

Septic Jugular Thrombophlebitis and Pulmonary Embolism: A Case Report

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ABSTRACT

Bacterial oropharyngeal infections in healthy young people rarely give rise to life threatening complications. Lemierre's disease, caused by Fusobacterium necrophorum, manifests as pharyngitis, jugular venous thrombosis and septic pulmonary embolism. A previously fit young male presenting with prolonged pharyngitis, complicated by severe pneumonia and septicaemia is presented. Recognition of this syndrome and early antibiotic therapy can prevent significant morbidity in otherwise healthy people (Critical Care and Resuscitation 2000; 2: 38-41)

Key words: Lemierre's syndrome, Fusobacterium necrophorum, external jugular thrombosis

In 1936 Lemierre described 20 cases of septicaemia in healthy young adults or adolescents caused by the organism Bacillus funduliformis. The disorder usually presented with a history of sore throat which was followed several days later by severe pyrexia, rigors, pulmonary infarcts (secondary to septic emboli originating from thrombosis of the internal jugular vein) with or without arthritic manifestations. Lemierre found the clinical picture so characteristic as to constitute a "syndrome whose diagnosis would be almost impossible to mistake".¹ Courmont and Cade reported the first case of Lemierre's syndrome in 1900.² A century has elapsed since then and while the responsible pathogen is susceptible to antibiotics, there continues to be reports which highlight not only the characteristic signs and symptoms, but also the delay that occurs in both diagnosis and appropriate therapy. We report one such case followed by a brief review of the literature.

CASE REPORT

A previously healthy 21 year old male was referred from his local doctor to the emergency department with dyspnoea and jaundice. He had been unwell for two weeks with a severe sore throat and a painful swelling just below his right jaw. Three days prior to presenting to his local doctor he described symptoms of progressive dyspnoea, productive cough, and bilateral

pleuritic pain. He also reported high fevers and sweats, severe lethargy, malaise and anorexia.

Physical examination revealed a sick, diaphoretic, jaundiced man. He had an oral temperature of 37.9°C, pulse rate 120/min, and blood pressure 90/70 mmHg. His respiratory rate was 28/min and on chest auscultation he had generalised bilateral coarse crepitations. Pharyngeal examination revealed pain on opening his mouth, a marked erythema in the right oropharynx and a fullness beneath the angle of the right jaw. Abdominal examination revealed right upper quadrant tenderness and hepatomegaly.

Initial laboratory testing revealed a white count of $17.2 \times 10^9/L$ (neutrophil count $14.9 \times 10^9/L$ and a shift to the left), haemoglobin 157g/L and a platelet count of $63 \times 10^9/L$. The serum sodium was 125 mmol/L, potassium 4.7 mmol/L, urea 11.6 mmol/L, creatinine 0.086 mmol/L, glucose 6.2 mmol/L, bilirubin 129 $\mu\text{mol/L}$, alkaline phosphatase 168 U/L, alanine amino transferase 257 U/L and albumin 32 g/L. Arterial blood gases, while receiving oxygen at 6 L/min via a face mask, revealed a pH 7.38, $p\text{CO}_2$ 47 mmHg, $p\text{O}_2$ 53 mmHg, bicarbonate 27 mmol/L, base excess 1 mmol/L and lactate of 2 mmol/L. Coagulation tests showed an INR of 1.7, APTT 33.3 s and fibrinogen of 4 g/L. The Chest X-ray revealed the presence of bibasal pleural effusions and multiple faint bilateral nodular densities throughout both lung fields.

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A thoracic CT scan showed bilateral pleural effusions and multiple peripheral 1.5cm nodules (Figure 1). The abdominal scan revealed hepatosplenomegaly and a normal biliary system. Mediastinal or retroperitoneal lymphadenopathy were not noted.



