CASE REPORT

Purpura fulminans and severe sepsis due to *Pasteurella multocida* infection in an immunocompetent patient

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SUMMARY

A 75-year-old woman was admitted into the intensive care unit, with severe sepsis and renal failure. She developed purpura fulminans (PF) of bilateral upper and lower extremities along with gangrene on the tips of her fingers and toes. Blood cultures confirmed *Pasteurella multocida* as the causative organism. Despite aggressive supportive measures, the patient remained dependent on high doses of vasopressors and the gangrene progressed. She ultimately succumbed to her underlying severe sepsis. PF is a rare and fatal dermatological emergency commonly seen in children, but it also occurs in adults. Acute infectious PF occurs secondary to severe sepsis and *P. multocida* is a rare cause of PF. To the best of our knowledge, this is only the second reported case of PF due to *P. multocida* in an adult.

BACKGROUND

Sepsis is a potentially life-threatening complication of infection with a high mortality rate. Several cutaneous findings may be associated with sepsis depending on the infection severity and causative organism. Findings range from mottling of skin due to poor perfusion to life-threatening conditions such as purpura fulminans (PF). PF is a rare and often fatal haemorrhagic disorder, characterised by disseminated intravascular coagulation (DIC), peripheral gangrene and end-organ damage. PF typically develops into symmetric gangrene and rapidly leads to tissue necrosis and extremity loss.¹ A retrospective study reported a mortality rate of 43% with PF and the most commonly associated bacteria are *Neisseria meningitidis*, *Haemophilus influenzae* and *Streptococcus pneumoniae*.²

We present a rare case of PF and severe sepsis due to a *Pasteurella multocida* infection in an immunocompetent patient.

CASE PRESENTATION

A 75-year-old woman presented to the emergency room (ER), with increased difficulty breathing and a temperature of 39.4°C. Her medical history included moderate mental retardation, hypertension, coronary artery disease, arthritis, macular degeneration (impaired vision), paroxysmal atrial fibrillation and obesity. On presentation to the ER, the patient was alert and answering questions; however, she was oriented to neither place nor time. Vitals were: respiratory rate 50/min, heart rate 140 bpm, temperature 38.4°C, O₂ saturation at

88% on room air and 93% when a 4 L nasal cannula was applied.

The patient was initially normotensive, but approximately an hour into her ER stay, her blood pressure dropped to 80/50 mm Hg. Her respiratory function worsened and required non-invasive positive pressure ventilation followed by endotracheal tube insertion and mechanical ventilation, and the patient was transferred to the intensive care unit (ICU).

INVESTIGATIONS

Laboratory testing in the ER indicated white cell count (WCC) $4.1 \times 10^9/L$ (reference range 4.0– $11.0 \times 10^9/L$) with $0.06 \times 10^9/L$ immature neutrophils (reference range 0– $0.04 \times 10^9/L$) and presence of Döhle bodies and 1+ toxic granulations on microscopy, haemoglobin 12.3 g/dL (reference range 12.0–16.0 g/dL), platelets $52 \times 10^9/L$ (reference range $140\text{--}440 \times 10^9/L$), lactic acid 6.3 mmol/L (reference range 0.7–2.5 mmol/L), blood urea nitrogen/creatinine 36, HCO₃⁻ 16 mmol/L, mildly elevated transaminases and total bilirubin (aspartate transaminase (AST) 80 IU/L, alanine transaminase (ALT) 37 U/L, total bilirubin 1.5 mg/dL), and blood glucose of 59 mg/dL (reference range 70–110 mg/dL). Troponin T was 0.19 ng/mL (reference range 0–0.03 ng/mL) and procalcitonin, 16.71 ng/mL (reference range <0.50 ng/mL). Urinalysis showed 16 white cells/high power field, 1000 mg/L protein, small leucocyte esterase and multiple bacteria. Blood cultures and urine cultures were also obtained.

ECG showed atrial flutter with variable block. Chest X-ray showed bibasilar atelectasis with small bilateral pleural effusions. A CT of the abdomen and pelvis revealed no significant abnormalities. An echocardiogram on day 2 of hospitalisation showed an ejection fraction of 45%.

TREATMENT

Owing to the diagnosis of sepsis—indicated by fever, decreased WCC, hypotension and lactic acidosis—broad-spectrum antibiotics, ceftriaxone and vancomycin, were initiated. A urogenital source was initially suspected due to abnormal urinalysis. Sepsis progressed rapidly into shock state with multiorgan dysfunction (renal and hepatic) and the patient required maximum doses of norepinephrine and vasopressin. Continuous renal replacement therapy was initiated later in the clinical course for management of acute renal failure.

