



Case report

Cavernous sinus thrombosis caused by *Streptococcus constellatus*-associated Lemierre syndrome presenting as an isolated abducens nerve palsy

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ABSTRACT

Purpose: To describe a patient with *Streptococcus constellatus*-associated Lemierre syndrome complicated by eventual cavernous sinus thrombosis (CST) that manifested as an isolated abducens nerve palsy.

Observations: A patient with a history of heavy alcohol use presented with Lemierre syndrome caused by an odontogenic infection due to *Streptococcus constellatus*. Despite initiation of intravenous antibiotics and eventual eradication of her bacteremia, she developed an isolated abducens nerve palsy on hospital day 7 due to associated CST.

Conclusions and Importance: CST is a rare complication of odontogenic infection and Lemierre syndrome. This case demonstrates the potential for primary odontogenic infections to progress to life- and sight-threatening diseases. This case also illustrates the importance of considering uncommon pathogens as the etiology of CST based on the suspected source of primary infection.

1. Introduction

Lemierre syndrome is a rare disease characterized by infectious thrombophlebitis of the internal jugular vein following an oropharyngeal infection.^{1–5} Lemierre syndrome is most commonly caused by *Fusobacterium necrophorum*, but cases involving *Staphylococcus*, *Klebsiella*, and *Streptococcus* species have been described.^{6–9}

Cavernous sinus thrombosis (CST) is a rare syndrome that occurs due to infectious and non-infectious causes and is an uncommon complication of Lemierre syndrome.^{1–5,10–22} The most common microorganism causing CST is *Staphylococcus aureus*,²³ and there are only few reports of CST due to *Streptococcus constellatus*, a saprophyte typically found in the oral mucosa.^{24–28} In this report, we describe a patient who presented initially with *Streptococcus constellatus*-associated Lemierre syndrome complicated by eventual CST that presented as an isolated abducens nerve palsy.

2. Case report

A 62-year-old woman with a history of alcohol abuse was brought to the emergency department for 3 days of dental pain, facial swelling, and altered mental status. Upon arrival, her Glasgow Coma Scale was 13 and she was not oriented to time or place. She was febrile with a temperature of 40° Celsius and a heart rate of 160 beats per minute.

Past medical history was significant only for hypertension and a family history of seizure disorder. Social history was significant for daily alcohol intake. She had no pertinent surgical history and took no medications. On examination, pupils measured 1 mm in diameter and were minimally reactive to light without an afferent pupillary defect. Visual acuity was unable to be adequately tested but was at least hand motion in both eyes. She was orthotropic in primary gaze and her ocular motility was full. Intraocular pressures were 19 and 14 mm Hg in the right and left eyes, respectively. She was noted to have right periorbital and temporal edema and erythema. There was inferior chemosis of the right conjunctiva but no conjunctival erythema. The rest of the examination including fundus examination was unremarkable.

Initial workup showed signs of septic shock with a serum anion gap of 23 mEq/L, lactic acid of 4.8 mmol/L, and white blood cell count of 15,000/mm³. The patient was immediately started on intravenous vancomycin, piperacillin/tazobactam, and metronidazole. Urinalysis was unremarkable but chest radiograph demonstrated a 2.7 cm right upper lung opacity in addition to heterogeneous basilar opacities (Fig. 1). Computed tomography (CT) of the chest without contrast was performed which revealed bilateral lung masses and nodules with a feeding vessel sign, consistent with septic emboli (Fig. 2). CT of the face with contrast revealed multi-fascial space abscesses with phlegmon and gas extending to the right lateral supraorbital soft tissues via a thrombophlebitic right retromandibular vein and superior temporal vein.

