Case Report

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Torcular herophili and lateral sinus thrombosis: An atypical presentation of Lemièrre's syndrome

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Summary **Lemièrre's syndrome (LS) is an uncommon disease characterized by septic thrombophlebitis of the jugular vein in the context of otorhinolaryngologic infections. These patients are often young and the pharyngotonsillar infection is the most frequent primary focus, but other foci like acute otitis media or otomastoiditis have been described. Although the internal jugular vein is the most commonly affected site, a few case reports have been published with thrombosis of other veins, such as the facial vein or transverse sinus. We report the case of a 93-year-old woman with an atypical presentation of LS presenting with thrombophlebitis of the internal jugular vein, transverse sinuses and Herophili torcula after an acute otitis media complicated with acute otomastoiditis. Infectious cerebral venous thrombosis (CVT) is rare and accounts for 6-12% of the total in large adult series and is usually associated to otorhinolaryngologic infections. CVT is an atypical presentation of LS that can be potentially lethal, especially during the acute phase. For this reason, clinical suspicion and early treatment are vital to improve the prognosis of these patients. Although surgical treatment is recommended in cases of LS complicated with CVT, conservative management with antibiotics and anticoagulation lead to ad integrum restitutio without neurological sequelae in our case, suggesting that surgical treatment may not be necessary in all cases of LS complicated with CVT.**

Keywords: Lemièrre's syndrome, torcula herophili, cerebral venous thrombosis, otomastoiditis

1. Introduction

Lemièrre's syndrome (LS) is an uncommon disease characterized by septic thrombophlebitis of the jugular vein in the context of otorhinolaryngologic infections, with an annual incidence of 3.6 cases per million people (*1,2*). The most commonly involved bacteria is *Fusobacterium necrophorum* but other bacteria such as fusobacteria, *Streptococcus*, *Staphylococcus*, and *Enterococcus* are commonly found in cultures. Although the internal jugular vein is the most commonly affected vein, a few case reports have been published with thrombosis of other veins, such as the facial vein or transverse sinus (*3-6*). In a recent systematic review of LS, a large proportion of cases had septic emboli in the lungs (*2*). Although less frequently, septic emboli were also found in other organs, such as the liver, spleen, joints, heart, and central nervous system. These patients are often young and the pharyngotonsillar infection is the most frequent primary focus, but other foci like acute otitis media or otomastoiditis have been described (*7*).

In the pre-antibiotic era, LS was associated with a case-mortality rate of 32-90%, with embolic events in 25%, and endocarditis in 12.5% (*8*). Currently, it is still a potentially life-threatening disease with a reported mortality of up to 17% (*1,2*). The recommended

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management includes several weeks of antibiotic therapy active against *Fusobacterium*, often combined with surgical drainage. However, the benefit of anticoagulation is uncertain. The recommended empirical antibiotic should include a beta-lactamase resistant beta-lactam antibiotic associated with metronidazole (*2,8*).

The purpose of this case is to present a case of LS complicated with cerebral venous thrombosis successfully managed with a conservative treatment that comprised anticoagulation and antibiotic therapy.

2. Case Report

A 93-year-old woman presented to the Emergency Department with a 48-hour history of left-sided neck swelling and pain. In the 3 weeks before admission, she noted purulent otorrhea through the left ear. She denied a recent history of fever or headache. Her past medical history was significant for hypertension, breast cancer diagnosed 30 years ago and currently in complete remission, pulmonary embolism 3 years before and paroxysmal atrial fibrillation. She did not take no other treatment. She was receiving oral levofloxacin for 2 days prior to admission.

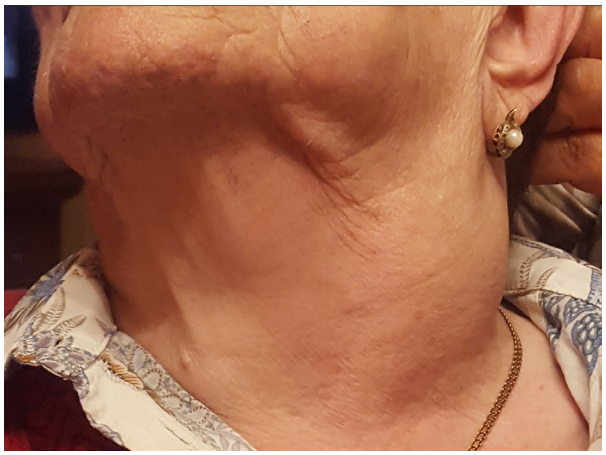

Figure 1. Physical exam revealed a left-sided neck swelling from the left submaxillary region to the supraclavicular region.

