BJCR
Brazilian Journal of Case Reports

PCAA
Publicações Científicas de Acesso Aberto

Case Report

Lemierre Syndrome Due to *Staphylococcus Aureus* Infection and Presenting with Periorbital Cellulitis and Bilateral Abducens Nerve Palsy

Lara Linhares Pierre [1], **Ana Camille Feijão Cisne** [1], **Lucas Linhares Pierre** [1], **Paulo de Tarso Ponte Pierre-Filho** [2,*]

[1] School of Medicine Uninta, Sobral, Ceará, Brazil.
[2] Department of Ophthalmology, Hospital Regional Norte, Sobral, Ceará, Brazil.

* Correspondence: paulopierre@hotmail.com.

Abstract: Lemierre syndrome is an uncommon and potentially fatal condition characterized by head or neck infection, thrombosis/thrombophlebitis of the internal jugular vein, and septic embolization to distant organs. This case report describes a 56-year-old male patient who made a home pimple drainage that resulted in periorbital cellulitis with progression to internal jugular vein thrombosis and septic embolism. Ophthalmological examination revealed bilateral abducens nerve palsy. Blood culture was positive for Staphylococcus aureus. He was managed with broad-spectrum antibiotics and anticoagulation. Response to treatment was satisfactory. Lemierre syndrome should be suspected in patients with bacteremia and radiologic imaging of pulmonary embolism or internal jugular vein thrombosis/ thrombophlebitis, even in the absence of signs and symptoms of oropharyngeal infection. Furthermore, uncommon pathogens should be considered conditions, based on the suspected source of primary infection.

Keywords: Lemierre Syndrome; Abducens Nerve Palsy; *Staphylococcus aureus*; Thrombosis; Septic Embolism.

Citation: Pierre LL, Cisne ACF, Pierre LL, Pierre-Filho PTP. Lemierre syndrome due *to Staphylococcus aureus* infection and presenting with periorbital cellulitis and bilateral abducens nerve palsy. Brazilian Journal of Case Reports. 2025 Jan-Dec;05(1): bjcr59.

https://doi.org/10.52600/2763-583X.bjcr.2025.5.1.bjcr59

Received: 3 December 2024
Accepted: 17 January 2025
Published: 18 January 2025

1. Introduction

Lemierre syndrome (LS) is life-threatening condition classically defined by thrombophlebitis of the internal jugular vein, bacteremia and septic embolism manifesting as a complication of a bacterial infection of the head and neck district – typically, a pharyngotonsillitis or an abscess. However, unusual forms of the disorder have been rarely reported. Atypical cases of LS involving facial vein, external jugular vein and superior ophthalmic vein septic thrombophlebitis have also been reported [1]. The bacterium most frequently involved is the obligate gram-negative anaerobic *Fusobacterium necrophorum*, but other bacteria such as *Streptococcus viridans*, *Staphylococcus aureus*, *Haemophilus influenzae*, and *Klebssiella pneumoniae* have been described most rarely. First described by Andre Lemierre in 1936 and published in the Lancet, LS is rare with a reported incidence of about 0.8 to 1.5 per million persons per year worldwide, occurring most commonly in otherwise healthy children and young adults [2,3]. It is a condition that can have high morbidity and mortality. If untreated LS results in a 90% mortality rate. Even with appropriate antibiotics and therapy, mortality has been reported to be between 2% and 5%. In only about 1% of cases have orbital infections been identified as triggers of LS [4].

Since the advent of antibiotics in the 1940s, the number of case descriptions of LS 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. The cause of this increase remains unclear, but improved imaging techniques to diagnose and the increased resistance, overprescription and modification in the prescription of antibiotics for pharyngotonsillitis, could be suppositions for this observation. Some cases of LS without an oropharyngeal infection also have been reported recently [3-6], mainly associated with periorbital cellulitis.

Ocular and neuro-ophthalmological signs are unusual in LS [7]. Periorbital cellulitis is often a localized infection; however, it can rarely lead to serious consequences including loss of vision and septic embolism if untreated. Infected material can penetrate in the bloodstream and disseminate to distant sites, resulting in infection of other organs, including the lungs, joints, spleen, kidneys, brain, liver and heart, leading to severe complications. We describe a serious complication in a patient who, during his routine, popped a pimple resulting in periorbital cellulitis, with progression to septic embolism and bilateral abducens nerve palsy. This case highlights the significance of detecting early signs of infection for prompt diagnosis and treatment.

