CASE REPORT

Sepsis-induced purpura fulminans caused by *Pasteurella multocida*Lisa Borges,¹ Nelson Oliveira,¹ Isabel Cássio,¹ Humberto Costa²¹Department of Vascular Surgery, Hospital do Divino Espírito Santo de Ponta Delgada, Ponta Delgada, Azores, Portugal²Intensive Care Unit, Hospital do Divino Espírito Santo de Ponta Delgada, Ponta Delgada, Azores, Portugal

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SUMMARY

A 52-year-old man was admitted with a cutaneous rash associated with septic shock and multiorgan failure, 6 days after a dog bite. He was started on empiric antibiotic therapy and supportive measures. The patient's condition aggravated, with need for invasive mechanical ventilation and intermittent haemodialysis, and evolution from a petechiae-like rash to purpura and gangrene, culminating in bilateral lower limb amputation. The blood cultures revealed only *Pasteurella multocida*, after 10 days of incubation.

P multocida infection is a rare cause of soft tissue infection that subsides with oral antibiotherapy. Infections causing sepsis are rare and appear in immunocompromised patients. *Purpura fulminans* induced by sepsis is a rare, life-threatening disorder. This syndrome should be recognised promptly, so early treatment is instituted. We found no case reports of *purpura fulminans* caused by *Pasteurella* infections in our literature review.

BACKGROUND

This is a unique clinical report of *purpura fulminans* caused by *Pasteurella multocida* infection and presents a wide spectrum of complications associated with a rare cause of sepsis.

CASE PRESENTATION

A 52-year-old man, previously healthy, was admitted with fever, nausea, vomiting, abdominal pain and intense myalgia starting 2 days ago. The patient denied history of similar symptoms and contact with people presenting the same symptoms, but referred a dog bite in the index finger of his right hand and in the nose, 6 days ago (4 days before the beginning of his symptoms). The patient had no history of chronic illnesses, including diabetes mellitus, alcoholism, liver, renal, cardiac or pulmonary diseases, neither did he have actual or previous haematological or immune conditions.

At admission, the patient presented fever (38.3°C), tachycardia (115 bpm), hypotension (83/45 mm Hg), a macular erythematous rash localised in the upper and lower limbs and face and excoriations on the nose and index finger of his right hand, with no signs of infection.

The patient was admitted in the Intensive Care Unit (ICU), with severe sepsis without known infectious focus and associated multiple organ failure (acute renal failure; liver dysfunction and haematological dysfunction characterised by leucopenia, neutropenia, thrombocytopenia and coagulopathy).

INVESTIGATIONS

The initial investigation comprehensively covered complete blood count, renal function, coagulation study, liver parameters, C reactive protein, erythrocyte sedimentation rate, lactates, urinalysis, blood, urine and faeces cultures and PCR for *Leptospira*. The results from this laboratory workup were as follows: haemoglobin 13.8 g/dL (normal range 14–18 g/dL), leucocytes 1300/mm³ (normal range 4000–11 500/mm³), neutrophils 1050/mm³ (normal range 2000–7500/mm³), platelets 23 000/mm³ (normal range 150 000–450 000/mm³), urea 65 mg/dL (normal range 10–50 mg/dL), creatinine 2.64 mg/dL (normal range 0.8–1.3 mg/dL), lactates 3.23 mmol/L (normal range <1 mmol/L), C reactive protein 19.37 mg/dL (normal range 0–0.3 mg/dL), alanine-aminotransferase 73 U/L (normal range <65 U/L), total bilirubin 2.15 mg/dL (normal range 0.2–1 mg/dL), direct bilirubin 1.23 mg/dL (normal range <0.2 mg/dL), prothrombin time 28.1 s (normal range 9.4–12.5 s), activated partial thromboplastin time 63.9 s (normal range 24–37 s), International Normalised Ratio 2.44 (normal range 0.75–1.18), fibrinogen 144 mg/dL (normal range 280–600 mg/dL), D-dimers 26 388 ng/mL (normal range 0–250 ng/mL); urine sediment: frequent erythrocytes, leucocytes and epithelial cells.

