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# Lemierre syndrome associated mycotic cavernous sinus thrombosis and carotid aneurysm after COVID-19

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ABSTRACT

*Purpose:* The purpose of this article is to report a case of Lemierre syndrome associated mycotic aneurysm of the intracavernous carotid artery leading to cavernous sinus syndrome in an otherwise healthy, young man in the setting of COVID-19 infection.

*Observations:* An 18-year-old, otherwise healthy male athlete developed fever, chills, and headache and was found to be positive for COVID-19 with gram negative bacteremia. While on systemic antibiotic treatment, he developed acute, left-sided, 6th nerve palsy and was found to have bacterial sinusitis, left-sided intracavernous mycotic aneurysm, and cavernous sinus thrombosis on imaging studies. Despite systemic antibiotic and antiplatelet therapy, he developed progressively worsening left-sided ophthalmoplegia and vision decline. He subsequently underwent left internal carotid artery embolization and cervical internal carotid artery sacrifice with excellent outcome.

*Conclusion and importance:* Lemierre syndrome can have atypical presentations and complications, including cavernous sinus thrombosis and mycotic aneurysms. Recognition of signs and symptoms, including progressive multiple cranial neuropathies, can aid in early diagnosis and management, which requires multidisciplinary care tailored to each individual based on risk of intervention.

## 1. Introduction

Lemierre syndrome, first described in 1936, is characterized by infectious thrombophlebitis, typically of the internal jugular vein (IJV), leading to multiorgan involvement. *Fusobacterium necrophorum*, part of the normal oral flora, is the most common associated organism. Although patients often present following oropharyngeal infection, few case reports have described other preceding infections such as sinusitis, otitis, and dental abscess.[1,2]

Secondary intracranial septic thrombophlebitis is rare, and cavernous sinus thrombosis secondary to Lemierre syndrome is uncommon.[2] Mycotic aneurysm is a potential, yet rare, finding associated with Lemierre syndrome and has only been described five times in the English literature.[3–7] In this report, we describe an atypical case of Lemierre's syndrome complicated by *Fusobacterium necrophorum* septicemia, bilateral sinusitis, cavernous sinus thrombosis and mycotic aneurysm of the intracavernous carotid artery (ICA).

## 2. Case report

An 18-year-old previously healthy, fully vaccinated, college athlete was brought to the emergency department for fever, chills, headache and groin pain. He was found to be positive for COVID-19 and was discharged home for quarantine. Over the next five days, he experienced worsening symptoms including nasal congestion, rhinorrhea, fevers, chills, headache, and left eye pain. He returned to the emergency room where his temperature was 103.8°F and peak heart rate was 156 beats/minute. He had no other past medical history. Initial workup revealed leukocytosis with white blood count (WBC) of 12.69; urinalysis was positive for 25 leukocyte esterase, 2+ bacteria, 6–10 WBC, and 30 proteins. Monoscreen test was positive. Computed tomography (CT) of the abdomen/pelvis was significant for hepatosplenomegaly and small bilateral pleural effusions. Blood cultures were positive for *Haemophilus influenza* and *F. necrophorum*. He was subsequently admitted and started on intravenous (IV) ceftriaxone and metronidazole.

Five days following admission, the patient noted acute onset of

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horizontal diplopia. CT imaging showed a left internal carotid artery (ICA) mycotic aneurysm with possible septic thrombophlebitis, loss of enhancement suggestive of cavernous sinus thrombosis, and bilateral sinusitis (Fig. 1). Vancomycin was added empirically at this time, and the patient was transferred to our tertiary medical center for further evaluation and management. On examination, the pupils were briskly reactive with no afferent pupillary defect. Visual acuity was 20/20 in both eyes and color vision was intact. Intraocular pressures were 15 and 8 mmHg in the right and left eye, respectively. He was noted to have a −3 abduction deficit of the left eye, consistent with left 6th cranial nerve (CN) palsy. Dilated fundus examination was unremarkable.

The same day, the patient underwent a cerebral diagnostic angiogram, which confirmed the presence of the mycotic aneurysm. Endoscopic sinus surgery disclosed extensive purulence. The following day, new onset ptosis, along with adduction, supraduction, and infraduction deficits were noted in the left eye, consistent with 3rd CN and likely partial 4th CN palsies (Fig. 2). The left pupil was apparently normal. Visual acuity of the left eye had decreased to 20/30 with preserved color vision. There was also a new loss of left CN V1 sensation, suggestive of cavernous sinus syndrome. The patient was started on Decadron to theoretically reduce inflammation and edema. Repeat MRI imaging showed interval worsening of the cavernous sinus thrombosis.

