Case Report

Infection by Panton–Valentine leukocidin-producing *Staphylococcus aureus* clinically mimicking Lemierre’s syndrome

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Lemierre’s syndrome is an oropharyngeal infection which leads to severe septic thrombophlebitis of the internal jugular vein and metastatic abscesses of the lungs and other organs. It is usually caused by *Fusobacterium necrophorum*, a Gram-negative obligate anaerobe. An unusual case of Panton–Valentine leukocidin (PVL)-producing *Staphylococcus aureus* infection masquerading as Lemierre’s syndrome is reported here. A 32-year-old fit and otherwise healthy male presented on Christmas morning with a boil on his left cheek for 2 days and generalized rash for 3 h. His general condition began to worsen, he developed facial swelling and loss of vision in the left eye and was transferred to the intensive care unit. His treatment was taken over by team of specialists and further investigations revealed thrombophlebitis of the left internal jugular vein and cavernous sinus thrombosis with multiple brain infarcts and lung abscesses. His condition remained critical with multiple cranial nerve involvement despite being on broad-spectrum antibiotics. Blood cultures grew *S. aureus* which was producing PVL toxin. He improved gradually over several weeks. He underwent intensive physiotherapy and made a good recovery. Although a rare entity, it is important to consider Lemierre’s syndrome in septic patients who present with rapidly worsening symptoms.

Introduction

Necrobacillosis or post-anginal sepsis was first described by Lemierre (1936). It is a condition characterized by oropharyngeal infection in otherwise healthy individuals, which leads to severe septic thrombophlebitis of the internal jugular vein in association with metastatic abscesses of the lungs and other organs. The condition is usually caused by *Fusobacterium necrophorum*, a Gram-negative obligate anaerobe. As a result of widespread antibiotic use, particularly in the community, this syndrome has become increasingly rare; hence it may present diagnostic difficulties. Moreover, if this condition is not detected and treated early, the condition itself can become rapidly fatal with very high rates of mortality. We report here an unusual case of Panton–Valentine leukocidin (PVL) (Holmes *et al.*, 2005)-producing *Staphylococcus aureus* infection masquerading as Lemierre’s syndrome.

Case report

A 32-year-old very fit and otherwise healthy male with no significant past medical history presented on Christmas morning to his general practitioner after having noticed a furuncle on his left face 2 days previously and after having episodes of vomiting the night before. His general practitioner prescribed him non-steroidal analgesics; however, that afternoon he noticed that the left side of his face had begun to swell and hence he was referred to Accident and Emergency.

On admission to Accident and Emergency, he was pyrexial and there was marked chemosis and swelling of the left eye and generalized erythematous rashes over the whole body. He was clinically alert and no focal neurological deficit was noted. Visual acuity in the left eye was 6/24. Blood cultures were obtained. He was commenced empirically on cefotaxime 1 g t.i.d., flucloxacillin 1 g q.d.s., gentamicin 240 mg, chlorphenamine 4 mg and hydrocortisone 100 mg. The possibility of orbital cellulitis and cavernous sinus thrombosis was entertained. A CT scan revealed periorbital swelling. He remained pyrexial and his clinical condition began to deteriorate rapidly. He developed dysartria, dysphagia and increased facial swelling and loss of vision in the left eye. He was urgently transferred to the local regional hospital for ophthalmological assessment.

On arrival, he was reviewed by Ophthalmology and orbital cellulitis was not felt to be the cause of his condition. The patient developed stridor and there was evidence of cranial nerve III, IV, V, VI, VII palsies. He was urgently transferred...
to the intensive care unit, where he was intubated and ventilated. The microbiologist was actively involved and the antibiotic regimen was changed to benzyl penicillin 2.4 g four hourly, metronidazole 500 mg t.d.s. i.v., gentamicin 240 mg o.d. i.v., meropenem 1 g t.d.s. and amphotericin B to cover the likely spectrum of pathogens. However, 9 h later his blood cultures grew *S. aureus*, hence benzyl penicillin was discontinued and replaced by flucloxacillin 2 g q.d.s. i.v., to which teicoplanin was added to cover the possibility of community-acquired MRSA until sensitivities were available. The strain proved to be flucloxacillin-sensitive hence the teicoplanin was discontinued. Amphotericin B was withdrawn as a fungal aetiology looked increasingly less likely.

Due to the unusual aggressiveness of the infection and its origin in the community, it was suspected from the outset that the *S. aureus* isolate might be a PVL-producing strain, which was confirmed 11 days later because of the holiday period. The isolate had an unrecognized phage pattern and therefore was thought to be sporadic in occurrence. The strain was positive for toxin genes enterotoxin H (seh) and PVL (*luk-PV*). PVL toxin was confirmed by PCR analysis. The rest of the screen for toxic genes, including that for toxic shock syndrome (*tst*), was negative. His Glasgow Coma Scale remained 3–5/15 with fixed and dilated pupils for nearly 2 weeks. Although he remained continually febrile, his further serial blood cultures were all sterile and his white cell count, erythrocyte sedimentation rate and C-reactive protein level were improving day by day (Table 1). He was haemofiltered as his renal functions were deranged.