Thoracic roentgenogram, ECG and echocardiogram were also performed, but revealed no abnormalities.

Index finger roentgenogram showed no signs of osteomyelitis or arthritis.

TREATMENT

The patient was started on empirical antibiotic therapy with ceftriaxone, clindamycin and tigecycline, fluid resuscitation, intravenous non-fractionated heparin, vasopressor amines and transfusion of fresh frozen plasma and platelets.

OUTCOME AND FOLLOW-UP

The patient's condition subsequently aggravated, with severe anaemia and need for recurrent transfusions of erythrocyte concentrate. He also presented diffuse alveolar haemorrhage, leading to suspension of intravenous heparin, orotracheal intubation and controlled mechanical ventilation, and acute renal failure with anuria, leading to intermittent haemodialysis. The erythematous macular rash, initially petechiae-like, evolved to a purpuric rash with cutaneous vesicles (figure 1) and then the patient presented a rapid progression to *purpura fulminans*, with gangrene of the lower limbs (figures 2 and 3), the index finger of his right hand (figure 4)

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Figure 1 Purpuric rash of the upper limb.

and his nose, which culminated in bilateral above-the-knee amputation, index finger amputation and debridement of nose skin and cartilage. Owing to the patient's condition, all the surgical interventions were performed at the same time, 9 days after the patient's admission at the ICU.

The blood cultures, presenting initially with non-specified slow growth bacteria, would only be conclusive by the 10th day of incubation, revealing *P multocida*, with no other microorganisms isolated. The antibiogram revealed that this bacterium was sensitive to penicillin, ampicillin, piperacilin—tazobactam, third generation cephalosporins, tetracycline, rifampicin and erythromycin, and it was resistant to gentamicin and clotrimoxazol. The antibiotics clindamycin and tigecycline were not tested. Owing to this new data, although the initial antibiotics prescribed included ceftriaxone which, according to the antibiogram, was effective against *P multocida*, the antibiotherapy prescribed was removed and piperacilin—tazobactam was initiated.

After this change in the antibiotherapy prescribed and the bilateral lower limb amputation, the patient progressively recovered, with normalisation of his renal function, thus suspending intermittent haemodialysis, and with improvement of respiratory function, with a clear thoracic roentgenogram and transition from mechanical ventilation to spontaneous breathing.

The patient was discharged from the hospital after total clinical and laboratory recovery, with no complications besides

Figure 3 Gangrene of the left foot.

bilateral lower limb and index finger amputation, and persisted to be stable during the entire follow-up.

DISCUSSION

P multocida can cause human infection and is transmitted to humans through dog or cat bite, scratch or lick. The clinical manifestations associated with *P multocida* are soft tissue, ocular, respiratory or intra-abdominal infections; septic arthritis, osteomyelitis, meningitis, endocarditis and, infrequently, sepsis.¹

Bacteraemia, in the majority of cases, occurs when there is evidence of localised infection and in patients who suffer from liver disease or diabetes mellitus. It can develop in 25–50% of patients with pneumonia, meningitis or septic arthritis.¹

The definitive diagnosis of *P multocida* infection relies on the culture of the microorganism.¹

P multocida infections have a good prognosis, with complete resolution when limited to the soft tissue. In case of meningitis, endocarditis or bacteraemia, the prognosis is poor and mortality amounts to 25–30% of patients.^{1,2}

Purpura fulminans is a rare but life-threatening disorder, characterised by haemorrhagic infarction of the skin, associated with disseminated intravascular coagulation and dermal vascular thrombosis. This may progress rapidly to multiorgan failure due to thrombotic occlusion of small-sized and medium-sized blood vessels. It is usually seen in children, but it can also occur in adults.^{3–10}

Figure 2 Gangrene of the lower limb.

Figure 4 Necrosis of the index finger of the right hand.