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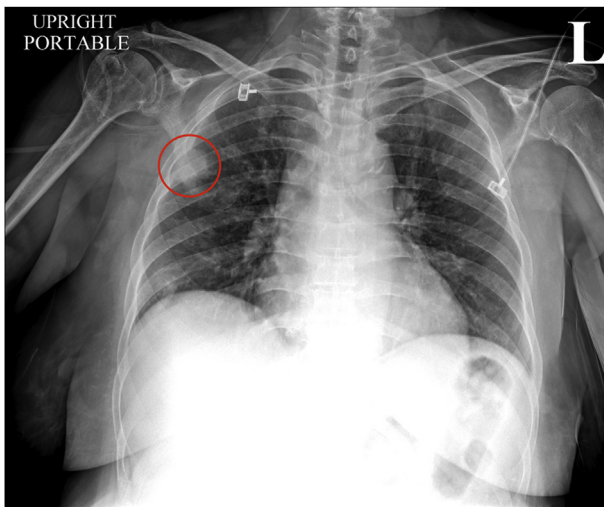


Fig. 1. Chest radiograph demonstrating a 2.7 cm right upper lung opacity in addition to heterogeneous basilar opacities.

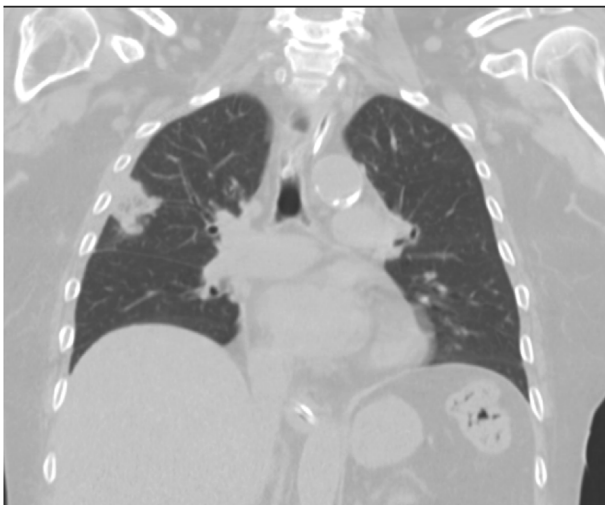


Fig. 2. Computed tomography (CT) of the chest without contrast revealing an irregular right upper lobe mass.

Periorbital cellulitis and thrombophlebitis of the right infraorbital facial vein and right internal jugular vein were also noted (Fig. 3). CT of the head without contrast was unremarkable. Transthoracic echocardiogram was performed due to concern for endocarditis in the setting of septic emboli, but revealed only mild to moderate aortic regurgitation and a small pericardial effusion without overt signs of valvular vegetation or intracardiac abscess.

After stabilization, she underwent incision and drainage of her facial abscesses with extraction of five carious teeth. On hospital day 3, initial blood and abscess cultures grew viridans group streptococci that were eventually identified as *Streptococcus constellatus*. Tracheal aspirate and urine cultures were negative. Blood culture susceptibilities revealed a minimal inhibitory concentration of $< 0.1 \mu\text{g/mL}$ to penicillin. Therefore, vancomycin, clindamycin, and piperacillin/tazobactam were discontinued and ampicillin/sulbactam was started. Anticoagulation for thrombophlebitis was considered but was held as subsequent blood cultures demonstrated eradication of the bacteremia.

The patient's clinical condition improved and she was eventually transferred out of the intensive care unit. However, on hospital day 7, she complained of binocular diplopia and was noted to have a large right incomitant esotropia with -4 abduction, consistent with lateral rectus paralysis due to a right sixth nerve palsy. Cranial nerve function

and extraocular movements were otherwise intact (Fig. 4) and signs of nystagmus were absent. Intraocular pressures and visual acuities were 16 mm Hg and 20/30 bilaterally. She had mild chemosis that was improved from admission and no conjunctival erythema. CT angiogram of the head revealed hypoenhancement of the right greater than left cavernous sinuses, concerning for CST (Fig. 5). CT of the face with contrast showed persistence of the multifascial abscesses so repeat incision and drainage was performed. Anticoagulation was again considered but was avoided due to a coinciding upper gastrointestinal bleed.