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OUTCOME AND FOLLOW-UP

The patient rapidly deteriorated clinically in the ICU with worsening of lactic acidosis from 6.3 to 12.1 mmol/L in a 5-hour period and developed consumptive coagulopathy that further decreased her platelet count to $9 \times 10^9/L$. A DIC panel revealed a D-dimer level of 35.20 $\mu g/mL$ (reference <0.50), fibrinogen 495 $\mu g/dL$ (reference 180–450) and two schistocytes/high power field. Furthermore, the patient developed significant liver dysfunction evidenced by elevated transaminases to 551 U/L AST and 167 U/L ALT in 24 hours and then to 1841 and 777 U/L in 72 hours from presentation.

She soon went into renal failure and required continuous renal replacement therapy. A symmetrical purpuric rash was noted on day 2 over bilateral upper and lower extremities (figures 1–3) along with gangrene of the tips of her fingers and toes, indicating PF. Preliminary results of blood cultures and Gram stain of urine specimen identified Gram-negative rods, and the patient's initial treatment with ceftriaxone and vancomycin on day 1 was changed to meropenem. Despite the change and aggressive clinical measures, the patient's condition continued to decline.

Initial urine cultures drawn in the ER grew *Klebsiella pneumoniae*. However, after changing the patient's Foley catheter and repeating the sample, urine cultures showed mixed flora. The blood cultures were positive for pan-sensitive *P. multocida* (susceptible to cefazolin, cefepime, ceftioxin, ceftriaxone, gentamicin, levofloxacin, meropenem, trimethoprim-sulfamethoxazole, tobramycin, ampicillin-sulbactam and piperacillin-tazobactam). We were also informed by the patient's nursing home that she had been exposed to cats and had had abrasions and lacerations due to recent falls prior to admission. No other organisms were detected on blood cultures.

After considering available options and discussing in detail the quality of life with amputations and existing chronic comorbid illnesses, the family and medical team both decided to change goals of care to comfort measures and the patient passed away some hours later.

DISCUSSION

Acute infectious PF develops from an acute systemic inflammatory reaction to bacterial endotoxins released during infection. These endotoxins ultimately cause cytokines to destroy protein C, protein S and antithrombin III. Depletion of these anticoagulant proteins results in an unchecked coagulation cascade that ultimately leads to DIC, in turn leading to PF.³

Figure 1 Purpura fulminans of bilateral lower extremities with formation of bullae. The picture also shows open wounds due to recent falls.

Figure 2 Purpura fulminans of bilateral upper extremities with gangrene of finger tips.

The dermatological lesions associated with PF begin with vascular leakage of red blood cells secondary to microthrombi-induced endothelial damage and rapidly progresses to haemorrhagic lesions with a raised and hardened erythematous circumference.⁴ The lesions progress to necrosis with formation of bullae and vesicles, and, ultimately, gangrenous necrosis, as the process extends into subcutaneous tissue, sometimes involving muscle and bone. Thus, patients often require amputation of gangrenous extremities during the course of illness and suffer significant morbidity. It is crucial to realise that PF is not simply a dermatological emergency, but that it can also lead to multiorgan failure by affecting the lungs, kidneys and adrenal glands.⁵ In our case, PF developed 36 hours after the patient was admitted.

Acute infectious PF is usually a result of severe sepsis, and has a mortality rate $>50\%$.⁶ To the best of our knowledge, there is only one other case report of PF due to *P. multocida* infection.⁵ Other reported infectious causes for PF include *Enterobacter cloacae*, *Staphylococcus aureus* and *Plasmodium falciparum* malaria.^{7–8} Systemic leptospirosis, *Capnocytophaga canimorsus* and rickettsial infection are rare causes of PF reported in the literature.^{9–11}

Figure 3 Gangrene of finger tips.

P. multocida are small Gram-negative coccobacilli that are primarily commensals or pathogens of animals. Cats are the most common reservoirs, but they can also be carried by dogs, pigs, horses and rabbits. Human infections occur by transfer into an open wound, and can result in a variety of infections involving soft tissue, lungs, joints and bone. Liver involvement is commonly observed in *P. multocida* bacteraemia, potentially resulting in refractory sepsis leading to death. Exposure to cats, with open wounds from recent falls, was thought to be the initiating factor for our patient's infection and the significant elevation of liver enzymes observed was likely due to liver involvement by *P. multocida* bacteraemia. Risk factors for *P. multocida* infection include diabetes mellitus, age >65 years, an immunocompromised state, history of chronic pulmonary disease and significant baseline chronic liver dysfunction.¹² In our case, our patient was 75 years old and had diabetes mellitus; the patient in the first reported case was a healthy 52-year-old immunocompetent man. *P. multocida* is typically susceptible to penicillin; however, penicillin-resistant strains of *P. multocida* have been reported in the literature, mandating use of second and third generation cephalosporin or fluoroquinolones.^{13 14} The diagnosis of acute infectious PF is based on the clinical findings of characteristic rash in a patient with severe sepsis and associated DIC. Thus, investigations helpful in diagnosis include DIC panel (fibrinogen, D-dimer and peripheral smear for schistocytes), prothrombin time, activated partial thromboplastin time, renal and liver function tests, and cultures of blood, urine and involved tissues, to identify the causative organism. A skin biopsy will also help in diagnosis and usually shows small vessel microthrombi, widespread haemorrhage and associated mild vasculitis.