2. Case Report

A previously healthy 56-year-old man arrived at emergency department (ED) after presenting fever, asthenia, nausea, progressive dyspnea, pain on opening the mouth, headache and double vision. He also complained of knees pain for 3 days. The patient denied prior history of trauma, consumption of tobacco, alcohol or drugs. He had a 12-day history of progressively worsening of erythema and swelling of the face that started after popping a pimple in his nose. Five days prior to hospitalization, he had consulted the general practitioner who established the diagnosis of periorbital cellulitis and recommended treatment with 500mg oral cephalexin four times per day and 200 mg ibuprofen three times per day for 7 days, however, his symptoms worsened.

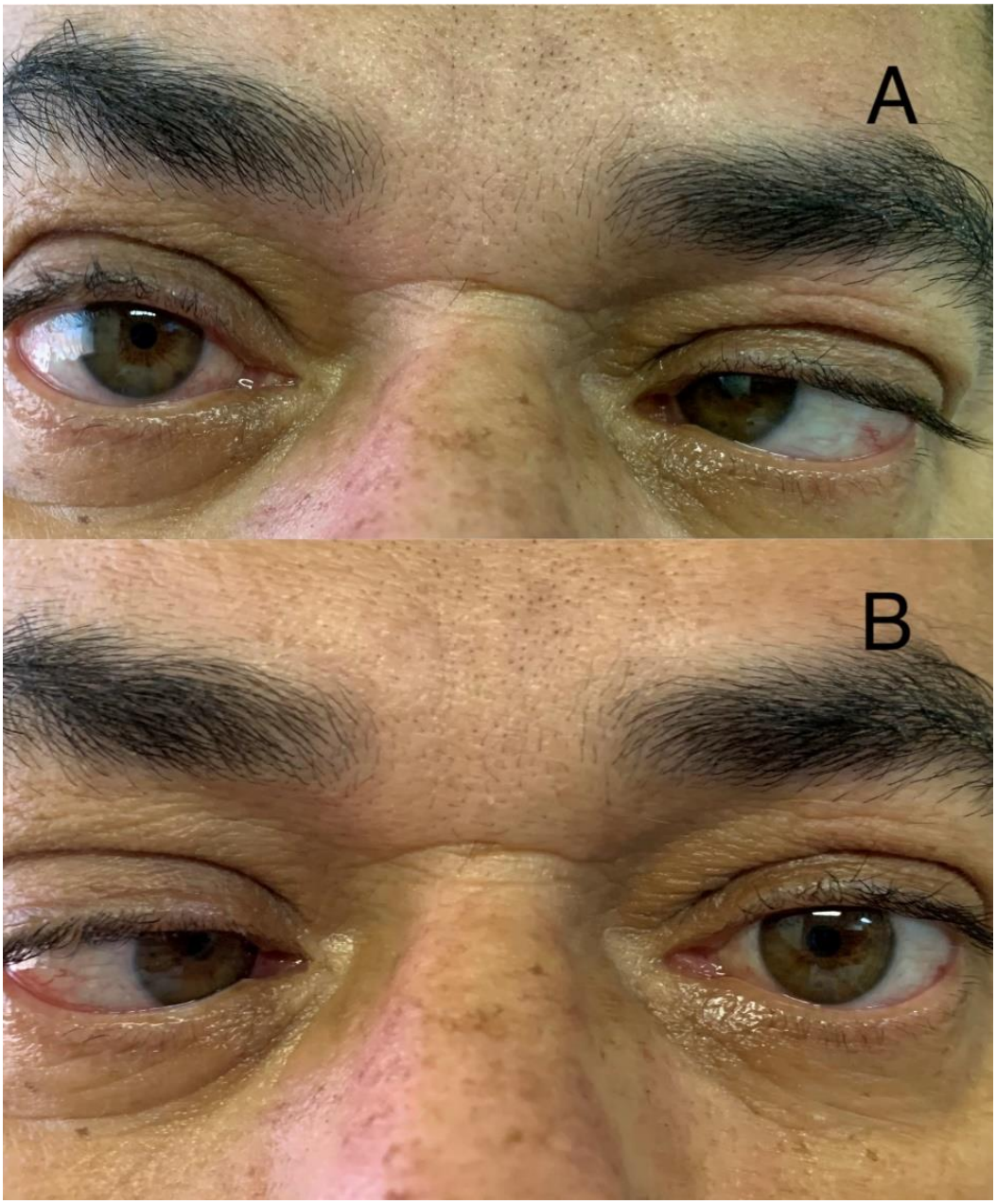
On admission, the patient had blood pressure (121x81mmHg), temperature 38.4°C, heart hate: 86, SpO_2: 92% (room air). The oropharynx was normal and there was no evidence of parapharyngeal abscess. The abdominal examination did not show any nodularity or hepatosplenomegaly. Laboratory data revealed hemoglobin 14.1 g/dL (11.5-16.4 g/dL), leukocytosis with a white blood cell count of 22.1 x 10^6 cells/L (4-10.5 x 10^6 cells/L), neutrophils of 86% (50-70%), platelets 340 K/μL (140-450 K/μL), prothrombin time of 14s (11-13.5s), activated partial thromboplastin time of 34.8s (25-35s), and international normalized ratio of 1.22 (<1.1).

