

Lemierre's syndrome: a sinister sore throat every clinician should remember

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SUMMARY: Paul SP, Beri R, Linney MJ. Lemierre's syndrome: a sinister sore throat every clinician should remember. Turk J Pediatr 2012; 54: 528-531.

Fusobacterium necrophorum is an anaerobic gram-negative bacterium that can present as a painful sore throat. Although uncommon, clinicians need to be aware of this condition as this can present a diagnostic challenge, with the initial symptoms being non-specific followed by a fulminant course. We present the case of a previously healthy girl who presented with a sore throat but later developed a full-fledged picture of Lemierre's disease. She developed bilateral pleural effusion and internal jugular venous thrombosis and needed intensive care management, a prolonged course of intravenous antibiotics and anticoagulation therapy.

Key words: Lemierre's disease, sore throat, internal jugular vein thrombosis, ultrasound.

Children and adolescents often have oropharyngeal infections and are managed by their primary care physicians¹. However, an apparently simple sore throat can give rise to severe complications and morbidity. Lemierre's disease, also known as postanginal septicemia, can present as a surprise pathology to clinicians because of its initial non-specific clinical symptoms, its increasing severity and often a fulminant course¹. We describe a case of Lemierre's syndrome in a teenaged girl who presented with a sore throat, together with a review of the related literature.

Case Report

A 16-year-old girl, fit and healthy, presented with rigors and cough and generally unwell status for two weeks. The cough was productive and had worsened at presentation. In the previous four days, she complained of knee pain, generalized body aches, neck stiffness, extremely painful sore throat, light headedness, shortness of breath, and chest pain. She also reported having intermittent headaches in the previous 10 days. Initial assessment revealed a temperature of 38°C, blood pressure 94/55 mmHg, pulse rate 100/min, and respiratory rate 22/min, with saturations of 97% in air. She was lethargic and clinically dehydrated. The respiratory examination revealed a few crackles over the right lung base, congested

tonsils, and palpable lymph nodes in the cervical chain. The neurological examination revealed slight neck stiffness but no photophobia or meningism with a normal fundoscopic examination. The right knee joint was tender with limited movement in flexion. The rest of the systemic examination was normal. She was admitted with a provisional diagnosis of sepsis or possible glandular fever.

She was started on intravenous (IV) fluids. IV antibiotics (cefuroxime 50mg/kg/dose 3 times daily and benzylpenicillin 25 mg/kg/dose 4 times daily) were started to cover for pneumonia and other common respiratory organisms. The doses were prescribed according to the British National Formulary for Children, 2010.

The initial blood investigations revealed a C-reactive protein (CRP) of 368 mg/L (0–10 mg/L), white cell count of $7.5 \times 10^9/\text{mm}^3$ ($4.5\text{--}11.5 \times 10^9/\text{mm}^3$) and platelet count of $34 \times 10^9/\text{mm}^3$ ($150\text{--}450 \times 10^9/\text{mm}^3$). The renal function results were suggestive of an acute pre-renal failure with a blood urea of 35 mmol/L (3.5–6.5 mmol/L) and a serum creatinine of 213 $\mu\text{mol/L}$ (60–100 $\mu\text{mol/L}$). Low serum albumin of 20 g/L (>40 g/L) was also detected. An ultrasound scan of the abdomen showed a large spleen, and the monospot test for glandular fever was reported as negative. The preliminary blood

culture results became available after 48 hours and showed a gram-negative bacillus (raising suspicion of *Fusobacterium*); therefore, a diagnosis of Lemierre's disease was considered. The antibiotics were changed to high-dose benzylpenicillin (50 mg/kg/dose 4 times daily), and IV cefotaxime (50 mg/kg/dose 4 times daily) and IV metronidazole (7.5 mg/kg/dose 3 times daily) were added as per hospital antibiotic guidelines. The IV cefuroxime was discontinued at this point as advised by the medical microbiologist. The IV fluids were stopped and nasogastric tube (NGT) feeding was started under the supervision of a dietician.

