and gave rise to distant septic emboli. He also described that patients presented initially with oropharyngeal infection and inflammation, fever, indurated submaxillary masses, internal jugular vein thrombophlebitis and, finally, distal metastatic abscesses more commonly localized in the lungs [2].

Since the advent of antibiotics in the 1940s, the number of case descriptions of Lemierre's syndrome has dropped significantly; however, an increase in frequency as of the 1970s has led to the conclusion that it may be a re-emergent disease [1], the change in incidence being the result of an increase in antibiotic resistance or misuse [3]. The reported incidence ranges between 0.6 and 2.3 per million, with mortality rates of 4–18%. Peak incidence occurs in patients 16–25 years of age with no history of immunosuppression [4]. Anaerobic organisms and gram-negative rods have been implicated in the etiology, typically *Fusobacterium necrophorum*, but also *Peptostreptococcus, Klebsiella pneumoniae, Peptostreptococcus anaerobius, Bacteroides fragilis, Eikenella corrodens* and *Escherichia coli*, among others. Some

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studies have even demonstrated that infection may be polymicrobial in 10–30% of all cases [1–4]. *Fusobacterium necrophorum* is responsible for the majority of bacteremia, and up to one-third of all patients will have polymicrobial bacteremia together with anaerobic streptococci and other gram-negative anaerobes. *Streptococcus anginosus* is part of the normal flora of the oral mucosa. Over the past few years, the pathogenic potential of this group has been underestimated because of the difficulty in identifying the species correctly. It has been found as a pathogen in abscesses of the oral cavity. Three species are part of the *Streptococcus milleri* group: *S. anginosus,* isolated predominantly in blood cultures, *S. constellatus*, and *S. intermedius,* which have been isolated in abscesses [5–9].

Clot formation in Lemierre's syndrome is unclear. Some authors have proposed the hypothesis of pathophysiological abnormalities in Virchow's triad: (1) systemic hypercoagulability caused by infection; (2) venous stasis due to intrinsic or extrinsic occlusion related to the infectious process or as a result of local inflammation; and (3) endothelial damage due to direct intravascular bacterial invasion or to perivascular inflammatory lesions [8].

Clinically, it manifests initially as pharyngeal pain, odynophagia, and tonsillar exudates. However, it can also occur after infections of the middle ear, paranasal sinuses, and mastoid and dental foci. Within 1–3 weeks, the patient develops symptoms related to internal jugular vein thrombophlebitis or metastatic emboli. Typical findings include neck pain, a palpable mass and pain with neck movement due to sternocleidomastoid involvement, mandibular angle pain, trismus, and fever. Pulmonary metastatic complications include pleural effusion, pneumonia, and empyema. Other embolic complications include osteomyelitis, septic arthritis, liver abscesses, brain abscesses and septic emboli of the central nervous system (meningitis and cavernous sinus thrombosis), septic shock, and multiple organ failure [10, 11].

High clinical suspicion is required for a diagnosis, and the first option for diagnosing jugular thrombosis is Doppler ultrasound, which is fast and noninvasive. Contrast CT of the neck has been shown to have advantages over Doppler, such as the visualization of thrombi under the mandible and the clavicle, characterization of lesions in the deep spaces close to the neck, and detection of embolic complications. Magnetic resonance imaging provides high-quality imaging of the soft tissues, but its use is limited by cost and availability. Lung metastasis is detected in 92% of all cases with chest X-rays, while CT of the chest is useful to detect multiple nodular infiltrates, necrotized cavitary lesions, abscesses, and empyema [10–12].

The mainstay of treatment is a multidisciplinary approach based on two essential pillars: appropriate antibiotic therapy and surgical drainage. Anticoagulation is controversial. Monotherapy with penicillin has been a good option in the past, but due to the growing number of beta-lactamase-producing strains, management has changed. There are no randomized controlled clinical trials on the optimal management. Numerous authors suggest the use of intravenous ceftriaxone and metronidazole. Other options include monotherapy with carbapenems, ampicillin-sulbactam, clindamycin, and antipseudomonal penicillins [4, 10, 11]. In previous reviews, the mean duration of antibiotic treatment was 3–6 weeks, anticoagulation therapy was used in 25% of the patients, overall mortality was 8%, and the mean time until diagnosis from the moment of hospital admission was 5 days [8].

This case is important because of the unusual presentation, the isolation of an infrequent pathogen, and the primary infection site (postseptal cellulitis), which are rare characteristics of this condition. An expanded review of the literature was conducted using PubMed, Embase, and Lilacs' databases in order to search for other cases of Lemierre's syndrome caused by *S. anginosus*, using the terms (*streptococcus* OR *streptococcus anginosus*) AND (Lemierre syndrome OR thrombophlebitis) with no limits regarding publication dates. The search resulted in 121 articles in PubMed, 376 in Embase, and 4 in Lilacs, with 7 cases of *S. anginosus* [5, 7, 13–17] of which only one was a pediatric patient under 18 years of age. This was a case

report published in 2016, describing a previously healthy 2-year-old boy who presented initially with suppurative lymphadenitis. Blood culture resulted in isolation of *S. anginious,* and a CT scan showed left jugular vein thrombosis requiring anticoagulation, with resolution on follow-up CT 2 months later [17].

Our case is relevant because this could be the second case of *S. anginosus* in a pediatric patient published in the literature, and it has an unusual presentation (primary focus: postseptal cellulitis).

Conclusion

Lemierre's syndrome is an infrequent complication of oropharyngeal and airway infections. It is a disease whose incidence has increased and which can be potentially fatal in the absence of early detection, adequate approach, and treatment. It is important for clinicians to be highly suspicious. Its different forms of clinical presentation, the different primary foci of the infection, and the different organs where the septic embolisms are located since the early diagnosis of this pathology can constitute a challenge for clinicians. With respect to the etiological agents of this pathology, *Fusobacterium necrophorum* is classically responsible in a large percentage of cases, without forgetting that other microorganisms can be isolated (in this case, *S. anginosus*); this aspect can be key to a correct approach regarding antibiotic treatment in order to improve the patient's prognosis.

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Statement of Ethics

The study protocol and case report were approved by the institute's Committee on Human Research and the medical Ethics Committee of the Hospital de San José.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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