She eventually required another incision and drainage due to radiographic concern for non-resolution of her facial infection but was discharged shortly thereafter. At discharge, she was switched from intravenous ampicillin/sulbactam to ertapenem for a total of six weeks of treatment from her first negative blood culture. At 6-week follow-up, she demonstrated no improvement of her sixth nerve palsy.

3. Discussion

Lemierre syndrome most commonly occurs in young, healthy adolescents but is also seen in immunocompromised patients.^{13,14,18,29,30} Most cases develop from primary infections of the head and neck such as pharyngitis and tonsillitis.³¹ Primary odontogenic infection is a less common cause of Lemierre syndrome, accounting for only about two percent of all cases.³²

Pulmonary manifestations, including septic pulmonary emboli, as seen in our patient, are the most common complications of Lemierre syndrome, occurring in up to 79% of patients.⁵ Neurologic impairments are much less common but have been reported, most often arising from local spread of infection to involve cranial nerves IX, X, and XII.¹³ While less frequent, central nervous system (CNS) involvement may also occur as a result of metastatic spread, manifesting as cerebral venous thrombosis, meningitis, ischemic stroke, mycotic aneurysm, and CST.^{1-5,10-16,18-22}

CST is a particularly rare but important complication of Lemierre syndrome. Hypothesized pathogenic mechanisms include progression of infection through the venous, arterial, or lymphatic systems and creation of a procoagulant cascade with subsequent thrombophlebitis.^{13,18,27} CST primarily manifests with ophthalmic findings including eye pain, ophthalmoplegia, proptosis, and chemosis. The abducens nerve is one of the most frequently affected structures in the cavernous sinus.³³

As alluded to above, Lemierre syndrome and CST are most frequently due to *Fusobacterium necrophorum* and *Staphylococcus aureus*, respectively. *Streptococcus constellatus* is a rare cause of both Lemierre syndrome and CST. However, uncommon pathogens, particularly those of odontogenic origin, should be suspected in immunocompromised patients presenting with signs of a preceding dental infection.²⁷ Indeed, etiology should be investigated in all patients presenting with suspected CST or Lemierre syndrome by obtaining blood cultures to allow for the administration of an appropriate and effective antimicrobial regimen.

A typical empiric regimen for CST includes a third-generation cephalosporin, an anti-staphylococcal agent, and metronidazole for coverage of anaerobes. An antifungal agent may be added in cases with suspected fungal etiology. Antibiotics with sufficient CNS penetration should be used in the treatment of Lemierre syndrome-associated CST. Indeed, the infection may be recalcitrant due to difficulty in achieving adequate concentrations of antibiotics in the CNS and penetrating septic emboli.¹⁸ Surgical management may be necessary to control the primary infectious source but is not recommended for the cavernous sinuses themselves.³⁴

The utility of anticoagulation in the treatment of Lemierre syndrome is controversial. A recent retrospective study involving twenty-four patients with Lemierre syndrome found no difference in the incidence of recurrent thrombosis or progression between patients who received antibiotics alone or antibiotics in conjunction with anticoagulation.³⁵ Indeed, anticoagulation has generally been reserved for