The girl continued to be febrile on day 3, and repeat clinical examination revealed reduced air entry on chest auscultation. A chest X-ray showed bilateral pleural effusion. To determine the size and nature of the pleural fluid collection, an ultrasound scan of the chest was done, which confirmed small bilateral pleural effusions. Ultrasound of the neck was requested as the neck swelling persisted. This demonstrated a thrombosed occluded left internal jugular vein (IJV), which extended from the angle of the jaw down to the left subclavian vein (Figs. 1, 2) and further substantiated a diagnosis of Lemierre's disease. She was transferred to the Intensive Care Unit (ICU) and subcutaneous tinzaparin was started.

On day 4, the final blood culture result confirmed the growth of *Fusobacterium necrophorum*; this was reported to be sensitive to metronidazole. She was continued on high dose of IV benzylpenicillin and metronidazole. IV clindamycin (500 mg/dose 4 times daily) was further added to the regimen following the confirmation of *Fusobacterium* in the blood

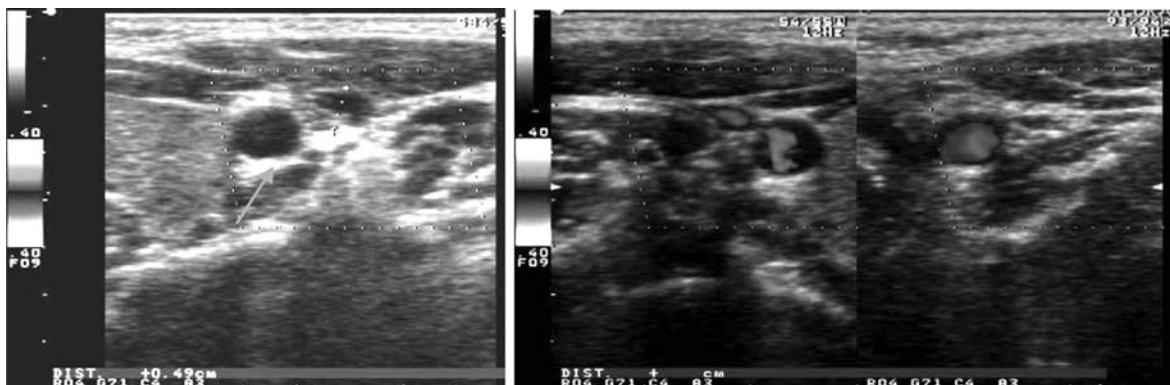
culture results.

Her temperature began settling on day 7 and signs of improvement were noted; she was transferred to the high dependency unit (HDU) in the pediatric ward. Her renal function also improved. Regular chest physiotherapy was continued. On day 9, she complained of chest pain, again became pyrexial and developed an oxygen requirement. A repeat chest X-ray, however, showed signs of improvement. She was continued on IV antibiotics and NGT feeding support with input from a dietician.

On day 12, she started feeling better, chest pain improved and oxygen therapy was discontinued. She continued to improve and NGT feeds were discontinued. On day 19, she eventually became afebrile and the antibiotics were changed to oral amoxicillin and metronidazole, and she was discharged from the hospital one day later on subcutaneous tinzaparin. The CRP level and renal functions had normalized at discharge. A clinical review five days later revealed further improvement, and she remained afebrile. She was advised to continue the oral antibiotics to complete a full six-week course. The tinzaparin was stopped one week later. At a clinic review after another four weeks, she reported being completely back to normal health and the clot in IJV (on repeat ultrasound scan 5 weeks later) showed signs of resolution. She was discharged to the general practitioner after the next clinic appointment another four months later as she continued to remain well.