On admission, temperature was 36.4ºC, blood pressure 110/50 mm Hg and heart rate 72 bpm. A left-sided neck swelling from the left submaxillary region to the supraclavicular region (Figure 1) and deviated uvula with an area of an inflamed tonsil were noted. An otoscopy showed low secretion at left tympanic box level, slight hyperemia of the malleus and integrity of the tympanic membrane. The remainder of the physical examination was normal.

Laboratory tests disclosed hemoglobin 14.4 g/dL, leukocytes 9400/mm^3, fibrinogen 965 mg/dl, INR 1.29, C-reactive protein 20.8 mg/dL and ferritin 499 mcg/L. A computed tomography (CT) with contrast showed left side thrombosis including innominate trunk, extra and intracranial jugular vein, sigmoid sinus and transverse sinus, and partial thrombosis of torcular herophili and soft-tissue density material occupying the tympanic cage and left mastoid cells (Figure 2). A funduscopy did not show papilledema. A chest X-ray was normal. Empirical treatment was initiated with intravenous amoxicillin/clavulanic acid and anticoagulation with weight-adjusted enoxaparin. The patient presented a good response to initial therapy and showed a rapid improvement of local cervical inflammation. Bacterial identification was not performed. After 6 days, she was discharged and amoxicillin/clavulanic acid was continued for 3 weeks and anticoagulation for 3 months, without evidence of recurrence or complications.

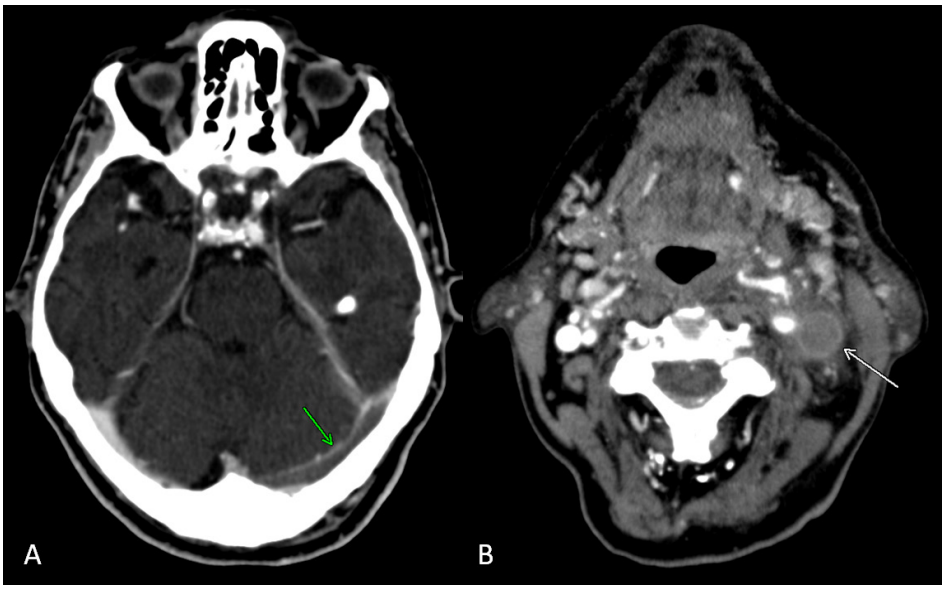

Figure 2. Combined sinus and jugular thrombosis. (A) A head CT scan shows a filing defect in the left transverse sinus (*green arrow*) and normal flow in the contralateral one. **(B)** The neck CT scan at the level of the oropharynx displays left internal jugular vein thrombosis (*white arrow*) and surrounding edema.

3. Discussion

Firstly described in 1936, LS is a septic thrombophlebitis of the jugular vein in the context of otorhinolaryngologic infections (*1*). However, the definition of LS still remains unclear in the literature. Some authors only include disseminated *F. necrophorum* infections originating from the throat, while others include all disseminated bacterial otorhinolaryngologic infections, as they have much in common, even though they may originate from different head foci and have different age distributions (*2*). LS with a primary otogenic focus predominantly occurs in otherwise healthy children, who mainly develop a spread of the infection into adjacent regions, e.g. mastoiditis and meningitis (*2*).