Treatment of underlying infection is the mainstay and early surgical consultation (first 24 hours) has been shown to improve morbidity and mortality in acute infectious PF.^{2 15} The surgeon's role in the management is focused on rapid diagnosis and treatment of compartment syndrome, debridement of all non-viable tissue and reconstruction of residual deformities, all of which can prevent muscle death and thereby avoid amputations. Amputation is necessary for patients in whom tissue perfusion is compromised despite the previously mentioned measures. More than 90% of patients with acute infectious PF require some level of limb amputation, a retrospective study

showed that eight out of nine survivors required amputation of at least one limb and four patients required amputations of all four limbs.¹⁶

Overall, the prognosis for acute infectious PF is often poor. However, early detection of causative agent, initiation of appropriate antibiotics and early surgical consultation, have shown to improve morbidity and mortality. PF associated with *P. multocida* infections is very rare and this is only the second reported case in the literature. With early identification of the commonalities among cases with *P. multocida* infection (immunocompromised with exposure to cats or dogs), it is possible to start appropriate early antibiotic therapy and prevent development of DIC.

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REFERENCES

- Nolan J, Sinclair R. Review of management of purpura fulminans and two case reports. *Br J Anaesth* 2001;86:581–6.
- Childers BJ, Cobanov B. Acute infectious purpura fulminans: a 15-year retrospective review of 28 consecutive cases. *Am Surg* 2003;69:86–90.
- Darmstadt GL. Acute infectious purpura fulminans: pathogenesis and medical management. *Pediatr Dermatol* 1998;15:169–83.
- Smith OP, White B. Infectious purpura fulminans: diagnosis and treatment. *Br J Haematol* 1999;104:202–7.
- Borges L, Oliveira N, Cássio I, et al. Sepsis-induced purpura fulminans caused by *Pasteurella multocida*. *BMJ Case Rep* 2014;2014:pil:bcr2013202441.
- Betrosian AP, Berlet T, Agarwal B. Purpura fulminans in sepsis. *Am J Med Sci* 2006;332:339–45.
- Taniyama D, Miyamoto K. Purpura Fulminans due to *Enterobacter cloacae*. *Intern Med* 2015;54:2425–6.
- Harikrishna J, Mohan A. Infectious purpura fulminans. *Indian J Med Res* 2015;141:130–1.
- Talwar A, Kumar S, Gopal MG, et al. Spectrum of purpura fulminans: report of three classical prototypes and review of management strategies. *Indian J Dermatol Venereol Leprol* 2012;78:228.
- Kullberg BJ, Westendorp RG, van 't Wout JW, et al. Purpura fulminans and symmetrical peripheral gangrene caused by *Capnocytophaga canimorsus* (formerly DF-2) septicemia—a complication of dog bite. *Medicine (Baltimore)* 1991;70:287–92.
- Katoch S, Kallappa R, Shamanur MB, et al. Purpura fulminans secondary to rickettsial infections: a case series. *Indian Dermatol Online J* 2016;7:24–8.
- Tattevin P, Souala F, Gautier AL, et al. Diabetes in patients with pasteurellosis. *Scand J Infect Dis* 2005;37:731–3.
- Nguyen Phuong T, Rosenau A, Phillipon A, et al. [Human pulmonary infection by a strain of *Pasteurella multocida* producing beta-lactamase]. *Presse Med* 1989;18:1886.
- Riera F, Priu R, Goreti Sauca M, et al. [Empyema caused by *Pasteurella multocida* resistant to penicillin]. *Enferm Infecc Microbiol Clin* 1993;11:169–70.
- Roughton MC, Agarwal S, Gottlieb LJ. Surgical management of acute infectious purpura fulminans. *J Burn Care Res* 2011;32:231–6.
- Davis MD, Dy KM, Nelson S. Presentation and outcome of purpura fulminans associated with peripheral gangrene in 12 patients at Mayo clinic. *J Am Acad Dermatol* 2007;57:944–56.

Learning points

- *Pasteurella multocida* sepsis can lead to purpura fulminans (PF) and significant morbidity and mortality.
- Our case report emphasises both the high mortality rate associated with sepsis-induced PF and the need for early detection and treatment of sepsis.
- Along with treatment of underlying infection, early surgical consultation and intervention, when necessary, in the form of debridement of non-viable tissue, fasciotomy or even amputations, have been shown to improve morbidity and mortality in acute infectious PF in retrospective studies.

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