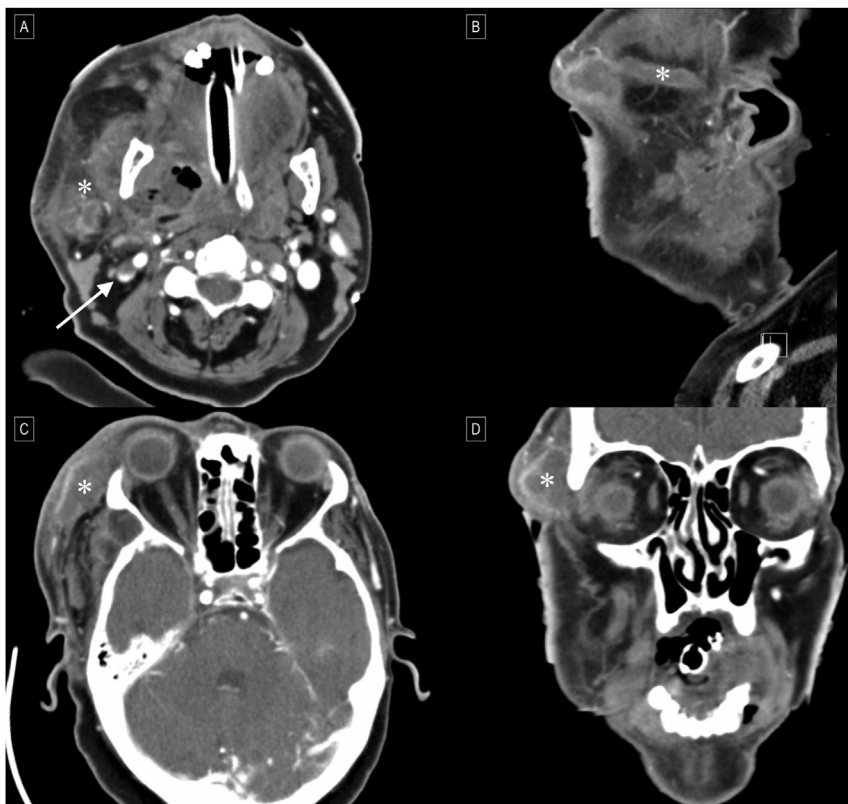


Fig. 3. Computed tomography (CT) of the face with contrast demonstrating (A) thrombophlebitis of the right internal jugular vein (arrow) and a complex, multiloculated, rim-enhancing fluid and gas-filled collection in the right masticator space consistent with an abscess (asterisk). (B) A thrombophlebitic right superficial temporal vein appears to communicate with the masticator space abscess (asterisk) and (C,D) a separate heterogeneously enhancing collection in the right lateral supraorbital soft tissues consistent with a developing abscess (asterisk).



Fig. 4. Ocular motility testing, demonstrating right-sided large-angle incomitant esotropia with a -4 abduction defect. Extraocular movements were otherwise intact.

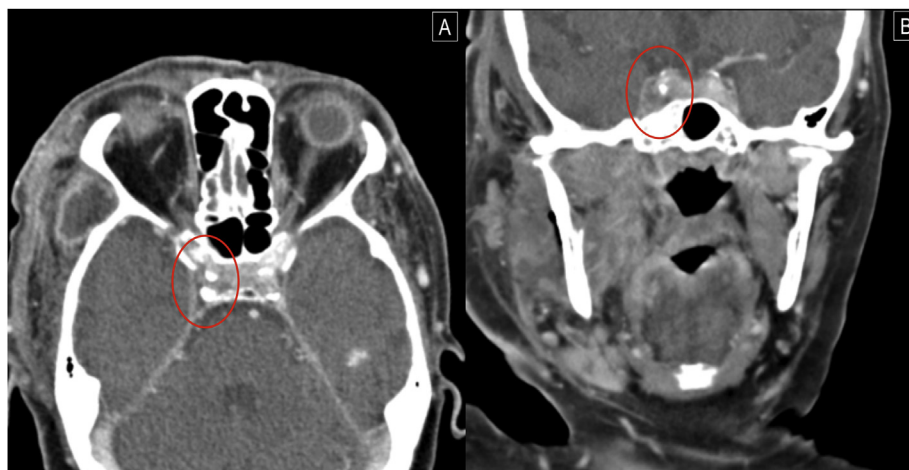


Fig. 5. Computed tomography (CT) of the face with contrast. (A) Axial and (B) coronal views demonstrating hypoenhancement of the right greater than left cavernous sinuses, indicative of cavernous sinus thrombosis (CST).

