Case Report

Lemierre's syndrome and septicaemia caused solely by *Arcanobacterium haemolyticum* in a young immunocompetent patient

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We present a case of septicaemia caused by *Arcanobacterium haemolyticum* in a previously healthy 23-year-old man suffering from acute pharyngotonsillitis, who developed complicated Lemierre's syndrome. Three blood cultures (both aerobic and anaerobic) revealed the exclusive presence of *A. haemolyticum*. The presence of *Fusobacterium necroforum* was not essential for the development of this pathology. To our knowledge, this is the first reported case of Lemierre's syndrome caused solely by *A. haemolyticum*. We confirm that this organism must be considered a potential pathogen in immunocompetent patients.

Case report

A 23-year-old male, weighing 84.5 kg, came in to the Emergency Department of Alto Guadalquivir Hospital (Andújar, Jaén, Spain) with a 6-day history of asthenia, anorexia, weight loss, arthromyalgia and a high temperature at night. The patient was suffering from a severe sore throat which worsened on swallowing. He was treated with erythromycin (500 mg per day, orally, for 7 days) and metamazole without improvement. The patient (a shepherd) was in contact with animals 4 days before the symptoms appeared.

On physical examination, the patient had a fever (39.2 °C), with blood pressure at 120/60 mmHg. The left laterocervical region was very stiff and painful, with a large adenopathic mass. The otorhinolaryngological examination showed a hyperaemic pharynx with exudate in the left tonsillar crypt. Throat swab samples were not taken, due to the age of the patient, as this is only indicated in children up to the age of seven (Cooper *et al.*, 2001; Isenberg & Campos, 2004). In addition, the routine microbiological diagnosis procedures for throat swabs do not include analysis for anaerobic micro-organisms, since they form a part of the normal flora in the oropharynx. Abdominal palpation revealed mild hepatomegaly, painful on palpation, without signs of peritonism. Blood samples showed $23\,580 \times 10^9$ leukocytes l^{-1} , 14.1 g haemoglobin dl^{-1} and $65\,000 \times 10^9$ platelets l^{-1} , with absence of schistocytes, and platelets without morphological changes. The serum biochemistry findings were: urea, 102 mg dl^{-1} ; creatinine, 2.46 mg dl^{-1} ; total bilirubin, 4.39 mg dl^{-1} ; direct bilir-

ubin, 3.51 mg dl^{-1} ; aspartate aminotransferase, 62 U l^{-1} ; alanine aminotransferase, 65 U l^{-1} . The urine was choluric with abundant red blood cells in the sediment, without cylinders. The serology was negative for cytomegalovirus, Epstein–Barr virus, human immunodeficiency virus, hepatitis B virus, hepatitis C virus and toxoplasma. Three different samples (two bottles each) were taken consecutively (every 2 h) for blood aerobic and anaerobic microbiological cultures. Thoracic and abdominal radiographs were normal. An abdominal–pelvic ultrasound scan showed an acute nephropathy. The patient was diagnosed with complicated left pharyngotonsillitis, acute renal failure and cholestatic liver failure.

Empiric treatment was started with high doses of amoxicillin/clavulanic acid and metronidazole, associated with intensive i.v. fluid therapy. The patient started to improve, with signs of a reduction in cervical inflammation and renal and hepatic failure.

On the second day, a cervical contrast-enhanced computed tomography (CT) scan demonstrated complete thrombosis of the left internal jugular vein (Lemierre's syndrome; Fig. 1). In addition, the CT scan showed low-density areas, consistent with no confluent microabscesses; for this reason any abscesses were not drained. The patient also presented small inflammatory adenopathies up to 1 cm. Treatment was started with full doses of enoxaparin.

On the third day, the patient developed progressive dyspnoea, with respiratory failure (O_2 saturation of 86 % basal), stridor and pathological noises in the lower lungs. A chest X-ray was done, showing right basal condensation, indicative of right basal pneumonia. The most significant

Abbreviation: CT, computed tomography.

Fig. 1. Contrast-enhanced CT scan of the neck showing an increase in size of the left amygdalar region (white star) with low density areas, consistent with no confluent microabscesses. The white arrow shows the complete thrombosis of the internal jugular vein, while the jugular vein common, and jugular external and carotid arteries are permeable.

analytical data were: $17\,160 \times 10^9$ leukocytes l^{-1} (93 % neutrophils); 13 g haemoglobin dl^{-1} ; $192\,000 \times 10^9$ platelets l^{-1} ; creatinine, 1.65 mg dl^{-1} ; aspartate aminotransferase, 44 U l^{-1} ; alanine aminotransferase, 51 U l^{-1} .

Treatment was started with imipenem (1 g intravenously t.d.s.) together with metronidazole. An improvement was seen in the hepatic and renal analytical parameters. When the thoracic control CT scan was performed, a bilateral pleural effusion was found. It was drained, and we obtained a transudate with negative microbiological culture, probably due to the antibiotic treatment.

The patient was discharged home in good general condition after 7 days of hospitalization. The treatment at home was acenocoumarol (for 3 months) and clindamycin (2 $\times$ 300 mg tablets t.d.s. for 10 days).

Microbiological findings

After 8 h of incubation of the three blood cultures (two bottles each) obtained previously (BD BACTEC Plus Aerobic/F and BD BACTEC Lytic/10 Anaerobic/F; Becton Dickinson), microbial growth was found in the three blood cultures (both aerobic and anaerobic), using the BACTEC system (BACTEC 9050; Becton Dickinson). All blood cultures (all bottles) were subcultured on blood agar plates,

both aerobically and anaerobically, for 72 h at 37 °C to exclude the presence of other anaerobic pathogens; indeed, all anaerobic plates were incubated for 4 days more to rule out *Fusobacterium necroforum* co-infection. In addition, the positive blood cultures were subjected to a Gram stain. In all cases, there was only growth of a Gram-positive, catalase-negative, oxidase-negative bacillus; a Gram-negative bacillus was not observed in any case. The micro-organism was identified as *Arcanobacterium haemolyticum* using API Coryne (bioMérieux).