Inflammatory markers were elevated: erythrocyte sedimentation rate (ESR) 136 mm/h and C-reactive protein of 114 mg/L (<10mg/L). Urine culture was negative. HIV test and viral hepatitis serologies were undertaken due to the atypical nature of infection which were negative. His lumbar puncture was normal and cerebrospinal fluid culture was negative. On ophthalmologic examination, the patient showed evident strabismus due to bilateral lateral rectus palsy (Figure 1). Pupils were equal, round, and reactive to light. There were no afferent pupillary defects. Visual acuity was 1.0 in both eyes with correction. Fundoscopic examination was negative bilaterally for signs of optic disc swelling. A chest X-ray showed bilateral infiltrates and nodular densities (Figure 2).

Computed tomography (CT) of the chest without contrast was performed, which revealed solid nodules affecting the lungs, some of them forming cavities of variable sizes; the largest measured 2.3cm, consistent with septic pulmonary emboli (Figure 3). Echocardiogram ruled out valvular vegetations or heart valve thrombosis. Magnetic resonance (MR) angiography of the brain confirmed reduction of flow at the right internal jugular vein (IJV) extending to the ipsilateral sigmoid sinus, suspecting partial thrombosis (Figure 4). On day 2 post-admission, Staphylococcus aureus was isolated from his peripheral blood culture. A diagnosis of Lemierre's syndrome was considered. He was initially put

on intravenous antibiotics vancomycin (500 mg every 6 hours), cefepime (1g every 12 hours) and heparin (5,000UI/day), which were later modified to meropenem (1 g every 8 hours), vancomycin (500 mg every 12 hours) and subcutaneous enoxaparin 60mg/day. The treatment continued for four weeks. During this time, the patient became afebrile and hemodynamically stable, but the diplopia persisted.

Figure 1. The patient was presented with clinical signs of bilateral abducens nerve palsy. As a result, he had an abduction limitation of the right eye in the right lateral gaze (A) and abduction limitation of the left eye in the left lateral gaze (B).



The laboratory test results returned to normal levels, and the blood cultures were sterile. Repeat imaging at that time showed the disease process had decreased significantly, and the patient was discharged home on per os clindamycin and levofloxacin for two weeks, as well as per os aspirin for six months. The patient was scheduled for monthly outpatient medical visits. Alternating occlusion patches were used to alleviate the symptoms of diplopia. After 6 weeks and minimal improvement of diplopia and abducens

nerve palsy, he was treated with Botox® (Allergan, Irvine, CA) application into the both medial rectus muscle (2.5 U - 0.05 ml) with topical anesthesia. This improved his ocular alignment in primary gaze. The abducens palsy recovered gradually and four months later, he had normal ocular movements, with no neurological deficits or abnormal findings on physical examination.

Figure 2. Anteroposterior chest x-ray showing multiple bilateral pulmonary infiltrations particularly in lower zones, consistent with septic emboli.

