Don't Forget the Forgotten Disease: Lemierre Syndrome. Case Report

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Abstract

We present the case of a three-year-old boy with Lemierre syndrome. He presented with the typical symptoms of an oropharyngeal infection, followed by bacteraemia and thrombophlebitis of the internal jugular vein. However, the infection was atypically caused by group A *Streptococcus*. The patient underwent surgical drainage of the abscess and received intravenous antibiotics and subsequently anticoagulation therapy. This case report highlights the importance of early recognition and initiatiniation of appropriate antibiotics with coverage for both gram-positive and anaerobic bacteria to prevent adverse outcomes. The indications for anticoagulation therapy in paediatric patients remain controversial, but in general, it should only be administered if the thrombus involves critical areas or if septic emboli occur or the thrombus progresses despite antibiotic therapy.

Introduction

Lemierre syndrome (LS) is a rare but serious condition first described by André Lemierre in 1936 (1). There is no standardized definition of LS, but it is usually characterized by a recent history of an oropharyngeal infection followed by bacteraemia, septic thrombophlebitis of the internal jugular vein (IJV) and at least one focus of septic metastasis. While *Fusobacterium necrophorum* remains the most common causative pathogen, recent reports suggest an increasing role for group A *Streptococcus* (GAS) (7). The rising incidence of severe GAS infections, particularly in children, raises concerns about its impact on presentation, treatment, and outcomes of LS. Compared to LS cases caused by *Fusobacterium necrophorum*, those caused by GAS may differ in terms of metastatic risk and response to treatment (2-4). This case of GAS-induced LS in a young child underscores the diagnostic challenges and evolving therapeutic considerations, highlighting the importance of early recognition and appropriate management.