Our case of a 93-year-old woman represents an uncommon clinical presentation of LS since it occurred in an elderly patient and showed extensive intracranial progression of the thrombosis. In our case, surgical treatment was not considered due to the patient's age and comorbidities, along with the rapid improvement of the symptoms with conservative treatment. The evidence available regarding LS complicated with cerebral venous thrombosis (CVT) is scarce, and mostly based in case reports or case series (*3-6*). In one of the largest case series of infection-associated CVT, all patients were treated with antibiotics combined with local surgical drainage or resection of the infected site; however, 50% of these patients showed an unfavourable outcome (*5*). In a case series of infectious CVT in pediatric population, all cases were treated with surgery and antibiotic therapy, and the reported outcome was favourable in all cases, although almost half of patients developed mild hearing impairment (*4*). In our case report, despite the conservative treatment, outcome was favourable, suggesting that surgical treatment may not be necessary in all cases of LS complicated with CVT.

F. necrophorum is still the major microbiological agent identified in LS. Other microbiological agents include *Streptococcus*, including *methicillin resistant S. aureus*, and *S. aureus*. However, a large proportion of the cases have not reported a microbiological agent. As with other bacteria, cultures can be falsely negative if antibiotics are administered before sample collection (*7*). In our case, blood cultures were not obtained because the patient was afebrile and she had received antibiotics prior to admission.

Clinically, LS begins as an oropharyngeal infection with odynophagia, cervical lymphadenopathy and peritonsillar abscess (*9*). Then, usually 1 to 3 weeks later, the infection spreads to the parapharyngeal space and jugular vein, disseminating directly or via the peritonsillar venous plexus. This causes thrombosis that often manifests as a tender and swollen cord anterior to the sternocleidomastoid muscle. Other complications are carotid artery rupture, Horner's syndrome, paralysis of the trapezius muscle and dysphagia. Septic thrombophlebitis of the jugular vein is the primary source of emboli, most commonly to the lungs, but also to the joints, soft tissues, liver, spleen, kidney and central nervous system. It is in this latter category where our case can be included (*7*).

CVT is an uncommon condition with an incidence of 1.3-1.6/100,000 in Western countries (*10*). Traditionally, the most prevalent aetiology of CVT was infections but nowadays aseptic CVT are more frequent. Infectious CVT accounts for 6-12% of the total in large adult series, mainly in developing countries. The most common infections associated with CVT are otitis, mastoiditis and sinusitis. *F. nucleatum* and *F. necrophorum*, normal flora of the oral cavity, are the most common pathogens involved in infectious CVT (*11*).

Severe headache is the most common presenting symptom of CVT. A minority of patients (10%) do not report headache at baseline, as in our case. Other typical CVT symptoms are seizures, focal deficits, intracranial hypertension (decreased visual acuity and papilledema) and diffuse encephalopathy (*12*). The confirmation of the diagnosis of CVT depends on the demonstration of thrombi in the cerebral veins or sinuses. Three imagining techniques can be used: magnetic resonance imaging (MRI) with MR venography, CT venography and angiography (*13*). MRI is the most sensitive technique and its sensitivity is even higher if venography is associated. CT-venography is a decent and less expensive alternative for the diagnosis of CVT, but it is inferior for the visualization of brain parenchymal lesions that can appear in this situation, such as intracerebral, subdural or subarachnoid haemorrhage (*12*). In our case, a contrast CT was performed showing thrombi in several cerebral structures, including the torcular herophili, site of the confluence of superior sagittal, straight, occipital and transverse sinuses.

A routine blood test including a chemistry panel, complete blood count and coagulation study should be performed in all patients with CVT. D-dimer measurements are not used frequently in the diagnostic work-up of patients with suspected CVT due to its limited sensitivity (*12*). In patients with infectious CVT, laboratory markers of infection should also be measured.

Management of LS should include these general principles: systemic antibiotic therapy, drainage of abscesses, and consider anticoagulation (*6,7*). The optimal antibiotic regime for this pathology is unknown, as the evidence is scarce. Normally, *F. necrophorum* is reported to be susceptible to penicillin, cephalosporins, metronidazole, clindamycin, tetracyclines and chloramphenicol. B-lactamase-producing strains of *F. necrophorum* have only rarely been reported (*8*), and still no resistant strains have been found in Europe. In our case, empiric treatment with amoxicillin/clavulanic acid was used, with an excellent outcome.