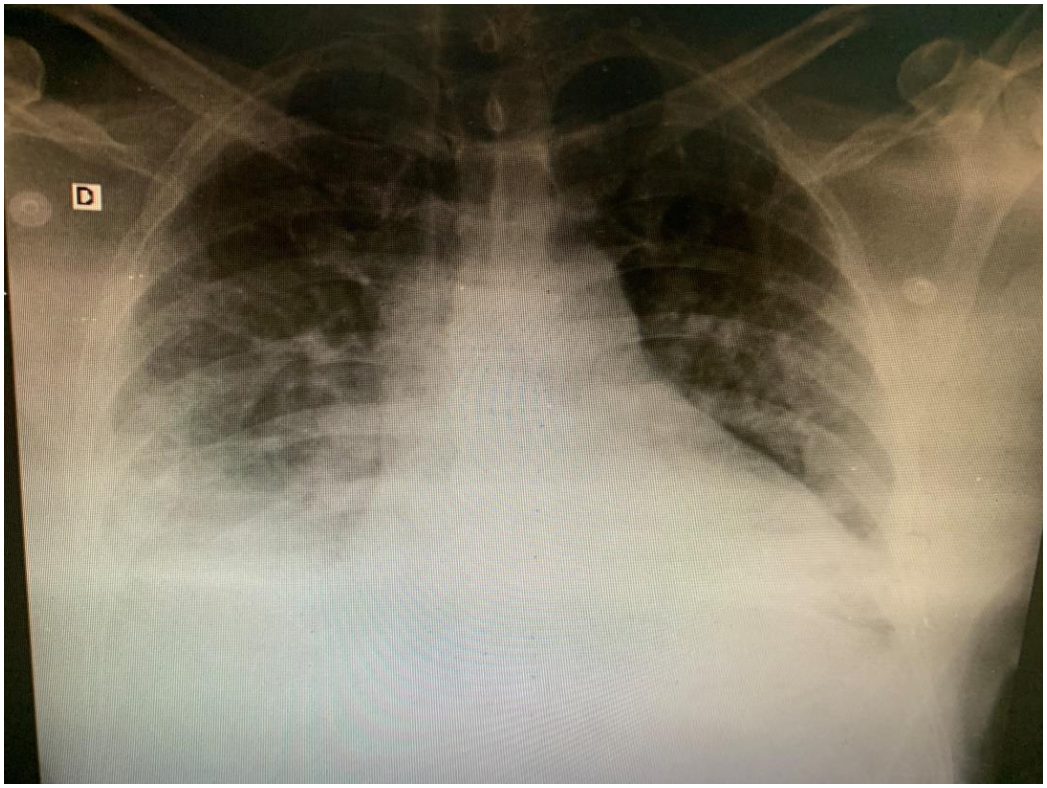
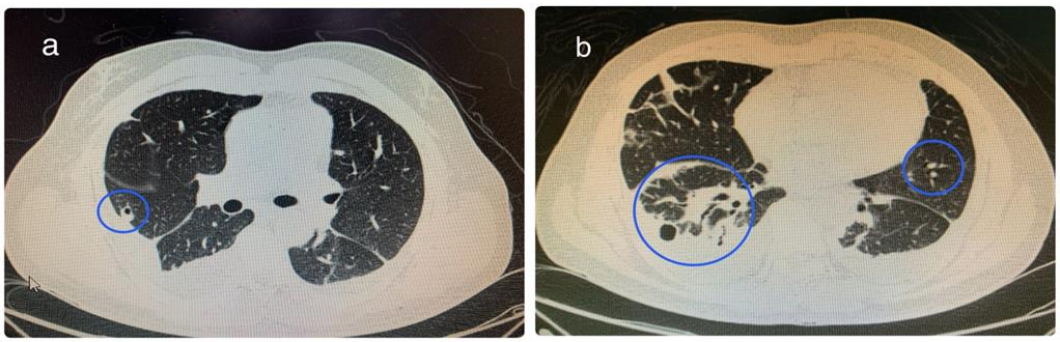


Figure 3. Anteroposterior chest x-ray showing multiple bilateral pulmonary infiltrations particularly in lower zones, consistent with septic emboli.

