Rare disease

Lemierre syndrome: from pharyngitis to fulminant sepsis

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Summary

We report a case of a previously healthy 33-year-old male who presented to his primary care physician with nausea, vomiting, diarrhoea and fever. One week prior to presentation the patient reported a history of sore throat which he presumed to be a viral infection and sought no medical attention. Upon hospital presentation, the patient was admitted and rapidly progressed to sepsis and respiratory failure. Goal directed therapy was initiated and the patient was intubated. Further clinical work up included blood cultures revealing *Fusobacterium varium* bacteraemia, and CT and ultrasound imaging demonstrated thrombosis of the internal jugular vein and septic pulmonary emboli. A diagnosis of Lemierre syndrome was made, and antibiotics as well as anticoagulation therapy were initiated. The patient's clinical condition improved with treatment, and he was discharged home on hospital day 12 with completion of an uneventful 4-week course of outpatient antibiotic and anticoagulation therapy.

BACKGROUND

Lemierre syndrome is a relatively rare, but potentially deadly complication of an acute oropharyngeal infection with *Fusobacterium* species (most commonly *Fusobacterium necrophorum*). It is characterised by septic thrombophlebitis of the internal jugular vein (IJV), bacteraemia and septic embolisation, leading to metastatic abscesses primarily to the lungs and large joints.

This once common syndrome carried a high mortality.¹ However, there was a substantial decrease in the incidence of Lemierre syndrome with the routine use of penicillin to treat pharyngitis in the postantibiotic era. Nonetheless, the incidence of Lemierre syndrome now seems to be on the rise.²

Given the large number of outpatients presenting with pharyngitis to primary care clinics,³ it is possible many cases are undiagnosed or are diagnosed late in the course when metastatic infection or sepsis becomes apparent.

A high clinical index of suspicion is essential. We highlight certain findings and features of the case which could lead to earlier diagnosis and treatment.

CASE PRESENTATION

Our patient is a 33-year-old previously healthy man who presented with a 4-day history of nausea, vomiting, diarrhoea and fever to his primary care clinic. The patient described a sore throat that started 7 days prior to presentation with fevers up to 40°C at home. Gradually, his pharyngitis resolved, but other symptoms to include vomiting and non-bloody diarrhoea worsened. On physical examination, the patient appeared acutely ill, but was in no respiratory distress. Mild erythema was noted in the oropharynx. The remainder of his examination was unremarkable.

Laboratory studies on admission revealed a white blood cell count of 7.3 with 93% neutrophils, 2.9% lymphocytes and 4.1% monocytes. Rapid strep test, faecal leucocytes, stool culture, throat culture, ova and parasites were all negative. A diagnosis of viral gastroenteritis was made and the patient was started on intravenous fluids and antiemetics. On hospital day 1, the patient developed fever up to 41.6°C with rigors. Cooling blankets were applied and blood culture gram stain showed gram negative rods. Ticarcillin/clavulanate, ciprofloxacin and metronidazole were initiated after infectious disease consultation.

On hospital day 2, the patient's pulmonary condition began to worsen with the development of hypoxaemia. A chest x-ray showed right lower lobe and left upper lobe consolidation (figure 1). His hypoxaemia persisted despite increased FiO₂. After developing hypotension, he was transferred to the intensive care unit where goal directed therapy was initiated. He was subsequently intubated.

INVESTIGATIONS

Blood cultures revealed *F. varium*. With infectious disease consultation, antibiotics were narrowed to ampicillin/sodium-sulbactam and metronidazole. At this point, Lemierre syndrome was first suspected. A D-dimer (ELISA) was drawn and found to be strongly positive at 9.52 µg/ml. Both venous Doppler ultrasound and CT of the neck (figure 2) were performed revealing thrombosis of the retro-mandibular vein with extension into the IJV. Images of the lung apices included in the neck CT showed a necrotic area containing fluid and air, concerning for developing abscess in the left upper lobe (figure 3). Additionally, multiple bilateral peripheral pulmonary nodular opacities were present suggesting an embolic origin (figure 4).

Figure 1 Frontal chest radiograph demonstrates left upper and right lower lobe air space opacities.