Anticoagulation is normally not advised in LS, and it has been reserved for cases of thrombosis progressing

retrogradely to the cavernous sinus, according to the recommendations of international guidelines; a course of intravenous heparin followed by up to 3 months of treatment with oral coumarin to reduce morbidity among survivors and to allow adequate collateral circulation has been recommended. The internal jugular vein does not usually recanalize after resolution of the infection (*8*). Endovascular treatment using intrasinus thrombolysis or mechanical thrombectomy should not be routinely used in patients with CVT (*12*).

Patients with the otogenic variant of LS may have a less severe course than oropharyngeal LS, as long as they remain at the mastoiditis stage and do not develop meningitis, which is reported to have a mortality of up to 31.5% (*2*). CVT usually has a good prognosis (*13*), but severe cases can result in death or permanent disability. Approximately 5% of patients die in the acute phase of the disorder, being transtentorial herniation secondary to a haemorrhagic lesion the main cause of death. Status epilepticus, medical complications and pulmonary embolism are among the other causes of early death. Deaths after the acute phase are due to the underlying conditions or to side effects of prolonged anticoagulant treatment. Prognosis is less favourable in patients at both extremes of age.

In conclusion, we report a case of LS complicated with infectious cerebral venous thrombosis in an elderly patient. This uncommon condition can be potentially lethal, especially during the acute phase. For this reason, clinical suspicion and early treatment are recommended. Surgical treatment, along with antibiotics are the treatment of choice. Anticoagulation should be considered. In our case, evolution was favourable with conservative medical treatment, suggesting that surgery may not be necessary in all cases of LS complicated with CVT.

References

1. Lemierre A. On certain septicaemias due to anaerobic organisisms. Lancet 1936, March 28. DOI: *https://doi.org/10.1016/S0140-6736(00)57035-4*
2. Hagelskjaer Kristensen L, Prag J. Lemierre's syndrome and other disseminated Fusobacterium necrophorum infections in Denmark: A prospective epidemiological and clinical survey. Eur J Clin Microbiol Infect Dis. 2008; 27:779-789.
3. Villamar MF, Lee JD. Cerebral venous sinus thrombosis secondary to otomastoiditis. Postgrad Med J. 2017; 93:569.
4. Bales CB, Sobol S, Wetmore R, Elden LM. Lateral sinus thrombosis as a complication of otitis media: 10-year experience at the children's hospital of Philadelphia. Pediatrics. 2009; 123:709-713.
5. Korathanakhun P, Petpichetchian W, Sathirapanya P, Geater SL. Cerebral venous thrombosis: Comparing characteristics of infective and non-infective aetiologies: A 12-year retrospective study. Postgrad Med J. 2015; 91:670-674.
6. Nakamura S, Sadoshima S, Doi Y, Yoshioka M, Yamashita S, Gotoh H, Onoyama K. Internal jugular vein thrombosis, Internal jugular vein thrombosis, Lemierre's syndrome; oropharyngeal infection with antibiotic and anticoagulation therapy--a case report. Angiology. 2000; 51:173-177.
7. Johannesen KM, Bodtger U. Lemierre's syndrome: Current perspectives on diagnosis and management. Infect Drug Resist. 2016; 9:221-227.
8. Hagelskjaer Kristensen L, Prag J. Human necrobacillosis, with emphasis on Lemierre's syndrome. Clin Infect Dis. 2000; 31:524-532.
9. Harper LK, Pflug K, Raggio B, April D, Milburn JM. Clinical images: Lemierre syndrome: The forgotten disease? Ochsner J. 2016; 16:7-9.
10. Wang L, Duan J, Bian T, Meng R, Wu L, Zhang Z, Zhang X, Wang C, Ji X. Inflammation is correlated with severity and outcome of cerebral venous thrombosis. J. Neuroinflammation. 2018; 15:329.
11. Fleet J, Birns J, Bhalla A. Cerebral venous thrombosis in Adults. J Neurol Disord Stroke. 2014; 2:1033.
12. Coutinho JM. Cerebral venous thrombosis. J Thromb Haemost. 2015; 13 Suppl 1:S238-S244.
13. Ferro JM, Canhao P, Aguiar de Sousa D. Cerebral venous thrombosis. Presse Med. 2016; 45:e429-e450.

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