Figure 1. Thoracic CT at level of the lower hilum demonstrating numerous pulmonary nodules (more noticeable on the right side) and bilateral effusions

A diagnosis of pneumonia with the possibility of an underlying malignancy (in view of the lung nodules and hepatomegaly) was made and the patient admitted to the high dependency unit. Blood and sputum were taken for microscopy and culture, although no antibiotics were given at this stage. Within a few hours the patient's condition deteriorated with increasing tachypnoea and worsening hypoxia so he was transferred to the intensive care unit for endotracheal intubation and mechanical ventilation. Following intubation, the patient became hypotensive and oliguric requiring intravenous fluid and noradrenaline. The initial results of sputum microscopy revealed multiple Gram negative rods resembling *Haemophilus* species so intravenous ticarcillin:clavulanic acid (3.1g 8-hourly) and erythromycin (1 g 6-hourly) were commenced along with a single dose of tobramycin (320 mg). Progressive hypoxaemia and hypotension with peripheral cyanosis supervened despite the initial treatment, so a pulmonary artery catheter was inserted via the right internal jugular vein. The cardiac index was 7.0 L/min/m², systemic vascular resistance index 704 dyne/sec/cm⁵/m² and pulmonary artery occlusion pressure was 12 mmHg. Bilateral intercostal catheters were inserted, draining purulent fluid (containing gram negative rods) which was associated with a marked improvement in gas exchange and haemodynamic status.

A repeat microbiological analysis of the pleural fluid and sputum suggested a *Fusobacterium necrophorum* infection. The patient's antibiotic therapy was changed to intravenous benzylpenicillin (2.4 g 4-hourly),

cefotaxime (1 g 6-hourly) and metronidazole (500 mg 8-hourly). Three days after presentation the organism was grown from blood and pleural cultures. No malignant cells were seen on pleural fluid cytology.

It was believed that the patient initially had *Fusobacterium* pharyngitis and developed jugular thrombophlebitis and septic pulmonary thromboembolism. A CT scan of the neck with intravenous contrast was performed after removal of the pulmonary artery catheter, which showed marked parapharyngeal oedema, an enlarged lymph node behind the right carotid vessels and right external jugular vein thrombosis. The internal jugular vein was free of clot. A transoesophageal echocardiograph was also performed, which did not demonstrate endocarditic valve lesions or clots in the superior vena cava or pulmonary arteries.

The patient made a satisfactory recovery with resolution of the pulmonary nodules, liver and coagulation abnormalities and was discharged from the intensive care unit. However, he had a continuing problem with bilateral loculated pleural effusions that required surgical drainage and a prolonged course of antibiotics before resolution occurred.

DISCUSSION

Lemierre's syndrome is primarily a disease of fit young adults and adolescents,³ with patients who are less than 10 years old being uncommon. In this age group the presentation is usually that of post otitis media meningitis,^{4,5} with or without cerebral vessel thrombosis.⁶ The decline of reported cases over the last few years is notable. Alston reported 269 cases in 1955,⁷ Gunn 148 in 1956,⁸ while Sinave found only 38 reported cases between 1974 to 1978.³ In the latter group the ages ranged from 7 to 38 years (with a mean age of 20 years) and there was a preponderance of males (60%).

Fusobacterium necrophorum is the organism most frequently associated with Lemierre's syndrome.⁹ It is synonymous with *Bacillus funduliformis*, *Bacillus necrophorum* and 50 other names that have been used in the past 100 years.¹⁰ It is an obligate anaerobe, a Gram negative, non-motile rod with distinct morphology. It constitutes part of the normal flora of the upper respiratory tract and is present in large numbers in the gingival crevice and subgingival plaque of all healthy adults.¹¹ It is also normally present in the female genital tract and large bowel, with reported cases of *Fusobacterium* septicaemias following bowel surgery and abortion.^{12,13} As an anaerobe, it has the unusual capacity to invade as a primary pathogen. It possesses a lipopolysaccharide endotoxin and various exotoxins including leukocidin, haemolysin, lipase, and a cytoplasmic toxin.¹⁴ The inflammatory response is largely dependent on the heat stable leukocidin. It has a

long incubation period (e.g. 4 days) and is susceptible to benzylpenicillin, metronidazole and clindamycin. However up to 40% of the isolates are beta-lactamase producing, explaining the failure of penicillin treatment alone in some cases. Other organisms less commonly associated with Lemierre's syndrome include Streptococci, Bacteroides, Peptostreptococci and Eikenella corrodens.¹⁵