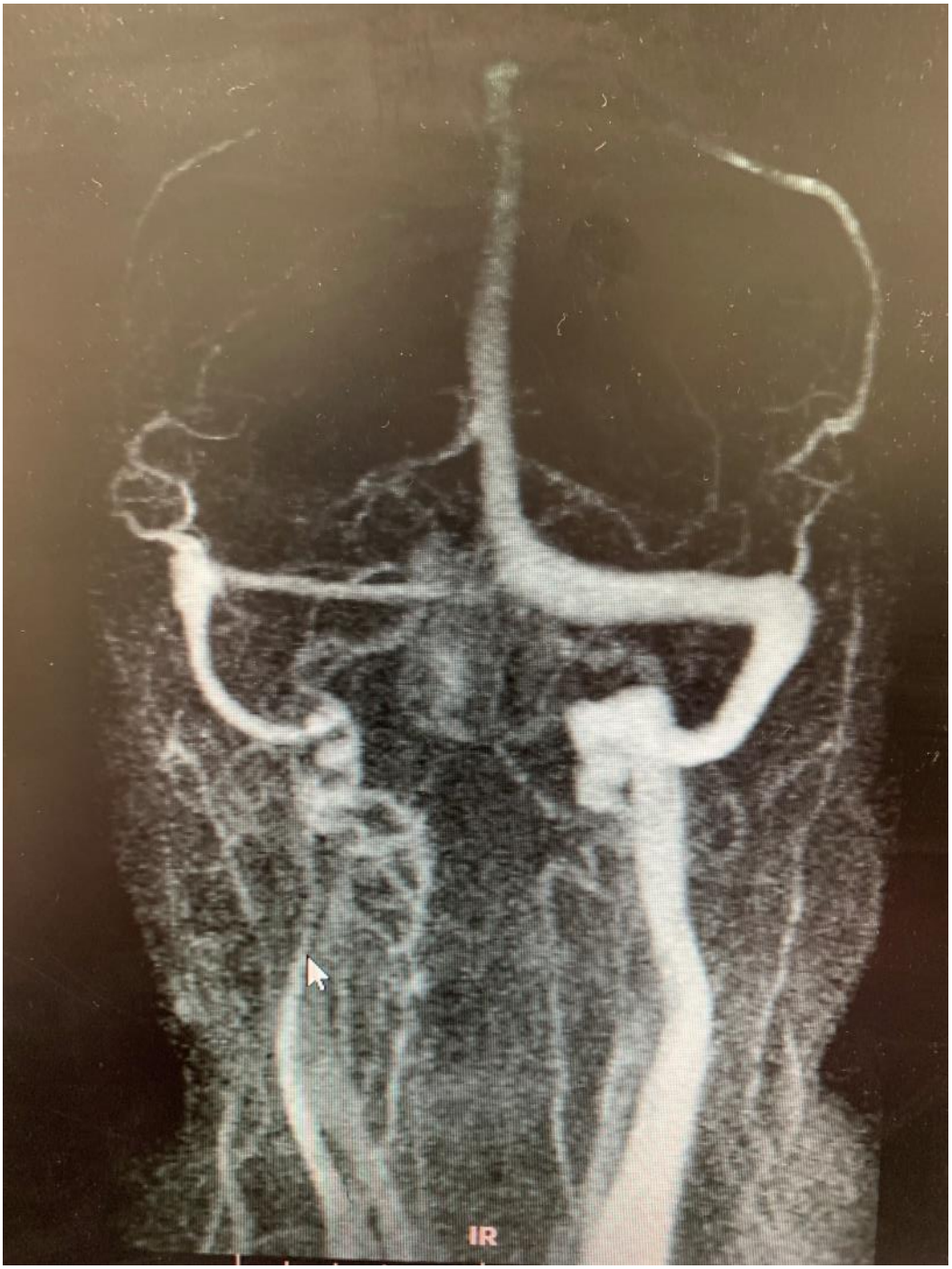


3. Discussion

LS is a medical emergency characterized by acute neck vein thrombosis and septic embolism, complicating a bacterial infection commonly following oropharyngeal infection. Variations to this presentation, however, can occur. The primary infection might arise from other sites, nasopharyngeal, including dental, sinus and ear infections, mastoiditis, cellulitis, intravenous drug abuse and catheterization of the IJV. The infection can progress by hematogenous spread to other organs. The most common distantly affected places are lungs, joints and central nervous system, as observed in our patient. Patients

with LS have a substantial risk of new thromboembolic complication, long-term sequelae and death [8]. They typically have neutrophil leukocytosis, and the C-reactive protein is invariably raised, which may indicate an infection or inflammatory condition. The mean age of patients with LS is 22 years [9]. So, our patient is older than this demographic.

Figure 4. Angio-MR image scan of the head and neck showing filling defect of right internal jugular vein, suspecting thrombosis (arrow). Additionally, we can observe reduction of flow in the right sigmoid and transverse sinuses because of thrombosis.