DIFFERENTIAL DIAGNOSIS

Given the patient's age and clinical picture of bacteraemia, acute respiratory failure and thrombosis of the IJV, Lemierre syndrome was the primary consideration. Other less likely considerations included primary bronchogenic carcinoma with central necrosis, necrotising pneumonia and metastatic disease.

TREATMENT

The patient was subsequently started on enoxaparin 1 mg/kg twice daily and antibiotics were narrowed to ampicillin/sodium-sulbactam and metronidazole. He continued to improve and on hospital day 6 was extubated. He was discharged home with outpatient therapy of augmentin and coumadin.

OUTCOME AND FOLLOW-UP

The patient completed an uneventful outpatient 4-week course of antibiotics and anticoagulation. A 3-month follow-up in the pulmonology clinic chest CT revealed mild apical scarring with resolution of air space disease.

DISCUSSION

Our case highlights some of the most commonly reported findings in Lemierre syndrome in addition to some specific features previously unreported in our review of the subject.

Our patient's sore throat had all but resolved by the time he presented to clinic. His primary complaints at presentation were vomiting, diarrhoea and fever. It is important to note that gastrointestinal complaints such as nausea, vomiting, diarrhoea and abdominal pain are common (49.5%) in Lemierre syndrome,⁴ and may be the presenting symptoms. Given the self-limited nature of the pharyngitis, it is the responsibility of the physician to elicit a history of oropharyngeal infection which can be found in 82–100% of the cases.^{3 5}

Spread of *Fusobacterium* into the lateral pharyngeal space via direct or lymphangitic spread ultimately leads to neck vein thrombosis. Contrast enhanced neck CT is the reported best imaging modality to evaluate for thrombosis. Ultrasound and MRI are also effective, but have limitations.⁶

Our case also highlights the role of other *Fusobacterium* species in Lemierre syndrome. *F. necrophorum* is most commonly reported and accounts for 81% of the reported cases. *F. varium* and other species account for 11% of infections.⁷ Any blood cultures revealing *Fusobacterium* should prompt the suspicion of Lemierre syndrome.

An almost invariable and critical characteristic of Lemierre syndrome is pulmonary septic embolisation (79–100% of cases).^{5 6 8 9} Non-cavitary pulmonary infiltrates are the reported most common finding on initial chest radiography. As in our case, cavitary lesions and evidence of

Figure 2 Coronal reformation contrast enhanced CT of the neck in soft tissue algorithm reveals low attenuation thrombus in the retromandibular and internal jugular veins (arrow).

septic embolisation are usually revealed soon after admission on CT.

Although the role of antibiotic therapy is well established, the role of anticoagulation in the treatment of Lemierre syndrome remains a controversial topic. Reports range from no anticoagulation therapy to treatment with 6 months of warfarin.⁹ There are no controlled studies evaluating the use of anticoagulation. Support for treatment is

based on the idea that anticoagulation speeds resolution of the source of septic emboli and hastens recovery. It is therefore reasonable to begin anticoagulation therapy if there is evidence of thrombus propagation or embolic events.^{5 10} The length of anticoagulation should be based on clinical judgment weighing therapeutic response against the bleeding risks of therapy.

Figure 3 Contrast enhanced axial image in soft tissue algorithm at the level of the lung apices reveals a necrotic gas containing mass with peripheral enhancement suggestive of developing abscess.

Figure 4 Contrast enhanced axial image in lung algorithm shows bilateral pleural effusions and peripheral nodular opacities in the right and left upper lobes with a possible feeding vessel noted on the right. This pattern is suggestive of embolic aetiology.

Learning points

- ▶ Lemierre syndrome is a rare condition which begins as an often self-limited oropharyngeal infection but evolves into a life-threatening form of sepsis.
- ▶ Some 50% of patients present with gastrointestinal symptoms, however pharyngeal symptoms may not be apparent and must be elicited by the physician.
- ▶ Septic embolisation in an otherwise healthy young patient or blood cultures revealing *Fusobacterium* species should suggest the diagnosis.
- ▶ Antibiotic therapy for a period of 3–6 weeks is recommended.
- ▶ Anticoagulation remains controversial, but has been recommended when there is evidence of thrombus propagation or septic embolisation.

Competing interests None.

Patient consent Obtained.

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