cases unresponsive to antibiotic therapy or in patients with predisposing thrombophilia.³⁶

On the other hand, anticoagulation for CST is generally recommended. Although prospective clinical trials have not been performed, retrospective reviews have demonstrated reduced morbidity and mortality with the use of anticoagulation therapy in CST.^{34,37,38} Indeed, most reported cases of concurrent Lemierre syndrome and CST have been treated with anticoagulation in addition to antibiotics, with resultant improvement in clinical status.^{1–3,5,10–16,18–22} However, in the two reported cases where anticoagulation was not used, both patients showed clinical improvement with only antibiotics.^{4,17} In our patient, we were unable to administer anticoagulation therapy due to an acute gastrointestinal bleed. Indeed, one must consider the risks and potential benefits of using anticoagulation therapy in each individual patient.

4. Conclusions

We present an uncommon complication of Lemierre syndrome manifesting as an isolated cranial nerve deficit. Through this case, we demonstrate the potential for primary odontogenic infections to progress to life- and sight-threatening diseases. Furthermore, we demonstrate the importance of considering uncommon pathogens as the etiology of CST based on the suspected source of the primary infection.

Patient consent

Consent to publish this case report was obtained from the patient in writing.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The following authors have no financial disclosures: LJR, SMG, DD, CJM, SD.