Ocular symptoms of LS are rarely documented and can occur with unusual characteristics. In this case, the patient was initially presented with typical signs and symptoms of periorbital cellulitis, including periorbital swelling, redness, and pain following pimple

drainage inside the nose. The visual acuity remained intact. He meets the diagnostic criteria for LS which includes positive blood cultures for Staphylococcus aureus, imaging evidence of IJV thrombosis and metastatic infection for the lungs. Like our case, Newman et al. described a case of LS originating from preseptal cellulitis due to Staphylococcus aureus without evidence of preceding pharyngitis [5]. Additionally, our patient presented with bilateral abducens nerve palsy and diplopia. Elhakeen et al. also reported an atypical case of a patient with history of recent herpes zoster infection who presented with orbital cellulitis secondary to malignant Staphylococcus aureus facial infection, as well as partial thrombosis of facial and superior ophthalmic vein [10].

The sixth cranial nerve is the most affected ocular motor nerve in adults. The main causes of bilateral abducens palsy are trauma, tumors, and vascular lesions including aneurysms, cerebrovascular accident and arteriovenous malformations [8]. Thrombosis of cerebral veins and sinuses have variable symptoms and signs. Diplopia is the most common symptom in patients with abducens nerve palsy and was present in our patients. The exact mechanism in our patient's bilateral abducens nerve palsy is unclear. The proximity of cavernous sinus to cranial nerves III, IV, V, and VI is of great importance. He possibly had IJV thrombosis on the right side that probably extended to the right cavernous sinus. Krezpointner et al. analyzed data of 27 (3.8%) patients with ophthalmic complications in a cohort of 712 patients with LS. IJV thrombosis was found in 21 (78%) and impaired eye movements/nerve palsy in 6 (21%) patients who presented with ophthalmologic complications [7]. Recently, Vu et al. reported a case of septic thrombophlebitis resulting in bilateral abducens nerve palsy and meningitis [11]. A literature review by Kupalli et al. in 2012 showed that patients suffering from meningitis usually have a poor outcome or unresolved neurologic deficit [12].

Staphylococcus aureus is an opportunistic gram-positive coccus bacterium that is part of the normal flora on skin, soft tissue and nasal passages. It is the leading cause of skin and soft tissue infections, and septic abscesses. It has emerged as a cause of LS in recent years [3,5,6]. Soft tissue infections in areas around the nose and upper lip (danger area of the face) can be dreadful, due to the presence of valveless venous channels [13]. So, furuncles about this zone should not be traumatized by squeezing or small incisions. The infection likely tracked through small facial veins and orbital veins into the dural sinus, ultimately leading to thrombosis of the IJV, septicemia and resultant septic embolization. Chanin et al. reviewed 11 cases of Staphylococcus aureus-associated LS published in the literature from 1965 to 2010. All these cases were published after 2002, and for all cases, metastatic spread to the lungs was reported; few involved the central nervous system [14].

The time of diagnosis is a very important prognostic factor. Some of the more frequent laboratory abnormalities include leukocytosis, mild to severe renal impairment, abnormal inflammatory markers like C-reactive protein and ESR, thrombocytopenia, as well as other evidence of disseminated intravascular coagulation. These are all well-known features of acute phase reaction and of sepsis [15]. Distinguishing between simple cellulitis and septic embolism during the early course of the infection can be a difficult task. Demonstration of infection is crucial to the correct diagnosis. When the disease is suspected, diagnostic imaging modalities are recommended as soon as possible to confirm thrombotic lesions and the presence of metastatic abscesses in distant organs, while awaiting blood cultures results. Chest x-ray is often the primary study performed in acute care and classically demonstrates bilateral pulmonary consolidation and small pleural effusions; however, chest x-ray appears normal in about 10% of patients [9]. Various other imaging modalities, such as CT or MR imaging scan with contrast, simple echography or Doppler ultrasound scan in the cervical region can be used to show filling failures or even the thrombus in the IJV and confirm the diagnosis. Retrograde venography is the gold standard for diagnosis of venous thrombosis, but this procedure is invasive [16].