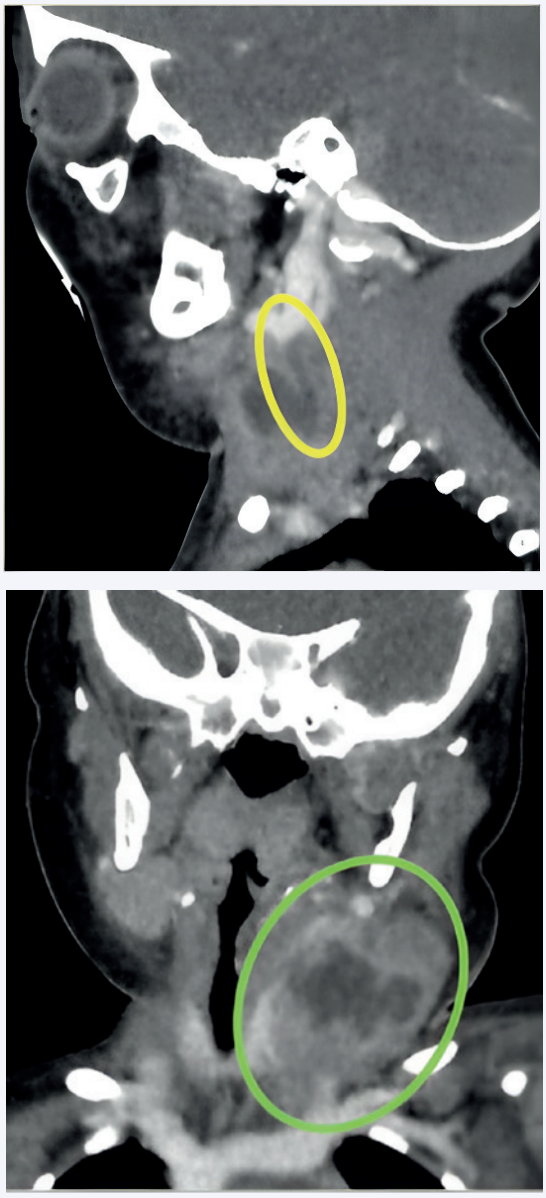
Case Presentation

A 3-year-old boy presented at the emergency department with a three-day history of fever, left neck swelling, vomiting, and decreased intake. He had been diagnosed with possible scarlet fever one week earlier but had not received antibiotics. On examination, he was non-ill appearing and had a temperature of 38.5°C, an erythematous pharynx, and a 4 x 4 cm firm, painful mass on the left side of the neck (figure 1). Further clinical examination was unremarkable. Laboratory results showed a white blood cell count of 21.5 x10³/mm³ [N 5.5-15.5 x10³/mm³], with 87.5% neutrophils , a haemoglobin level of 10.9 g/dL [N 12.5], a platelet count of 336 x10³/mm³ [N 150-350 x10³/mm³] and elevated erythrocyte sedimentation rate (>120 mm/h [N < 10 mm/h]) and C-reactive protein (189 mg/L [N 5 mg/L]). Urine culture was sterile. Serology for Epstein-Barr virus, *Toxoplasma* and cytomegalovirus were negative. Blood cultures were positive for GAS. Doppler ultrasound (US) of the neck revealed unilateral lymphadenopathy of 1.4 x 2 cm, with (?) secondary abscess formation, along with a thrombus in the IJV. He was admitted and treated with intravenous (IV) clindamycin, amoxicillin-clavulanic acid, and metronidazole. Subsequently, a contrast-enhanced computed tomography (CT) scan of the neck confirmed an abscess beneath the left mandible and IJV thrombosis, consistent with LS without lung emboli (Figure 2). The abscess was surgically drained, and culture of the puncture fluid grew GAS, which was sensitive to penicillin, ceftriaxone, and clindamycin. Given the polymicrobial nature of LS, with frequent involvement of anaerobes, we switched to monotherapy with IV amoxicillin-clavulanic acid. Anticoagulation therapy was not started due to the lack of progression of the thrombus and the absence of septic lung emboli. The patient showed progressive clinical improvement. After 10 days, the patient was discharged with oral clindamycin for another 10 days.

Follow-up imaging after 3 weeks showed insufficient thrombus reduction leading to initiation of low molecular weight heparin. Gradual thrombus regression and development of collateral circulation were subsequently observed. Initial follow-up included monthly ultrasounds and multidisciplinary consultation by ENT and haematology. This was later extended to every 6 months, and at 2.5 years post-discharge, follow-up could be fully discontinued given the stable partial thrombosis and well-developed collateral circulation.

FIGURE 1: clinical presentation of swelling on the left side of the neck.

FIGURE 2 AND 3: CT scan of neck. On the left side confirmation of thrombosis of the internal jugular vein. On the right side unilaterally enlarged lymphadenopathy (1.7 x 1.7 x 1.2cm) with possible abscess.



Discussion

LS was common before the advent of antibiotics, incurring a high mortality rate. With the introduction of antimicrobials and the routine use of penicillin in treating oropharyngeal infections, the incidence began to decline, and LS became the "forgotten disease" (2,3,6). Unfortunately, there has been an increase in reported cases over the past 10 years, particularly in the paediatric population. This is likely due to the accumulation of antibiotic resistance, the increasingly judicious use of antibiotics for pharyngitis in recent years and the rise in GAS infections (6,7). The worldwide incidence of LS varies, with reports ranging from 3.6 cases to 14.4 cases per million persons per year (3,5).

Clinical suspicion for LS arises when patients with any ENT infection show signs of IJV thrombophlebitis, sepsis, or organ failure due to septic emboli (2). Diagnosis is confirmed through laboratory studies, with a positive blood culture for *Fusobacterium necrophorum*, the main pathogen, often being the initial clue. Diagnostic delays can lead to metastatic spread by the time of official diagnosis (2). The initial clinical presentation usually involves oropharyngeal, dental, middle ear, or sinus infections, accompanied by fever (80%), sore throat (50%), nausea, vomiting, and neck pain, stiffness, or swelling. During this stage, there are no pathognomonic symptoms for LS. The second stage may manifest various clinical symptoms depending on the site of invasion, including IJV vascular involvement or cranial nerve palsies. IJV thrombophlebitis typically presents as painful unilateral swelling at the mandible angle, sometimes with trismus and dysphagia, serving as an initial indication of LS. The final stage leads to septic emboli development, often in the lungs or central nervous system (CNS), causing pleural effusions, abscesses, or cavitary lesions in the lungs, and meningitis or epidural abscess in the CNS, causing high morbidity and mortality (2). Other possible metastatic locations include joints, liver, spleen, muscles, kidneys, bones, and heart (5). In our case, the combination of pharyngitis, neck tenderness/swelling, and left IJV thrombosis raised suspicion for LS.

In 70-80% of cases, *Fusobacterium necrophorum* is the main pathogen (2). About 20-30% of patients have polymicrobial infections involving other organisms, including *Bacteroides* spp., *Staphylococcus* and *Streptococcus* spp., *methicillin-resistant Staphylococcus aureus* (MRSA), *Enterococcus* spp., and Candida spp. (3,7). Polymicrobial infections typically present as a monophasic, progressive, and pyogenic illness, differing from the typical triphasic presentation of LS caused by *Fusobacterium* infection (5). In our case report, cultures from blood, throat swab, and puncture fluid from the abscess, showed positive results for GAS only, which is rarely the solitary pathogen in LS (7). Similar to other paediatric LS cases caused by GAS, there was no progression to septic emboli. Although GAS is a highly invasive pathogen capable of causing severe infections, cases of GAS-associated LS tend to have a lower incidence of septic emboli compared with cases of *F. necrophorum*-associated LS. This may be due to differences in virulence factors. Another hypothesis is that the robust immune response that GAS infections often elicit leads to earlier clinical recognition and intervention (7).