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References

- Miller B, Khalifa Y, Feldon SE, Friedman DI. Lemierre syndrome causing bilateral cavernous sinus thrombosis. *J Neuro Ophthalmol*. 2012;32(4):341–344. <https://doi.org/10.1097/WNO.0b013e31825e42ae>.
- Shibuya K, Igarashi S, Sato T, Shinbo J, Sato A, Yamazaki M. A case of Lemierre syndrome associated with infectious cavernous sinus thrombosis and septic meningitis. *Rinsho Shinkeigaku*. 2012;52(10):782–785. <https://doi.org/10.5692/clinicalneuro.52.782>.
- Rudski Ricondo L, Ramos Gómez MJ, Aguilar Cantador J, Bravo-Rodríguez FA. Lemierre syndrome: thrombosis of the cavernous sinus and internal carotid artery occlusion secondary to acute sphenoid sinusitis. *Acta Otorrinolaringol*. 2013;64(1):75–77. <https://doi.org/10.1016/j.otoeng.2013.02.004> (English Ed).
- Bababegy SR, Almarzouki H, Buffenn AN. Isolated abducens nerve palsy secondary to Lemierre syndrome. *J AAPOS*. 2011;15(6):587–589. <https://doi.org/10.1016/j.jaapos.2011.06.010>.
- He J, Lam JCL, Adlan T. Clival osteomyelitis and hypoglossal nerve palsy-rare complications of Lemierre's syndrome. *BMJ Case Rep*. 2015;2015. <https://doi.org/10.1136/bcr-2015-209777>.
- Yaita K, Sugi S, Hayashi M, et al. The co-existence of Lemierre's syndrome and Bezold's abscesses due to *Streptococcus constellatus*. *Medicine*. 2018;97(26) <https://doi.org/10.1097/MD.00000000000011228> (United States).
- Chuncharunee A, Khawcharoenporn T. Lemierre's syndrome caused by *Klebsiella pneumoniae* in a diabetic patient: a case report and review of the literature. *Hawaii J Med Public Heal*. 2015;74(8):260–266.
- Garbati MA, Ahsan AM, Hakawi AM. Lemierre's syndrome due to *Klebsiella pneumoniae* in a 63-year-old man with diabetes: a case report. *J Med Case Rep*. 2012;6. <https://doi.org/10.1186/1752-1947-6-97>.
- Jariwala RH, Srialluri S, Huang MZ, Boppana SB. Methicillin-resistant *Staphylococcus aureus* as a cause of Lemierre's syndrome. *Pediatr Infect Dis J*. 2017;36(4):429–431. <https://doi.org/10.1097/INF.0000000000001460>.
- Morelli N, Rota E, Sacchini D, et al. Lemierre syndrome: more than the forgotten disease. *Neurology*. 2013;81(13):1179–1180. <https://doi.org/10.1212/WNL.0b013e3182a55f30>.
- Golan E, Wong K, Alahmadi H, et al. Endoscopic sphenoid sinus drainage in Lemierre syndrome. *J Clin Neurosci*. 2014;21(2):346–348. <https://doi.org/10.1016/j.jocn.2013.02.020>.
- Gutzeit A, Roos JE, Portocarrero-Fäh B, et al. Differential diagnosis of Lemierre's syndrome in a patient with acute paresis of the abducens and oculomotor nerves. *Korean J Ophthalmol*. 2013;27(3):219. <https://doi.org/10.3341/kjo.2013.27.3.219>.
- Stauffer C, Josiah AF, Fortes M, et al. Lemierre syndrome secondary to community-acquired methicillin-resistant *Staphylococcus aureus* infection associated with cavernous sinus thromboses. *J Emerg Med*. 2013;44(2) <https://doi.org/10.1016/j.jemermed.2012.02.075>.
- Ridgway JM, Parikh DA, Wright R, et al. Lemierre syndrome: a pediatric case series and review of literature. *Am J Otolaryngol - Head Neck Med Surg*. 2010;31(1):38–45. <https://doi.org/10.1016/j.amjoto.2008.09.006>.
- Lim SC, Lee SS, Yoon TM, Lee JK. Lemierre syndrome caused by acute isolated sphenoid sinusitis and its intracranial complications. *Auris Nasus Larynx*. 2010;37(1):106–109. <https://doi.org/10.1016/j.anl.2009.02.012>.
- Touitou D, Deltour S, Bonneville F, et al. Hemiplegia in Lemierre syndrome: a neuroimaging strategy. *Eur J Neurol*. 2006;13(4):424–426. <https://doi.org/10.1111/j.1468-1331.2006.01155.x>.
- Yamaguchi M, Nishizawa H, Yasumoto T, et al. Lemierre syndrome with blepharoptosis. *Intern Med*. 2010;49(8):753–757. <https://doi.org/10.2169/internalmedicine.49.2779>.
- Westhout F, Hasso A, Jalili M, et al. Lemierre syndrome complicated by cavernous sinus thrombosis, the development of subdural empyemas, and internal carotid artery narrowing without cerebral infarction. *J Neurosurg Pediatr*. 2008;106(1):53–56. <https://doi.org/10.3171/ped.2007.106.1.53>.