LS remains a serious disease even in this millennium. Treatment is primarily medical management with fluids and antimicrobial therapy. Despite advances in detection and

treatment, mortality for LS remains high. Broad-spectrum antibiotics should not be delayed, and the median duration is 3-6 weeks to allow for complete penetration of the fibrin clot and abscess [16,17]. When the infection is controlled, therapy can be completed orally. Fortunately, our patient was immediately placed on broad-spectrum antibiotics. Once Staphylococcus aureus was identified on culture, he was maintained with vancomycin and meropenem to maximize the bactericidal activity against gram-positive cocci with good central nervous system penetration. An antifungal agent may be added in cases with suspected fungal etiology. Surgical exploration is rarely required. Minimally invasive catheter drainage may be necessary to drain parapharyngeal, cervical, or pulmonary abscesses. A more drastic therapy with ligation and excision of the IJV is only indicated in cases of persistent septic emboli despite antibiotic treatment [17].

The utility of anticoagulation therapy in LS is considerable controversial, with uncertainties regarding indications, choice of agent, dosage and duration. Due to the rarity of this syndrome, there are no controlled trials to validate this practice. Although studies have shown the efficacy and safety of anticoagulation in preventing septic embolic events originating from IJV thrombosis [18,19], further controlled studies are needed. A retrospective analysis of 712 reported cases showed anticoagulation therapy reduced in-hospital new venous thromboembolism and new peripheral septic lesions with less major bleeding [19]. Meanwhile, a recent meta-analysis was performed on 194 patients to examine the effect of anticoagulation on mortality, and on 50 patients to evaluate the effect of anticoagulation on vessel recanalization on follow-up imaging.

Neither relationship was statistically significant, showing no significant effect on mortality or vessel recanalization with anticoagulation in these subsets of LS patients [20]. Additionally, Karkos et al., after reporting a case and performing a brief literature review, concluded that there is no evidence for a beneficial effect of anticoagulant therapy [9]. Some authors claim that anticoagulation appears to be relatively efficacious and safe in LS, with no attributed bleeding complications, increasing the rate of thrombophlebitis resolution with clot destruction [21]. Indeed, one must consider its risks and benefits in each individual patient. In our case, due to the sudden onset of respiratory compromise, possible IJV thrombus and absence of potential risks, anticoagulation therapy was considered.

4. Conclusion

Ophthalmological manifestations of LS can show atypical symptoms, such as diplopia and strabismus, if the cranial nerve is affected. This case illustrates bilateral abducens nerve palsy, an unusual presentation of LS and highlights the importance of considering uncommon pathogens as the etiology of based on the suspected source of the primary infection. The suspected initial infection was staphylococcus aureus mediated periorbital cellulitis. Our patient was middle aged and immunocompetent man with no underlying predisposing disease, who responded well to intravenous treatment. Early and accurate diagnosis through a combination of clinical symptoms, inflammatory markers, imaging findings, and blood cultures can facilitate aggressive treatment and contributes for a favorable outcome of this rare disease which may require a multidisciplinary approach to patient care. Therefore, LS should be suspected in patients with signs of sepsis and cranial nerve palsy. Future research and randomized trials are needed to develop consensus guidelines for diagnosis and treatment of Lemierre disease.

Funding: Not applicable.

Research Ethics Committee Approval: We declare that the patient approved the study by signing an informed consent form and the study followed the ethical guidelines established by the Declaration of Helsinki.