A CT scan of the chest showed bilateral consolidation and abscesses of the lungs. His condition slowly improved over 8 days to the stage where an MRI scan of his brain could be performed. MRI of the head and neck revealed cavernous sinus thrombosis and also thrombosis of the left internal jugular vein extending to the jugular bulb above and into the transverse sinus. There were bilateral cerebellar and brain stem infarcts and a left frontal infarct.

In effect, the patient had one very large thrombus extending from the cavernous sinus and in continuity with the left internal jugular thrombus (Fig. 1). It became clear that the patient had severe *S. aureus* sepsis leading to cavernous sinus thrombosis. At this point it was felt possible to rationalize antibiotic treatment to flucloxacillin 2 g q.d.s., linezolid 600 mg b.d. and rifampicin 600 mg b.d. Despite this aggressive antimicrobial treatment, the patient remained pyrexial for 30 days. Although surgical options were considered, they proved impossible as the thrombus had already extended too far proximally.

Initial treatment of the thrombus was with activated protein C and heparin infusion followed by long-term warfarinization with a target international normalized ratio of 2–3. A tracheostomy was required and over the next 2-week period he gradually began to improve. He was weaned off inotropes and sedation and eventually extubated. After an intensive care unit stay of 36 days, he was discharged to his local hospital for rehabilitation.

During the phase of rehabilitation, his initial antibiotic therapy was discontinued and he was commenced on rifampicin and flucloxacillin for a further 6 weeks. Gradually his dysphagia, dysarthria and motor functions improved. A repeat MRI showed resolution of the previously noted infarct, and some reconstruction and flow in the left transverse sinus. However, there was no flow seen in the left internal jugular vein (Fig. 2).

After a considerable period of rehabilitation, he was discharged home. The patient continued antibiotics for another 4 weeks. At review, his inflammatory markers were normal. The patient has returned to work as a quantity surveyor and driving a car with loss of vision in his left eye.

<table>
<thead>
<tr>
<th>Day</th>
<th>White cell count (×10⁹)</th>
<th>Erythrocyte sedimentation rate (mm h⁻¹)</th>
<th>C-reactive protein (mg l⁻¹)</th>
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<tbody>
<tr>
<td>1</td>
<td>10.3</td>
<td>54</td>
<td>141</td>
</tr>
<tr>
<td>8</td>
<td>8.9</td>
<td>93</td>
<td>221</td>
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<tr>
<td>30</td>
<td>5.6</td>
<td>37</td>
<td>17</td>
</tr>
<tr>
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<td>4.6</td>
<td>26</td>
<td>11</td>
</tr>
<tr>
<td>90</td>
<td>5.6</td>
<td>16</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 1. Inflammatory markers during the course of illness
Discussion

Prior to the availability of antibiotics, Lemierre’s syndrome led to fulminant sepsis and death in the majority of patients (Lemiale et al., 2001). In Lemierre’s series (Lemierre, 1936), 18 of the 20 patients that he reported died. Lemierre’s syndrome is most often caused by anaerobic Gram-negative bacilli such as *Fusobacterium necrophorum*, but other pathogens such as *Streptococcus* species, *Peptostreptococcus* species, *Bacteroides* species and other *Fusobacterium* species have been implicated (Bach et al., 1988; Lustig et al., 1995). Our patient had septic thrombophlebitis of the internal jugular vein, a rare complication of *S. aureus* skin infection. As a result of backpressure he also developed cavernous sinus thrombosis and multiple brain infarcts and pulmonary abscesses. In our case, the PVL toxin (Holmes et al., 2005) produced by the *S. aureus* enhanced the virulence of the organism. The case described here involved a penicillin-sensitive strain of *S. aureus*. A similar case involving MRSA was described in Australia (Fong & Watson, 2002).

Conditions mimicking Lemierre’s syndrome usually affect young adults. Lung manifestations are pneumonia, empyema, lung abscesses and pleural effusion. Other common complications include endocarditis, meningitis and disseminated intravascular coagulation (Sinave et al., 1989; Golpe et al., 1999). A high index of clinical suspicion is crucial for the diagnosis. The definitive diagnosis is made with positive culture of the organism responsible and detection of the toxin gene by PCR. High-resolution CT thorax identifies specific lung abscesses as in this case. MR angiogram would be the best modality of imaging to demonstrate vascular complications.

As this syndrome is usually caused by *F. necrophorum*, prolonged i.v. administration of antimicrobial agents known to have a good anti-anaerobic coverage along with drainage of pus-filled cavities will usually be successful in the majority of patients. The recommendation that patients receive at least 4–6 weeks of i.v. antibiotics would appear to be appropriate. However, other antibiotic regimes may be necessary as one must consider the possibility of other organisms causing a condition clinically similar to classical Lemierre’s syndrome. In our case, antibiotic therapy was carried out for 3 months due to the large size of the thrombus, the slow resolution of pyrexia and concern over possible viable organisms embedded in the clot. Due to the thromboembolic nature of the condition, the patient was anticoagulated. A recent review (Moore et al., 2002) showed that 11 of 41 patients with extensive thrombosis improved following the addition of anticoagulants heparin followed by warfarin for up to 6 months.

References