Since there is no standardized method for studying the antibiotic susceptibility of *A. haemolyticum*, this was determined by the diffusion disc-plate method (Kirby–Bauer). The isolated micro-organism showed sensitivity to penicillin, oxacillin, tetracycline, erythromycin, clindamycin, cefotaxime, ciprofloxacin and vancomycin, and resistance to colistin.

A. haemolyticum must be differentiated from *Arcanobacterium pyogenes*. *A. pyogenes* is part of the normal flora in many domestic animals. *A. pyogenes* ferments xylose while *A. haemolyticum* does not. Indeed, *A. pyogenes* is a rare cause of pyogenic infections in humans (Hermida Amejeiras *et al.*, 2004).

Discussion

A. haemolyticum can be found on the skin and in the pharynx of healthy humans. Occasionally it has been isolated from pharyngeal exudates in patients suffering from acute pharyngitis (White & Foshee, 2000), the highest incidence being observed in individuals between 15 and 18 years old (Mackenzie *et al.*, 1995). It has also been described as a cause of a systemic invasive disease, often in combination with other pathogens, with a special predilection for males (Skov *et al.*, 1998), presenting two preferential types of pattern: young men without risk factors and older men with an underlying disease (Carlson *et al.*, 1999). Thus Tan *et al.* (2006) showed cases of bacteraemia caused by *A. haemolyticum* in immunocompetent diabetic patients, indicating a higher risk of infection by this micro-organism in diabetes diseases. These results are in agreement with those obtained by other authors (Carlson *et al.*, 1999). Minárik *et al.* (1997) described two cases of serious infections caused by *A. haemolyticum* in immunocompromised patients (neutropenic) suffering from lymphoma.

Young healthy people can also suffer from septicaemia caused by *A. haemolyticum*. van der Eerden *et al.* (2006) described a case of an immunocompetent 20-year-old woman who presented with pharyngitis, rash and necrotizing pneumonia. As *A. haemolyticum* was identified in blood cultures, the patient's condition improved after treatment. Recently, Therriault *et al.* (2008) described a severe sepsis, cavitory pneumonia and pyomyositis caused by *A. haemolyticum* in an 18-year-old male with a medical history of mild asthma.

Lemierre's syndrome is characterized by peritonsillar infection followed by unilateral swelling and tenderness along the sternocleidomastoid muscle owing to thrombophlebitis of the internal jugular vein. The incidence of Lemierre's syndrome caused by *F. necroforum* (typical pathogenic agent involved in the appearance of this syndrome) was described by Hagelskjaer Kristensen & Prag (2008) as being 14.4 cases per million people per year in 15–24-year-old Danes. Younus *et al.* (2002) reported the first case of Lemierre's syndrome caused by co-infection with *A. haemolyticum* and *F. necroforum*.

In the case in question, the patient was immunocompetent and was not suffering from any other underlying disease that could predispose him to the progression of *A. haemolyticum* infection. To our knowledge, this is the first reported case of Lemierre's syndrome caused solely by *A. haemolyticum*. In relation to this, Bomke *et al.* (2009) described a case of a 20-year-old patient with multiple peritonsillar abscesses caused by *A. haemolyticum*; due to the extremely virulent behaviour of the micro-organism in that case, these authors suggested that in certain clinical situations, some patients could be developing Lemierre's syndrome.

Two different biotypes have been described that enable the classification of *A. haemolyticum* (Carlson *et al.*, 1994a): smooth and rough. The micro-organism isolated in our case was a rough biotype, because of the morphological appearance of the colonies, the absence of β -haemolysis, and it was negative for sucrose and trehalose fermentation. Also, in accordance with other studies (Carlson *et al.*, 1994a), this biotype is more frequently associated with isolation from the respiratory tract.

The clinical experience of treatment of septicaemia caused by *A. haemolyticum* is limited. This organism remains susceptible to most classes of antimicrobials, including penicillins, cephalosporins, carbapenems, macrolides, tetracyclines, clindamycin and vancomycin (Carlson *et al.*, 1994b; Therriault *et al.*, 2008). Erythromycin and the newer extended-spectrum macrolides commonly used in upper respiratory tract infections such as tonsillitis, otitis media and maxillary sinusitis are not active against fusobacteria (Murray *et al.*, 1999). This could mean a possible presence of *Fusobacterium* in this case. However, all *A. haemolyticum* strains studied so far have been uniformly susceptible to macrolides (Carlson *et al.*, 1999). Although it is a micro-organism which has frequently been shown to be sensitive to erythromycin (Carlson *et al.*, 1999; Mackenzie *et al.*, 1995), the treatment administered before our patient came into the hospital failed. It is possible that this uncontrolled antibiotic treatment provided by primary care services had not been carried out correctly. It is likely that the amount of erythromycin reaching the throat infection (abscess) would not be enough to eradicate the micro-organism (Younus *et al.*, 2002).

Conclusions

As reported by other authors (van der Eerden *et al.*, 2006; Therriault *et al.*, 2008; Younus *et al.*, 2002), we must

consider that *A. haemolyticum* infections that are not treated correctly may progress and lead to serious complications. *A. haemolyticum* alone can cause Lemierre's syndrome, the presence of *F. necroforum* not being essential for the development of this pathology. This micro-organism must be considered a potential pathogen in immunocompetent patients.

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