Investigation of the Association between Recreational Scuba Diving and a Case of Acute Lemierre's Syndrome: Will it Recur?

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Abstract: - Lemierre's Syndrome (LS) is a septic thrombophlebitis of the internal jugular vein following acute pharyngitis commonly caused by anaerobic bacteria. We postulate a rare source of infection in a young male never before cited in the literature, scuba diving. We discuss the patient's risk factors which we postulate likely caused an altered innate immunity, and when combined with superimposed barotrauma, likely provoked the infection. We then consider the possibility of disease recurrence and make certain recommendations for prevention. Additionally, we highlight the importance of early diagnosis in potentially critical diseases such as LS.

Key-Words: - Lemierre's Syndrome, septic thrombophlebitis, allergic rhinosinusitis, barotrauma, diving, altered immunity.

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1 Background

Lemierre's Syndrome (LS) has been identified to be a complication of oropharyngeal infection classically presenting as sore throat and persistent fevers progressing to septic thrombophlebitis of the vascular region of the lateral neck, [1], [2].

In a recent systemic review of 84 case reports, the most common source of infection was found to be the pharynx and tonsils with sources of lungs, larynx, teeth, eyes, and the mastoid process being less common, [3]. The most commonly identified causative agent, Fusobacterium necrophorum, is part of the normal flora of the human upper respiratory tract, [3], [4]. Another recent systemic review of 712 cases found that 84% of patients had acute thrombosis of head/neck vasculature, and 82% had septic embolisms, [5]. LS affects young individuals with a median age of 21 years and has a substantial risk of major clinical sequelae, various new thromboembolic complications, and even death, [4], [5].

Antibiotics are the mainstay of treatment, with carbapenems, metronidazole, and piperacillin-tazobactam being the initial choice targeting gram-negative bacilli and anaerobic microorganisms common in the disease, [6]. Recommendations and guidelines regarding systemic anticoagulation, however, are inconsistent and have not been investigated in clinical trials. Some systemic reviews of cases have shown lower rates of new venous thromboembolisms and septic peripheral lesions in those that received anticoagulation, [5].

Here, we present a case of Lemierre's Syndrome with a likely unique cause of infection. Although difficult to prove without a doubt, it is likely the patient acquired his infection from his diving activities. A case associated with recreational scuba diving has never prior been cited in the available English literature. Additionally, we highlight the importance of further thorough investigation and testing when a diagnosis is unable to be made initially or does not fit the clinical picture appropriately.

2 Case Description

Our patient is a 24-year-old male who presented to our institution as an international transfer from Trinidad and Tobago. His medical history consisted of a deviated septum, chronic allergic rhinosinusitis, and recurrent sinus pain diagnosed by ear, nose, and throat (ENT) specialists as neuropathic in nature. Of note, the patient's profession is as a commercial diver. It requires him to dive to a maximum of 70 feet underwater for at least 60 minutes at a time.

His symptoms began while on vacation in Barbados as a left-sided sore throat. He went

recreational scuba diving one time 6-12 hours prior to symptom onset. After the dive, he had some self-limited mild diarrhea. However, 4 days after symptom onset, he had an episode of light headedness, headaches, sweats, chills, and fever that prompted him to go to the emergency room (ER) upon return to Trinidad. After multiple daily visits to the ER, he was eventually admitted to the hospital on day 10 of his illness. A chest radiograph (RA) showed bilateral patchy infiltrates and he was admitted for presumed viral pneumonia with a possible superimposed bacterial infection. Multiple COVID-19 antigen and PCR tests were negative and it was noted that he had received the Sinopharm COVID vaccination. He was treated with 3 days of azithromycin, ceftriaxone, and oseltamivir, and due to symptomatic improvement of his sore throat, he was subsequently discharged on day 13 of his illness. However, 2 days later, on day 15, he returned with worsening leukocytosis and continued fever and chills which at this point had lasted almost 2 weeks. He was started on piperacillin/tazobactam and levofloxacin. Further testing including blood cultures was negative. After 6 days of total antibiotics, his computed tomography (CT) of the chest showed worsening bilateral pleural effusions and cavitating pulmonary lesions.

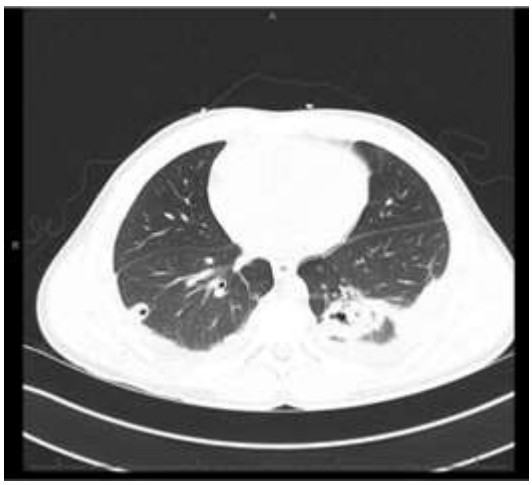

Fig. 1: CT chest with IV contrast of our patient on 1/22/2022. Bilateral lung cavitary nodules and pleural effusions, likely septic pulmonary emboli, left lower lobe consolidation with some pockets of air may represent developing abscess.