Given the patient's progressive ophthalmoplegia consistent with cavernous sinus syndrome, the decision was made to perform cerebral angiogram with plan to sacrifice the ICA. Aspirin (ASA) 325mg was given prior to the procedure. However, intra-operatively, the aneurysm was found to be largely thrombosed, and the embolic risk of sacrificing the ICA at this time was deemed too high. The patient was subsequently started on ASA 81mg.

Repeat imaging four days later showed stable appearance of the aneurysm, and the patient was started on a heparin infusion at 800 units/hour, with an anti-factor Xa goal of 0.2–0.5. However, he developed an acute onset headache the following morning and the infusion was stopped. Urgent CT head imaging was stable, and the patient underwent repeat cerebral angiogram for further evaluation. After ensuring adequate collateral flow, embolization of the mycotic aneurysm with proximal ICA sacrifice was successfully performed with coils and high-density Onyx by neurosurgery without any clinical deficits.

Post-operatively, the patient showed remarkable recovery of V1 sensation and improved CN 3 function. He was transitioned to ASA 81mg twice a day following surgery. Visual acuity improved to 20/20 in the left eye with resolution of diplopia at distance on post-operative day five. His diplopia resolved at both distance and near 3 months following intervention but continues to have mild ptosis of the left eye. In addition, he reports forgetfulness, word finding difficulty, difficulty in multitasking and concentrating after returning to college 4 months later. Neuropsychological testing revealed relative difficulties on measures of verbal memory, organization, and naming/word retrieval. He was recommended to meet with a learning specialist at school to address these difficulties. Repeat MRI at 6 and 9 months showed stable post-operative changes with no new ischemic event and the patient continues to do well without any neurological deficits.

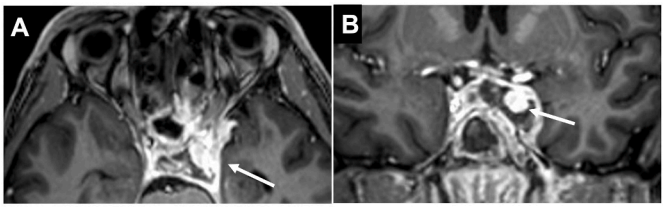


**Fig. 1.** A-B Axial and coronal magnetic resonance images (T1-weighted) demonstrating saccular enlargement of the left intracavernous carotid artery (arrows in A-B).

## 3. Discussion

Lemierre syndrome is a potentially fatal disease most commonly affecting young, healthy adolescents.[2,3] Prior to antibiotics, the disease carried a mortality rate of 32–90% compared to 5–18% with antibiotic treatment.[8] It is characterized by thrombosis of the internal jugular vein with septic thrombophlebitis associated with gram-negative septicemia, most commonly *F. necrophorum*. Classically, this develops from primary infections of the head and neck such as pharyngitis, but it has also been described following sinusitis, as in our patient.[1,4,9] Up to 92% of patients experience pulmonary complications such as septic pulmonary emboli.[10] Though less common, central nervous system (CNS) involvement can occur due to retrograde metastatic spread.

Cavernous sinus thrombosis (CST) is a rare complication of Lemierre syndrome.[11–14] The presumed pathophysiology involves extension of the primary infection into nearby vascular structures. The cavernous sinus is especially susceptible to septic thrombosis due to its extensive direct and indirect vascular connections.[15] Involvement of the cavernous sinus results in ophthalmological symptoms such as eye pain, proptosis, chemosis, ophthalmoplegia and, if severe, vision loss.[3,10,16]

Lemierre syndrome most often involves venous structures, and extension into the carotid artery is extremely uncommon.[2,3,5,6] Arterial extension can result in thrombosis, stenosis, and aneurysm formation. Chamseddin and Kirkwood described a case of ICA thrombosis and mycotic aneurysm of the external carotid artery (ECA) in a healthy 18-year-old patient.[3] Similarly, Gupta et al. described a case of bilateral mycotic aneurysms of the vertebral arteries. These cases demonstrate the variable locations of mycotic aneurysms associated with Lemierre syndrome. In our literature search, we did not find any reported cases of mycotic intracavernous carotid aneurysms secondary to Lemierre syndrome.