The onset the syndrome is usually heralded by a sore throat. The primary site of infection in greater than 90% of cases is the palatine tonsil. In Sinave's review, 97% had tonsillitis or peritonsillar abscess, with one case of odontogenic infection.³ Parotiditis, otitis media and mastoiditis represent other potential sources. Typically, one week elapses between the initial infection to the development of the septicaemia, coining the term 'post anginal septicaemia'. At this stage there can be a wide variation in tonsillar appearance ranging from normal to exudative, thus local findings of pharyngitis may be absent on presentation. High fever, dyspnoea, pleurisy and haemoptysis, as originally described by Lemierre, often occur. Chest X-ray and CT typically show nodular shadowing, cavitations and effusions.

The presence of unilateral tenderness around the angle of the mandible and/or over the anterior border of the sternocleidomastoid muscle, with trismus and dysphagia are indicative of internal jugular vein thrombosis, a cardinal feature of the syndrome. The exact cause of the thrombosis is unknown. Possible mechanisms include propagation of thrombus from the tonsillar veins, luminal thrombosis due to perivenous lymphadenopathy, or direct extension through the fascial planes of the neck. Palpable induration of the thrombosed internal jugular vein (the cord sign) may be mistaken for lymphadenopathy. Internal jugular vein thrombosis is best demonstrated by contrast enhanced CT and MRI of the neck.^{16,17} Its significance lies as a source for septic emboli, invariably to the lungs and less frequently to joints, bones, meninges, liver and soft tissues. Up to 75% of cases have abdominal pain with hepatosplenomegaly and jaundice, adding to the complex clinical picture.¹⁸ Metastatic liver abscess and purulent peritonitis have been reported rarely.

The diagnosis is often not immediately evident. Doubts may be cast on the level of immunocompetency of a seriously ill young adult with no previous history of chronic disease. Multiple organ dysfunction is manifested by abnormal liver function, renal failure and coagulopathy. Neutrophil leukocytosis, anaemia and thrombocytopenia are common. A false positive monospot can occur in the presence of Fusobacterium necrophorum, so serological confirmation (e.g. IgG and IgM antibodies to Epstein Bar virus) is required to confirm a diagnosis of infectious mononucleosis.¹⁹

Confirmation of growth on blood cultures takes 2-7 days.

With the increase in beta-lactamase producing Fusobacterium necrophorum, benzylpenicillin alone is inadequate therapy. Antibiotics with beta-lactamase resistance (e.g. clindamycin, ticarcillin:clavulanate, ampicillin:sulbactam, and metronidazole) are recommended.²⁰ Resistance to metronidazole has not been reported, and often the addition of metronidazole to penicillin leads to clinical improvement. Prognosis improves with early treatment. The mortality in Leugen's series was 1 in 29 if treated at presentation compared with 1 in 8 when antibiotics were delayed for greater than 4 days.²¹ If there is continued evidence of sepsis despite antibiotic therapy, ligation and excision of the internal jugular vein should be considered. Anticoagulation is indicated if there is retrograde cavernous sinus thrombosis.²²

Our case report contains many of the typical features of Lemierre's syndrome, but highlights the difficulty and delay in diagnosis of a now rare disease which is associated with considerable morbidity in the young. External jugular thrombosis in the absence of internal jugular vein thrombosis has not been reported before, however the possibility of displacement by the insertion of the pulmonary artery catheter exists, therefore it is advisable to avoid the use of jugular veins for central venous cannulation when this condition is suspected.

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