Due to a lack of clinical improvement, and new worsening cavitary pulmonary nodules, the patient was internationally transferred to our institution on day 22. CT chest with contrast showed persistent cavitary pulmonary nodules bilaterally, small sub-segmental septic pulmonary emboli, small bilateral pleural effusions, and a lower left consolidation with pockets of air concerning developing an abscess, (Figure 1). Our final blood cultures were negative, although this is likely due to previous antibiotic treatment. Due to concern for LS, a venous ultrasound doppler (US) of the upper left extremity was completed revealing a deep vein thrombosis (DVT) of the left internal jugular vein (IJV), (Figure 3 A-B).

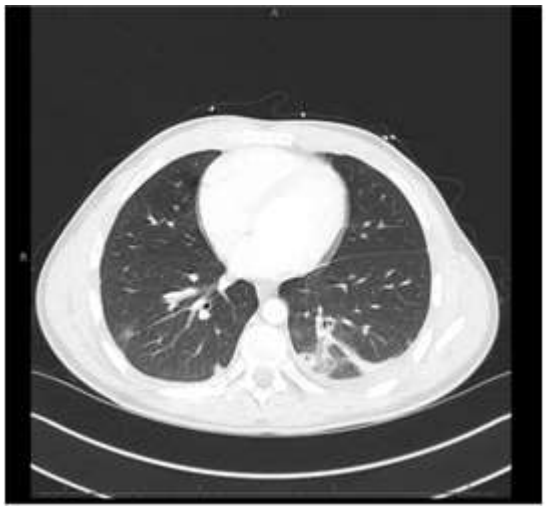

Fig. 2: CT chest with IV contrast of our patient on 1/27/2022. Overall significant improvement inflammatory process and decreased size cavitary nodules and pleural effusions.

A diagnosis of LS was made based on the characteristic clinical course of the sore throat followed by fevers accompanied by IJV thrombus and septic pulmonary emboli. The patient was continued on intravenous piperacillin-tazobactam and therapeutic anticoagulation throughout his hospitalization. He was discharged on day 32 with 6 weeks of oral metronidazole, 3 months of oral anticoagulation, and close follow-up appointments with the infectious disease specialist. Prior to discharge, the patient's repeat venous US doppler and CT chest with contrast showed marked improvement in the size of the DVT and septic pulmonary emboli (Figure 2 and Figure 3 C-D).

3 Discussion

Our patient's initial symptoms of sore throat and fever were nonspecific and overlooked requiring multiple ER visits. Despite eventual hospitalization, a definitive diagnosis reflecting his condition wasn't established until far into his clinical course. We would like to highlight the importance of maintaining a wide differential and pursuing diligent diagnostic workup when a

common presumed diagnosis doesn't match the clinical course. Especially in the younger patient population, it is imperative to keep not only LS in mind but also various other rare medical conditions as they can be easily overlooked due to nonspecific presenting symptoms. In many diseases such as LS, an earlier diagnosis prevents devastating complications.

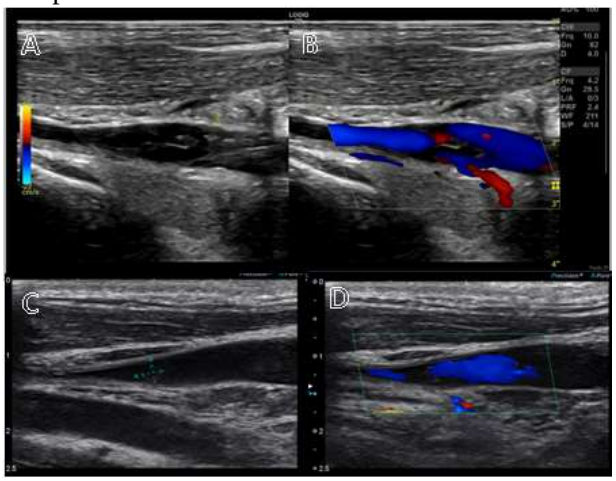

Fig. 3: Doppler Ultrasounds of Left Internal Jugular Vein
A-B: US Doppler on 1/25/2022 reveals a large DVT of Left Internal Jugular Vein and superficial partial thrombophlebitis involving the left cephalic vein.
C-D: US Doppler on 1/31/2022 show considerable improvement in DVT of Left Internal Jugular Vein and minimal improvement in thrombus in left cephalic vein.