The three most common aetiological categories of *purpura fulminans* are idiopathic, inherited or acquired coagulation abnormalities or sepsis induced, being the last and the most frequent of all.^{7–9} The septic causes of purpura are known to be direct invasion of the vascular wall and lumen by the microorganisms, septic embolism, septic vasculitis, thrombocytopenia and disseminated intravascular coagulation.³

The most common agent of sepsis-induced *purpura fulminans* is meningococcus, followed by pneumococcus, but there are also clinical cases described of *purpura fulminans* associated with infection by *Haemophilus influenzae*, *Streptococcus* of groups A and B, *Staphylococcus aureus*, *Enterococcus faecalis*, Enterobacteriaceae, varicella zoster virus and *Plasmodium falciparum*.^{3–9} We found in the literature one isolated case of *purpura fulminans* secondary to systemic leptospirosis and two cases of *purpura fulminans* caused by *Capnocytophaga canimorsus*, after a dog bite.^{7 10 11}

The cutaneous lesions seen in *purpura fulminans* start with petechiae-like lesions, caused by leaking of red blood cells from vascular disruption, progressing to haemorrhagic purpuric lesions with a surrounding erythematous border, later to vesicles and culminating with necrosis of the dermis and subcutaneous tissue. In extreme cases, this necrosis may lead to symmetrical peripheral gangrene.^{4 7 8} This process also affects the lungs, kidneys and adrenal glands, leading to multiorgan failure.^{4 9}

The diagnosis of *purpura fulminans* and its underlying infectious cause can be made on measurement of fibrinogen, D-dimers, platelets, PT, aPTT, protein C, protein S and antithrombin III levels; renal and liver function; blood, urine and tissue cultures and even cutaneous biopsy.^{3–5 7–9 12 13}

The basis of treatment of *purpura fulminans* is addressed to the underlying cause, which in case of sepsis-induced *purpura fulminans* involves prompt empiric antibiotherapy. Given the most common agents of this syndrome being meningococcal and *Streptococcus*, the first-line antibiotic considered should be a third-generation cephalosporin.^{3–8 13 14}

Supportive measures, consisting of fluid therapy, mechanical ventilation, renal replacement therapy, correction of electrolyte and acid-base abnormalities, plasma and platelets transfusion and non-fractionated heparin perfusion are also important in the management of the patient.

Surgical management involves debridement of necrotic lesions, early fasciotomy when there is evidence of compartment syndrome, skin allograft, sympathectomy or limb amputation.^{8 15–18} Some reports have shown that sympathetic blockade, either acquired or induced by local anaesthesia or

surgery, improves skin perfusion and can reverse the development of *purpura fulminans*.^{19 20}

Purpura fulminans causes multiorgan dysfunction and long-term morbidity and is associated with a mortality rate of more than 50%.^{3–6}

The patient was treated accordingly to the guidelines and even though the infectious agent would only be known in a late phase of the patient's evolution, one of the antibiotics that were initially prescribed was directed against it. Nevertheless, the early empiric antibiotherapy and the supportive measures instituted, although responsible for the patient's survival, did not prevent him from a bilateral lower limb amputation.

Contributors LB participated in conception, design, acquisition, analysis and interpretation of the data; drafting of the article and final approval given. NO and IC participated in analysis and interpretation of the data, critical revision of the manuscript and final approval given. HC participated in acquisition, analysis and interpretation of the data; critical revision of the manuscript and final approval given.

Competing interests None.

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Learning points

- ▶ *Pasteurella multocida* infections are associated with a good prognosis and rarely cause sepsis.
- ▶ Sepsis induced purpura fulminans is a rare disorder and its treatment relies on prompt empiric antibiotherapy.
- ▶ Despite early therapeutic and supportive measures, purpura fulminans carries a bad prognosis, leading to multiorgan failure and significant mortality.
- ▶ We found no clinical reports of sepsis induced purpura fulminans caused by *P multocida* in our literature review.

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