Acknowledgments: None.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Risoud M, Mortuaire G, Chevalier D, Rysman B. Atypical Lemierre syndrome. Eur Ann Otorhinolaryngol Head Neck Dis. 2016 Apr;133(2):123-4. doi: 10.1016/j.anorl.2015.12.001.
2. Dasari SP, Jha P. A Systematic Review of Lemierre's Syndrome With a Focus on Ophthalmologic Complications. Cureus 2020;12(7):e9326. doi: 10.7759/cureus.9326.
3. Salami A, Assouan C, Garba I, Konan E. An unusual cause of Lemierre Syndrome. J Stomatol Oral Maxillofac Surg. 2019;120(4):358-360. doi: 10.1016/j.jormas.2019.02.009.
4. Branson SV, McClintic E, Yeatts RP. Septic cavernous sinus thrombosis associated with orbital cellulitis: a report of 6 cases and review of literature. Ophthal Plast Reconstr Surg 2019;35:272-80.3. doi: 10.1097/IOP.0000000000001231.
5. Newman N, Bantikassegn A, West TG, Peacock JE Jr. An Unusual Etiology of Lemierre-Like Syndrome: Preseptal Cellulitis due to Methicillin-Resistant Staphylococcus aureus. Open Forum Infect Dis 2022;9(5):ofac143. doi: 10.1093/ofid/ofac143.
6. Kadhiravan T, Piramanayagam P, Banga A, Gupta R, Sharma SK. Lemierre's syndrome due to community-acquired methicillin-resistant Staphylococcus aureus infection and presenting with orbital cellulitis: a case report. J Med Case Rep 2008;2:374. doi: 10.1186/1752-1947-2-374.
7. Kreuzpointner R, Valerio L, Corsi G, Zane F, Sacco C, Holm K, Righini C, Pecci A, Zweifel S, Barco S. Ophthalmic complications of Lemierre syndrome. Acta Ophthalmol 2022;100(1):e314-e320. doi: 10.1111/aos.14871.
8. Durkin SR, Tennekoon S, Kleiinschimidt A, Casson RJ, Selva D, Crompton JL. Bilateral six nerve palsy. Ophthalmology 2006;113(11):2108-9. doi: 10.1016/j.ophtha.2006.06.026.
9. Karkos PD, Asrani S, Karkos CD, Leong SC, Theochari EG, Alexopoulou TD, Assimakopoulos AD. Lemierre's syndrome: A systematic review. Laryngoscope. 2009;119(8):1552-9. doi: 10.1002/lary.20542.
10. Elhakeem IA, Al Shokri SD, Elzouki AY, Danjuma MI. An Unusual Case of Modified Lemierre's Syndrome Caused by Staphylococcus aureus Cellulitis. Am J Case Rep 2020;21:e916575. doi: 10.12659/AJCR.916575.
11. Vu VN, Savino PJ, Robbins SL. Bilateral abducens nerve palsy due to septic thrombophlebitis. Am J Ophthalmol Case Rep 2019;16:100566.
12. Kuppalli K, Livorsi D, Talati NJ, Osborn M. Lemierre's syndrome due to Fusobacterium necrophorum. Lancet Infect Dis 2012;12 (10): 808-15. doi: 10.1016/S1473-3099(12)70089-0.
13. Maes U. Infections of the dangerous áreas of the face: their pathology and treatment. Ann Surg 1937;106(1):1-10. doi: 10.1097/00000658-193707000-00002.
14. Chanin JM, Marcos LA, Thompson BM, Yusen RD, Dunne WM Jr, Warren DK, Santos CA. Methicillin-resistant Staphylococcus aureus USA300 clone as a cause of Lemierre's syndrome. J Clin Microbiol. 2011;49(5):2063-6. doi: 10.1128/JCM.02507-10.
15. Fumagalli RM, Gloor E, Kaufmann PA, Frehner M, Voci D, Konstantinides SV, Kucher N, Nicoletti TF, Pecci A, Valerio L, Barco S. Common laboratory tests and their correlation with the clinical presentation and prognosis of Lemierre syndrome. Anaerobe 2023;83:102773. doi: 10.1016/j.anaerobe.2023.102773
16. Hadjinicolaou AV, Philippou Y. Lemierre's syndrome: a neglected disease with classical features. Case Rep Med 2015;2015:846715. doi: 10.1155/2015/846715
17. Lee WE, Jean SS, Chen FL, Hsieh SM, Hsueh PR. Lemierre's syndrome:A forgotten and re-emerging infection. Journal of Microbiology, Immunology and Infection 2020;53(4):513-7. doi: 10.1016/j.jmii.2020.03.027.
18. Adedeji A, Chukwura O, Obafemi T, McNulty SB, Reinert JP. Anticoagulation Strategies in the Management of Lemierre Syndrome: A Systematic Review of the Literature. Ann Pharmacother 2021;55(5):658-65. doi: 10.1177/1060028020957620.
19. Valerio L, Zane F, Sacco C, Granziera S, Nicoletti T, Russo M, et al. Patients with Lemierre syndrome have a high risk of new thromboembolic complications, clinical sequelae and death: an analysis of 712 cases. J Intern Med 2021;289(3):325–39. doi: 10.1111/joim.13114.
20. Gore MR. Lemierre Syndrome: A Meta-analysis. Int Arch Otorhinolaryngol 2020;24(3):379–385. doi: 10.1055/s-0039-3402433.
21. Adedeji A, Chukwura O, Obafemi T, McNulty SB, Reinert JP. Anticoagulation Strategies in the Management of Lemierre Syndrome: A Systematic Review of the Literature. Ann Pharmacother. 2021 May;55(5):658-665. doi: 10.1177/1060028020957620.