LS can develop from the local spread of certain oropharyngeal pathogens, [1]. It can be associated with regional thrombophlebitis in an otherwise normal host, in patients with a history of allergic rhinosinusitis, or with predisposing viral or bacterial nasal-oropharyngeal infection, [1], [2]. Our patient did have a history of allergic rhinosinusitis which we hypothesize was likely a factor predisposing him to infection due to altered innate immunity from chronic inflammation and impaired clearance of sinus ostia, [9]. Among the oropharyngeal pathogens normally found in the human respiratory tract, Fusobacterium necrophorum is one of the most virulent species capable of causing opportunistic infections, especially in the setting of altered innate immunity, [4]. This species and various others may share virulence factors that facilitate regional septic thrombophlebitis. Heparinase, an exotoxin, enables invasion without tissue destruction, [7]. Another exotoxin, hemolysin, develops an anaerobic environment for other anaerobic organisms such as Fusobacterium necrophorium to grow. Additionally, endotoxins such as Leucocidin may play a role, by lysing neutrophils. To prevent the propagation of our patient's internal jugular thrombus further into the cerebral vasculature, or the formation of further thrombi, we initiated therapeutic dose anticoagulation. Recall, recommendations regarding systemic anticoagulation are inconsistent, [5]. Regardless, on repeat imaging, our patient had marked improvement in the size of the IJV thrombosis and septic pulmonary emboli. Treatment with anticoagulation in addition to antibiotics may be beneficial. Further clinical trials are needed to establish guidelines.

Now, our hypothesis is that the recreational scuba dive may have predisposed the patient to develop LS. The offending pathogens had not been identified in our patient's case, likely due to the receipt of empiric broad-spectrum antibiotics prior to blood culture draws. However, our patient may have acquired a virulent pathogen via a contaminated mouthpiece or other scuba equipment. He may also have acquired LS from swallowing contaminated water which may explain his self-limited diarrhea, [8].

Our patient also had anatomical anomalies that likely predisposed him to LS. He had a surgically uncorrected deviated septum and probable mucosal thickening from chronic allergic rhinosinusitis leading to sinus obstruction from blocked ostia, subsequently preventing nasal passage clearance, predisposing him to infection, [7]. Given our patient's chronic rhinosinusitis, we cannot rule out an altered innate immunity as a predisposing factor to the spread of virulent pathogens, [9].

Additionally, the role of barotrauma must also be seriously considered as a contributing factor, leading to the pathophysiology of our patient's LS, [10], [11], [12]. His recurrent sinus and facial pain are likely a consequence of said barotrauma. Barosinusitis can be explained by Boyles law, when the pressure of a gas is decreased, the volume of gas increases. When the diver ascends, there will be decreased pressure causing an increase in volume, consequently compressing the mucosa, and thus leading to ischemia. When the diver descends, there is increased pressure causing decreased volume which could lead to tugging with increased mucosal capillary congestion, leaky capillaries, and bleeding. These results will also lead to inflammatory thrombogenic host responses, and possibly strip endothelial cells or cause endothelial dysfunction causing changes in the coagulation system. Additionally, in cases due to

such anaerobes as fusobacterium, barosinusitis may add to the microaerophilic local anatomical environment by causing further ischemia and allowing the anaerobic microbes to proliferate. In other words, the change in barometric pressure during diving causes irritation and damage to the mucosal lining of the paranasal sinuses by failing to equalize intranasal pressures with ambient environmental pressure.

Finally, diving can result in barosinusitis, and barosinusitis is an additional risk factor with our patient's underlying altered anatomy, [10], [11]. These risk factors in the setting of our patient's altered innate immunity secondary to chronic allergic rhinosinusitis likely contributed to the pathophysiology of LS. Hence, we can conclude that there would be a probable risk of recurrence of LS with subsequent dives in our patient's case.

Without standard-of-care treatment guidelines, we would recommend in cases of LS, six weeks of antibiotic treatment for endovascular infection, to cover empirically for mixed aerobic and anaerobic oropharyngeal flora. The antibiotics could also be further narrowed to target likely pathogens identified from blood cultures. Additionally, we recommend anticoagulation be prescribed for three months although the issue of utilizing anticoagulation in LS to minimize embolic phenomenon remains unresolved in the medical literature. We also recommend follow-up imaging such as chest CT's and venous doppler ultrasounds to evaluate the course of the patient's septic thrombi.