To confirm IJV thrombosis and assess its extent and size, the gold standard is a contrast-enhanced CT scan of the neck. This scan is also useful for evaluating additional complications in the head and neck. The typical findings in LS are distended neck veins, enhancing vessel walls, low-attenuation intraluminal filling defects, and soft tissue swelling. US utility is limited due to poor imaging quality in the mandibular and clavicular regions and the risk of missing a thrombus with low echogenicity. MRI and magnetic resonance venography remain the preferred modalities for tracking the progression or regression of thrombosis, particularly in the intracranial space (9).

In suspected LS cases, prompt initiation of high dose IV antibiotic therapy is essential. The choice of antibiotics is primarily directed toward gram-positive and anaerobic bacteria to target the most common microorganisms (5-7). As soon as cultures become available, antibiotic therapy can be adjusted accordingly, with treatment typically lasting 4 to 6 weeks, which is longer than standard duration for other ENT-abscesses. Transitioning from IV to oral antibiotics can be considered upon clinical improvement (5). The initiation of anticoagulation therapy in paediatric patients remains controversial due to the lack of randomized controlled trials evaluating its risks and benefits. The existing evidence and recommendations rely on anecdotal case reports, theoretical assumptions, and extrapolation from the adult population (6).

Anticoagulation therapy is usually used only in cases involving thrombus extension into the cerebral sinuses, large or bilateral clots, or ongoing sepsis and disease progression despite antibiotic therapy, provided there are no contraindications (5). Although there was no clear evidence of thrombus progression or septic emboli in our case, anticoagulation therapy was started one month after diagnosis of LS. Given the slow and incomplete resolution of the thrombus in our case, one could argue that anticoagulation was started too late, or that this would have been the outcome regardless of its use. The most documented anticoagulant in children is low molecular weight heparin (LMWH), due to its predictable pharmacokinetics and favourable safety profile (3). If used, anticoagulation is typically continued for three months, assuming resolution of the septic thrombophlebitis (9).

Conclusion

As LS is becoming more prevalent, clinicians should consider it in paediatric patients presenting with fever and unilateral neck swelling. In parallel with the rising incidence of invasive GAS infections in children, there is an increasing number of cases of GAS-associated LS. Although these cases tend to have a lower incidence of septic emboli, prompt diagnosis and the initiation of antibiotic treatment are essential for preventing complications and improving outcomes. The use of anticoagulation therapy in the treatment of paediatric LS is controversial and requires further study.

All authors state that they have no conflict of interest to declare in relation to the realization of this case report.

REFERENCES

1. Lemierre A. On certain septicaemias due to anaerobic organisms. Lancet. 1936;227(5874):701-3.
2. Ridgway JM, Parikh DA, Wright R, Holden P, Armstrong W, Camilon F, et al. Lemierre syndrome: a pediatric case series and review of literature Am J Otolaryng. 2010;31(1):38-45.
3. Patel PN, Levi JR, Cohen MB. Lemierre's syndrome in the pediatric population: trends in disease presentation and management in literature. Int J Pediatr Otorhinolaryngol. 2020;136:110213.
4. Rafati F, Bhalla V, Chillal V, Thyagarajan M. Lemierre syndrome: a diagnostic dilemma in paediatric patients. J Surg Case Rep. 2017(12): rjx210.
5. Alves S, Lorena S, Carvalho I, Moreira D. Lemierre's syndrome: a disguised threat. BMJ Case Rep. 2019.;12(4): e228397.
6. Phan T, So TY. Use of anticoagulation therapy ofr jugular vein thrombus in pediatric patients with Lemierre's syndrome. Int J Clin Pharm. 2012. 34(6):818-21.
7. Shah RK, Wofford MM, West TG, Shetty AK. Case report Lemierre syndrome associated with group A streptococcal infection. Am J Emerg Med. 2010 (5): 643.e5-8.
8. Waterman JA, Balbi HJ, Vaysman D, Ayres RA, Caronia CG. Lemierre syndrome a case report. Pediatr Emerg Care. 2007;23(2):103-5.
9. Koo J, Pong A, Dory C, Farnaes L, Thronbur CD. Management and outcomes of pediatric septic thrombophlebitis: a case series. Ped Hematol Oncol. 2020; 37(4):344-352.
10. Goldenberg NA, Kittelson JM, Abshire TC, Bonaca M, Casella JF, Dale RA, et al. Effect of Anticoagulant Therapy for 6 Weeks vs 3 Months on Recurrence and Bleeding Events in Patients Younger Than 21 Years of Age With Provoked Venous Thromboembolism: The Kids-DOTT Randomized Clinical Trial. JAMA 2022;327(2):129-137.