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<b>TITLE OF CASE</b>
An unusual case of Lemierre's syndrome.
<b>AUTHORS OF CASE</b> <i>Please indicate corresponding author by *(after the author's name)</i>
Issrah Jawad*, Arjun Chandna, Stephen Morris-Jones, Sarah Logan
<b>SUMMARY</b> <i>Up to 150 words summarising the case presentation and outcome</i>
<p>A young previously healthy patient presented with sepsis and cavitating pneumonia. <i>Campylobacter rectus</i> was isolated from blood cultures and subsequent CT neck showed an internal jugular vein thrombosis. Treatment was with antibiotics, anticoagulation and supportive management.</p> <p>Lemierre's syndrome is an infectious thrombophlebitis of the internal jugular vein. Although a rare diagnosis since the use of penicillin for treatment of acute pharyngitis, it is being reported with increasing frequency[1,2]. Usually associated with <i>Fusobacterium</i> species, we believe that this is the first reported case of Lemierre's caused by <i>Campylobacter rectus</i> - an anaerobic member of the human oral cavity flora, usually associated with localised periodontal disease. The bacillus was isolated from blood during the acute presentation.</p>
<b>BACKGROUND</b> <i>Why you think this case is important – why you decided to write it up</i>
It is widely known that Lemierre's syndrome may be caused by a variety of, mostly anaerobic, oral cavity flora. With the advent of more advanced laboratory identification methodologies, clinicians should be alert to the implications of isolating more unusual organisms.
<b>CASE PRESENTATION</b> <i>Presenting features, medical/social/family history</i>
A 29-year old Sardinian man presented to the emergency department (ED) complaining of a sore throat, fever and myalgia. He had blood tests and a chest radiograph and was

subsequently discharged with a diagnosis of glandular fever. A week later he re-presented with symptoms of chest pain, shortness of breath and recrudescence of his fever.

He was normally fit and well and had a quiescent history of Glucose-6-phosphate dehydrogenase (G6PD) deficiency from which he had never suffered complications. He had a previous excision of a hydatid liver cyst in his early teens in Italy. He had been living in London for three years and working as a waiter.

At presentation he was tachycardic (110 bpm), hypotensive (systolic BP 91mmHg) and febrile (38.1°C). His blood tests showed a new anaemia with a haemoglobin (Hb) of 83 g/L fallen from a value of 115 g/L seven days earlier, a neutrophilia with a count of  $24.47 \times 10^9/L$  and a C-reactive protein (CRP) of 251.9 mg/L.

A repeat chest radiograph showed new changes: multiple bilateral lung nodules with prominent opacification and cavitation in the right upper zone. He was admitted and treatment commenced for a cavitating community-acquired pneumonia with intravenous (IV) co-amoxiclav.

The following morning a repeat full blood count showed worsening anaemia with a Hb of 68 g/L, the blood film showed target cells, infrequent keratocytes and polychromatic cells but no other specific features of oxidative haemolysis. The patient was transfused 2 units of packed red blood cells with the haematological opinion of an acute G6PD deficiency crisis.

His respiratory viral screen was positive for coronavirus, but all other major respiratory and blood-borne viruses were negative. Blood cultures, which had been drawn at admission, flagged positive for a Gram-negative coccobacilli on day three. There was initial improvement, but he deteriorated over the next 48 hours, complaining of pleuritic chest and neck pain, and developing tachycardia, hypotension, increasing oxygen requirements and worsening anaemia. A repeat chest radiograph demonstrated new bilateral pleural effusions.

He was transferred to the critical care unit where his right sided pleural effusion was drained, a morphine PCA commenced and he received a further red blood cell transfusion.

#### **INVESTIGATIONS *If relevant***

A CT pulmonary angiogram confirmed extensive bilateral parenchymal nodules with evidence of cavitation; the distribution was (considered) more suggestive of a cavitating pneumonia than septic emboli (figure 1, figure 2).

The patient's marked and continuing neck and throat pain warranted further investigation specifically to exclude possible abscess formation. A CT neck with contrast showed a 65 mm filling defect in the left internal jugular vein (IJV) with a central thrombus extending from the level of the distal left common carotid artery to the level of the left lobe of the thyroid (figure 3).

The isolation of the culprit organism was problematic. It took three days for the anaerobic blood culture bottle to flag, and even after the identification of Gram-negative coccobacilli, the culture on solid medium was challenging. A satisfactory species-level identification by MALDI-TOF was achieved, and this confirmed by molecular 16S rDNA sequencing from the isolate colonies. Susceptibility testing was not possible as the isolate failed to cultivate.

Once the blood cultures confirmed that the patient was bacteraemic, a transthoracic echocardiogram was requested to screen for evidence of valvular seeding. This showed no evidence of infective endocarditis.

#### **DIFFERENTIAL DIAGNOSIS *If relevant***

Common causes of rapidly-developing cavitating pneumonias include *Klebsiella pneumoniae* and *Staphylococcus aureus*. The IJV thrombosis raised the suspicion of Lemierre's syndrome. Expecting the blood culture to isolate *Fusobacterium necrophorum*, we were surprised by the identification of a different organism.