Mycotic aneurysms account for approximately 2.5–6.2% of all intracranial aneurysms, and mycotic aneurysms of the intracavernous carotid artery represent an exceeding rare entity. There have been to date less than fifty cases of mycotic intracavernous carotid aneurysms (ICCA) in the English literature.[17] In a sentinel autopsy study by Weisman of cavernous sinus thrombophlebitis, he found neutrophil infiltration of the arterial adventitia and media as well as reactive intimal proliferation.[18] His findings suggest that focal infection and inflammation of the artery in the setting of cavernous sinus thrombophlebitis leads to weakening of the vessel wall and aneurysm formation, likely the case in our patient. Similar to CST, mycotic ICCA can present as a cavernous sinus syndrome, with abducens nerve palsy often as the first sign[19]

The role of anticoagulation in the treatment of Lemierre syndrome is unclear. Valerio et al. demonstrated in their analysis of 712 patients that only 56% of patients receive anticoagulation despite its various thromboembolic manifestations.[20] Our patient was given a very limited dose of heparin infusion before it was terminated due to acute onset of headaches (with no acute intracranial changes on imaging). This reflects the perceived complications, such as major bleeding and fragmentation of septic thrombus leading to new septic lesions, associated with anticoagulation use in such cases. The authors found lower proportion of anticoagulant use in patients with new or recurrent thromboembolic events and recommend the consideration of routine anticoagulant treatment in patients without contraindications.[20]

In addition, there are currently no established guidelines for managing myotic ICCA. Its friable nature and precarious location make management extremely difficult and unpredictable. In contrast to non-infectious intracranial aneurysms, mycotic aneurysms are prone to rupture and carry a significantly high mortality rate of 60–90%.[21] Management strategies have ranged from conservative treatment, ICA ligation, balloon or coil occlusion, to stenting with variable outcomes.[22] Yuen et al. described a case that was treated with antibiotics and balloon occlusion which resulted in thromboembolic complications and ultimately death.[23] Arkilo et al., reported a similar case of progressively

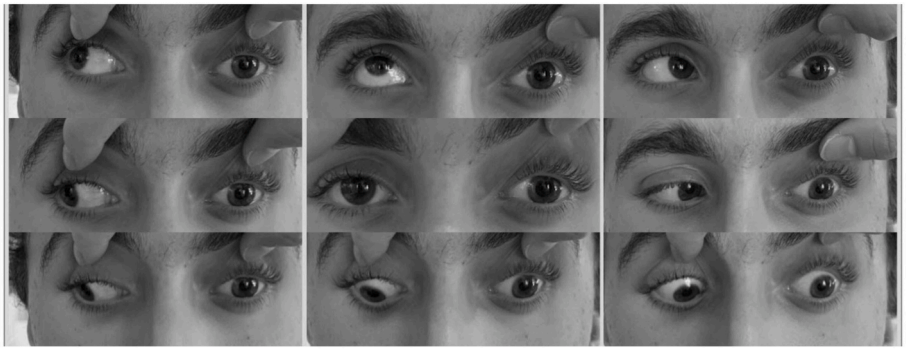

**Fig. 2.** External photography showing nine gaze directions demonstrating significant abduction, supraduction, infraduction, and adduction limitations of the left eye consistent with 3rd, 4th, and 6th cranial nerve palsies.

enlarging left internal carotid aneurysm in the setting of sphenoid sinusitis in an 8-year-old who was managed with internal carotid occlusion with a good neurologic outcome.[24] Due to the variable outcomes and lack of standardized guidelines, the management of mycotic aneurysms, especially in the pediatric population, should be tailored to the individual and the clinical presentation. With this approach, our patient had excellent outcomes without any additional ischemic events or neurologic deficits following discharge. Compared to the 10% of patients with Lemierre syndrome who experience debilitating long-term clinical sequelae,[20] our patient has returned to school and resumed playing basketball.

Interestingly, our patient's symptoms occurred within the backdrop of a recent COVID-19 infection. The novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has been associated with a wide range of bacterial and fungal co-infections.[25–27] Turbin et al., described two healthy adolescents who developed fulminant cellulitis, sinusitis, and local thrombosis following COVID-19.[26] These severe co-infections may be attributed to the documented immune dysregulation associated with COVID-19. It is unclear if COVID-19 is a contributing factor in the pathogenesis of these infections, although secondary upper respiratory congestion may have compromised mucociliary clearance leading to secondary sinus obstruction.[27]

## 4. Conclusions

We describe a highly unusual presentation of Lemierre syndrome causing cavernous sinus thrombosis and mycotic intracavernous carotid aneurysm in the setting of COVID-19 infection. In the COVID-19 era, co-infection may have created a pro-thrombotic environment that facilitated the spread of *F. necrophorum* in our patient, leading to septic cavernous sinus thrombophlebitis. Progressive loss of cranial nerve function also warrants immediate intervention which may include high dose steroid, neurosurgical intervention, and anticoagulation. Lastly, we present the importance of managing mycotic ICCA aneurysms via a multidisplinary and tailored approach.

## Patient consent

The patient and patient's legal guardian both consented to publication of the case verbally.

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## Authorship

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

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## Proprietary interest

None.

## Declaration of competing interest

None.

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