Discussion

In 1936, Lemierre first described this condition as 'anaerobic postanginal septicemia' as a



Figs. 1, 2. Left internal jugular vein showing thrombus on ultrasound scan.

complication of oropharyngeal infection following a review of 20 cases¹⁻⁵. This condition later came to be known as Lemierre's syndrome. In 1955, Alston used the term "necrobacillosis" for infections caused by *F. necrophorum*¹. *Fusobacterium* species are anaerobic, non-motile, gram-negative bacilli^{1,2} usually found in the oral cavity, female genital tract and gastrointestinal tract in healthy individuals. *F. necrophorum* and *F. nucleatum* are the most commonly isolated pathogens in Lemierre's syndrome, the former being more virulent, and can be isolated in up to 80% of cases⁴. *F. necrophorum* has the unique ability to invade as primary pathogen in previously healthy individuals, and this was seen in the case described. Multiple pathogens may also be isolated in the same patient¹. It affects both sexes and all ages; however, a predilection for male adolescents and young adults is seen¹. The oropharynx is the main site of infection in the majority of cases². The initial presentation of Lemierre's syndrome (some of which were present in our case) are described below⁶:

- Sore throat (33%)
- Neck mass (23%)
- Neck pain (20%)
- Bone/joint pain (8%)
- Otalgia and/or otorrhea (8%)
- Dental pain (5%)
- Orbital pain, gastrointestinal symptoms,

Limb weakness (1% each) Lemierre's syndrome is a condition with multisystem involvement. In the pre-antibiotic era, most cases were fatal within 7 to 15 days². The interval between oropharyngeal infection and septicemia is usually ≤ 1 week². A high degree of clinical suspicion is necessary to make an early diagnosis. The diagnostic criteria^{1-3,5} are:

- 1) A history of recent oropharyngeal infection.
- 2) Clinical or radiological evidence of thrombophlebitis of the internal jugular vein
- 3) Isolation of an anaerobic pathogen

Blood investigation will usually reveal raised inflammatory markers, although cases of pancytopenia have also been reported in two, with bone marrow necrosis in one⁸. In a study

of 77 children in Chichester, UK, CRP value of >300 mg/L was found to be associated with severe infections, and 2 out of 8 positive blood culture results showed *Fusobacterium* spp. (25%)⁷. Biochemical abnormalities may reveal abnormal liver and renal functions; this was seen in the case described. Radiological features of Lemierre's syndrome may include pleural effusion, pneumothorax and thrombosis of the IJV. However, thrombosis of the external jugular vein (EJV) has also been described in the literature⁵. Any suspicion of IJV or EJV thrombosis should initiate an urgent ultrasound of the neck, which has been found to be equally effective in demonstrating the thrombosis². Contrast computed tomography scan is preferred over ultrasound scan in pleural effusion, as it can provide better anatomical information³. The role of anticoagulation therapy in IJV thrombosis remains controversial and is usually decided by the clinician taking into consideration the severity of symptoms, treatment response and degree of thrombus extension⁵. The treatment of Lemierre's syndrome involves a prolonged course of antibiotics, and this should initially be through the IV route. The initial choice of antibiotics should include broad-spectrum antibiotics, although there is no general consensus for the best antibiotic therapy. However, a common choice for beta-lactam antibiotic cover is found throughout the literature^{2,3}. *F. necrophorum* has been found sensitive to penicillin, clindamycin and chloramphenicol². Intensive care support is often required and nutritional needs should be managed by a pediatric dietician. A surgical team may need to be involved early for drainage of abscesses and chest drain insertion^{2,3}. The overall mortality rate can be up to 15%; however, the mortality can reach up to 80% where there is a delay in identifying the condition or starting antibiotics². In conclusion, Lemierre's syndrome is often referred to as a "forgotten disease", and this is due to the very limited number of cases in current clinical practice. It should be suspected in previously healthy adolescents with a fever and severe neck pain after a minor oropharyngeal infection. We hope this article will leave the readers with a heightened awareness of this seemingly rare but life-threatening condition.

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