The differential diagnosis of his anaemia included an acute phase response, haemorrhage and haemolysis. It was felt most likely to be related to haemolysis, secondary to his underlying G6PD deficiency, triggered by sepsis.

#### **TREATMENT *If relevant***

At the start of his admission, the patient was treated with IV co-amoxiclav 1.2g three times a day (TDS) and clarithromycin 500mg twice a day for a community-acquired pneumonia. As his clinical condition deteriorated his antimicrobials were briefly broadened to piperacillin-tazobactam 4.5g TDS and metronidazole 500mg TDS, both IV. As the diagnosis became clear, on microbiological advice, the piperacillin-tazobactam and metronidazole were discontinued. The co-amoxiclav was restarted on the grounds of possible polymicrobial infection, and the potential for cryptic  $\beta$ -lactamase activity. He was converted to oral therapy to complete a total of six weeks treatment.

Although the patient gave no history of recent dental treatment an inpatient maxillofacial and ear nose and throat review was organised. There was no evidence of periodontal disease and no further investigations were recommended.

Anticoagulation with low molecular weight heparin was commenced, subsequently converted to a direct oral anticoagulant, Rivaroxaban, on hospital discharge. He was anticoagulated for three months in total.

#### **OUTCOME AND FOLLOW-UP**

Our patient made a full recovery and returned to work six weeks after discharge. His chest radiograph appearances had completely resolved at his two month follow up.

He was also seen in the haematology clinic because of his unusual deep vein thrombosis and G6PD crisis. Risk factor screening for recurrent venous thromboembolism (VTE) was negative. The decision was made to stop his anticoagulation after three months as this was a provoked first VTE. His haemoglobin was stable at this review, the haematology opinion was that his haemolytic crisis had been driven by sepsis. He was counselled about future management of his G6PD deficiency. He was advised to start prophylactic folic acid 5mg once daily to help promote his reserves in case of future haemolytic crises.

#### **DISCUSSION *including very brief review of similar published cases (how many similar cases have been published?)***

Lemierre's syndrome, which is also referred to as post-anginal sepsis or human necrobacillosis, is an infectious thrombophlebitis of the internal jugular vein. It is a rare complication of bacterial tonsillitis first reported by André Lemierre in 1936[3]. Suggestive clinical features include persistent neck or throat pain which may or may not be associated with swelling. With the advent of penicillin treatment for tonsillitis, the incidence of this syndrome has dramatically declined with a risk of 0.8 cases per million in the general population[4], although there are suggestions that the condition may be re-emerging[1,2].

Lemierre's syndrome mostly follows infections of the pharynx but can develop after other upper airway and sinus infections. As the causative organism colonises beyond the primary infection site into the parapharyngeal spaces they have access to the peritonsillar blood vessels which allows further spread onto the internal jugular vein[5]. Thrombophlebitis, resulting in both local inflammation and a septic thrombus, carries the potential to embolise[6]. Embolisation most commonly occurs to the lung, but abscesses and septic metastases can occur throughout the body[5].

The organisms most frequently associated with Lemierre's syndrome are those found in the normal oropharyngeal flora[7], in particular *Fusobacterium necrophorum* which is strongly associated with recurrent tonsillitis[8, 9]. More uncommon presentations with *Eikenella corrodens*[10], streptococcal and *Bacteroides*[11,12,13] species have been reported in the literature. To our knowledge, there are currently no reported cases of Lemierre's caused by *Campylobacter rectus* as in our patient.

*Campylobacter rectus* is a Gram-negative, facultative anaerobic bacillus. It is a recognised oral commensal that is associated with dental infections especially early[14, 15] and chronic periodontitis[16], and root canal infections[17]. Case reports have implicated it in more severe cases of invasive sepsis such as subdural abscesses and even necrotising soft tissue infection[18]. Microbiologically the organism is fastidious, but it will grow under routine anaerobic conditions, although this may require prolonged culture of around 7 days, and some have recommended additional atmospheric hydrogen to improve isolation[19]. Organisms are typically susceptible to a range of antimicrobials including  $\beta$ -lactams.

#### **LEARNING POINTS/TAKE HOME MESSAGES 3 to 5 bullet points**

- Lemierre's syndrome is a rare but important differential in patients with a history of recent sore throat and signs of sepsis
- Most commonly caused by *Fusobacterium necrophorum*, other organisms have been associated, predominantly anaerobic bacteria found in the oral cavity
- Supportive management of the septic patient is needed including antibiotics with anaerobic spectrum of activity and anticoagulation
- With the advent of advanced laboratory techniques, unusual organisms may more often be identified. Clinicians need to be alert to classic clinical syndromes caused by more atypical organisms.
- Isolation of anaerobic bacteria from bloodstream is often associated with significant underlying pathology.

#### **REFERENCES Vancouver style (Was the patient involved in a clinical trial? Please reference related articles)**

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### Figure captions

**Figure 1:** A CT of the chest demonstrating extensive bilateral parenchymal nodules with evidence of cavitation in the axial plane

**Figure 2:** A CT of the chest demonstrating extensive bilateral parenchymal nodules with evidence of cavitation in the coronal plane.

**Figure 3:** A CT neck with contrast showing a filling defect in the left internal jugular vein (IJV).

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