- Nishida A, Ogata T, Kudo M, et al. A case with both infectious cavernous sinus thrombosis and Lemierre syndrome due to intraoral resident flora. *Rinsho Shinkeigaku*. 2015;55(7):483–489. <https://doi.org/10.5692/clinicalneuro.cn-000676>.
- Martel A. Septic thrombosis of cavernous sinus extended to the ipsilateral internal jugular vein and transversal sinus with favorable outcome: clinical and radiological features of a Lemierre syndrome. *Orbit*. 2018;37(2):94–96. <https://doi.org/10.1080/01676830.2017.1383458> (London).
- Wang YH, Chen PY, Ting PJ, Huang FL. A review of eight cases of cavernous sinus thrombosis secondary to sphenoid sinusitis, including a 2-year-old girl at the present department. *Infect Dis*. 2017;49(9):641–646. <https://doi.org/10.1080/23744235.2017.1331465> (Auckland).
- Budhram A, Shettar B, Lee DH, et al. Bilateral cavernous sinus thrombosis in Lemierre's syndrome. *Can J Neuro Sci*. 2017;44(4):424–426. <https://doi.org/10.1017/cjn.2016.438>.
- Dinkin M, Patsalides A, Ertel M. Diagnosis and management of cerebral venous diseases in neuro-ophthalmology: ongoing controversies. *Asia-Pacific J Ophthalmol*. 2019;8(1):73–85. <https://doi.org/10.22608/apo.2018239>.
- Chang WN, Chen SD, Lui CC, et al. Septic cavernous sinus thrombosis due to *Streptococcus constellatus* infection. *J Formos Med Assoc*. 2003;102(10):733–736.
- Hoshino C, Satoh N, Sugawara S, et al. Septic cavernous sinus thrombosis complicated by narrowing of the internal carotid artery, subarachnoid abscess and multiple pulmonary septic emboli. *Intern Med*. 2007;46(6):317–323. <https://doi.org/10.2169/internalmedicine.46.6202>.
- Goawalla A, Mansell N, Pearson A. Septic cavernous sinus thrombosis with bilateral secondary orbital infection. *Orbit*. 2007;26(2):113–116. <https://doi.org/10.1080/01676830600675418>.
- Jones RG, Arnold B. Sudden onset proptosis secondary to cavernous sinus thrombosis from underlying mandibular dental infection. *BMJ Case Rep*. 2009;2009:1671. <https://doi.org/10.1136/bcr.03.2009.1671> bcr03.2009.
- Allegrini D, Reposi S, Nocerino E, Pece A. Odontogenic orbital cellulitis associated with cavernous sinus thrombosis and pulmonary embolism: a case report. *J Med Case Rep*. 2017;11(1):164. <https://doi.org/10.1186/s13256-017-1309-0>.
- Golan E, Wong K, Alahmadi H, et al. Endoscopic sphenoid sinus drainage in Lemierre syndrome. *J Clin Neurosci*. 2014;21(2):346–348. <https://doi.org/10.1016/j.jocn.2013.02.020>.
- Tewfik TL, Husein M, Shapiro RS, Oudjhan K. Lemierre syndrome in an immunocompromised patient. *Int J Pediatr Otorhinolaryngol*. 1999;51(3):195–199. [https://doi.org/10.1016/S0165-5876\(99\)00264-5](https://doi.org/10.1016/S0165-5876(99)00264-5).
- Moore BA, Dekle C, Werkhaven J. Bilateral Lemierre's syndrome: a case report and literature review. *Ear Nose Throat J*. 2002;81(4):234–236 238–40, 242 passim.
- Malis DD, Busaidy KF, Marchena JM. Lemierre syndrome and descending necrotizing mediastinitis following dental extraction. *J Oral Maxillofac Surg*. 2008;66(8):1720–1725. <https://doi.org/10.1016/j.joms.2007.12.002>.
- Azarmina M, Azarmina H. The six syndromes of the sixth cranial nerve. *J Ophthalmic Vis Res*. 2013;8(2):160–171.
- van der Poel NA, Mourits MP, de Win MML, et al. Prognosis of septic cavernous sinus thrombosis remarkably improved: a case series of 12 patients and literature review. *Eur Arch Oto-Rhino-Laryngol*. 2018;275(9):2387–2395. <https://doi.org/10.1007/s00405-018-5062-9>.

35. Cupit MC, NageswaraRao A, Warad DM, et al. Lemierre's Syndrome: role of anticoagulation and thrombosis outcomes, a retrospective study. *Blood*. 2015;126(23):2296-2296.
36. Phan T, So TY. Use of anticoagulation therapy for jugular vein thrombus in pediatric patients with Lemierre's syndrome. *Int J Clin Pharm*. 2012;34(6):818-821. <https://doi.org/10.1007/s11096-012-9684-5>.
37. Southwick FS, Richardoson EP, Swartz MN. Septic thrombosis of the dural venous sinuses. *Medicine*. 1986;65(2):82-106. <https://doi.org/10.1097/00005792-198603000-00002> (United States).
38. Levine SR, Twyman RE, Gilman S. The role of anticoagulation in cavernous sinus thrombosis. *Neurology*. 2012;38(4):517-522. <https://doi.org/10.1212/wnl.38.4.517>.