Our patient was made aware that diving may have contributed to the development of LS and that we are unsure of the risk of recurrence from continuing diving. We made certain recommendations that may ameliorate the risk of recurrence. First, we recommend using mouthpieces that are disinfected, according to the CDC guidelines, [13]. Second, we recommend he avoid contaminated environments and minimize swallowing water, e.g., when feasible, wear a full-face mask. Third, we recommend in order to minimize sinus obstruction, he should consider normalizing his deviated septum if surgically amenable and perform allergy testing and hyposensitization. Fourth, one should avoid or postpone a dive if there is active infectious or acute allergic rhinosinusitis, [11]. Fifth, it is imperative to practice good dental hygiene. Sixth, one must remain up-to-date on vaccinations against respiratory pathogens. Seventh, a diver should repeatedly practice maneuvers to equalize pressures between sinuses and ambient environmental pressure. These include Valsalva (pinching nostrils and gently blowing), Frenzel (pinching nostrils closed and attempting to make a 'k' sound), and Toynbee (pinching nostrils and swallowing or yawning), [14]. Eighth, we should consider if there is a role for chemoprophylaxis, e.g., PrEP with antibacterial rinses or medications.

4 Conclusion

This is an interesting case of LS demonstrating a unique cause of infection. No other cases of LS associated with diving were found in the English scientific literature. Our patient likely developed LS due to a combination of circumstances. He suffered from recurrent barotrauma and mucosal injury causing blocked ostia from his long history of dives. His chronic allergic rhinosinusitis also led to altered innate immunity. Subsequently, he was exposed to contaminated scuba equipment and likely swallowed contaminated water duringhis recreational dive. Therefore, these combined circumstances were likely the "perfect storm" that led to his upper respiratory tract infection predisposing him to LS. The risk of developing recurrent LS will remain until he is able to alter these circumstances. Therefore, if our hypothesis is correct, LS may recur. Due to its rarity, the optimal approach to prevent LS is unknown. Here, we provide a foundation for an approach as we await further corroborating evidence.

Clinical Message:

Further clinical trials and research are needed to make guidelines not only regarding the role of anticoagulation but also to study the possibility of recurrence of LS due to diving and the methods of prevention.

Consent:

Informed consent was obtained from the patient to publish case details, test results, and images.

Competing Interests:

No competing interests to disclose.

References:

[1] Lemierre, A., On Certain Septicaemia Due to Anaerobic Organisms, *Lancet*, Vol.227, No.5874, 1936, pp. 701-703.

[2] Eilbert W., Singla N., Lemierre's syndrome, *Int J Emerg Med*, Vol.6, No.40, 2013.

[3] Kushawaha A., Popalzai M., El-Charabaty E., Mobarakai N., Lemierre's syndrome, reemergence of a forgotten disease: a case report, *Cases J*, Vol.2, No.6397, 2009.

[4] Karkos PD., Asrani S., Karkos CD., Leong SC., Theochari EG., Alexopoulou TD., Assimakopoulos AD., Lemierre's syndrome: a systematic review, *Laryngoscope*, Vol.119, No.8, 2009, pp. 1552–1559.

[5] Valerio L., Zane F., Sacco C., 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*, Vol.289, No.3, 2021, pp. 325-339.

[6] Litt, Michael J., Montgomery, Mary W., Small, Kirstin M., Miller, Amy L., Loscalzo Joseph, Hard to Swallow, *N Engl J Med*, Vol.385, No.15, 2021, pp. 1421-1427.

[7] Williams, Michael D., Kerber, Caroline A., Tergin, Helen F., Unusual presentation of Lemierre's syndrome due to Fusobacterium nucleatum, *J Clin Microbiol*, Vol.41, No.7, 2003, pp. 3445-3448.

[8] Schijven, Jack, de Roda Husman, Ana Marie, A survey of diving behaviour and accidental water ingestion among Dutch occupational and sport divers to assess the risk of infection with waterborne pathogenic microorganisms, *Environ Health Perspect*, Vol.114, No.5, 2006, pp. 712-717.

[9] Hulse K.E., Immune Mechanisms of Chronic Rhinosinusitis, *Curr Allergy Asthma Rep*, Vol.16, No.1, 2016.

[10] Jamil RT., Reilly A., Cooper JS., Sinus Squeeze, In: *StatPearls*, 2022.

[11] Battisti AS., Lofgren DH., Lark JD., Barosinusitis, In: *StatPearls*, 2022.

[12] Mitchell, Simon J., Bennett, Michael H., Moon, Richard E., Decompression Sickness and Arterial Gas Embolism, *N Engl J Med*, Vol.386, No.13, 2022, pp. 1254-1264.

[13] Brnich, MJ., et al., Cleaning, Disinfecting, and Sterilizing Self-Contained Self-Rescuer Mouthpiece Assemblies Used in Hands-On Training, *U.S. Department of the Interior, Bureau of Mines*, No.9236, 1989, pp. 1-7.

[14] Wolber, P., Meyer, M.F., Knesic, K., et al., Prospective study on the Eustachian tube function during Frenzel maneuver in a hypobaric/hyperbaric pressure chamber, *Eur Arch Otorhinolaryngol*, Vol.279, No.4, 2022, pp. 1843-1850.

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Conflict of Interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.