Purpura fulminans in a child secondary to Panton–Valentine leukocidin-producing *Staphylococcus aureus*

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A case of purpura fulminans (PF) in a child secondary to infection with meticillin-sensitive *Staphylococcus aureus* (MSSA) encoding the Panton–Valentine leukocidin (PVL) toxin genes is presented. Occasional cases of PF have been documented secondary to *S. aureus* infection in adults, but, to the authors’ knowledge, not in children. Here the first UK case of MSSA-PVL leading to PF is presented.

**Case report**

A 10-month-old girl presented to her local emergency department in profound septic shock. She had been unwell for 10 days with a coryzal illness and had been pyrexial for 72 h. Initial blood results were: total white cell count 3.0 \( \times 10^9 \) l\(^{-1} \), platelet count 114 \( \times 10^9 \) l\(^{-1} \), international normalized ratio 1.7 and fibrinogen >4.5 mg l\(^{-1} \).

On arrival, she had a capillary refill time of 5 s with a heart rate of 170 beats min\(^{-1} \) and grunting respirations. Examination revealed a widespread, macular erythematous rash, with three punctate petechiae on her shoulder. Suspecting meningococcal septicaemia, she was commenced on intravenous ceftriaxone, fluid resuscitated, intubated and ventilated by 3 h post-presentation.

Despite 100 ml kg\(^{-1} \) fluid boluses and maximal inotropic support, she remained acidotic, at which point teicoplanin was added. The rash became bullous, spreading rapidly and affecting the lower limbs (Fig. 1).

In view of the atypical progression of the rash, clindamycin was added. Bacterial cultures of the fluid from the bullae correlated with initial blood cultures, confirming invasive *Staphylococcus aureus* infection, which was resistant to penicillin, but sensitive to flucloxacillin, erythromycin, tetracycline, vancomycin, clindamycin and rifampicin. The isolates were sent to the Staphylococcus Reference Laboratory, Health Protection Agency (HPA), Colindale, London, for toxin gene profiling and were confirmed as encoding the Panton–Valentine leukocidin (PVL) genes.

Over the next 48 h she remained critically ill on maximal intensive care support. She developed acute respiratory distress syndrome, multiorgan failure and disseminated intravascular coagulopathy requiring significant blood product support. After an initial ventilatory improvement, she deteriorated on day 8 secondary to a pneumothorax.

She continued to develop multiple pneumothoraces and abscesses requiring bilateral chest drains and she was eventually weaned off respiratory support 5 weeks after the initial presentation. The chest X-rays remained abnormal with bilateral, multiple pneumatoceles which were eventually managed with a surgical pleurectomy.

Blood and endotracheal cultures remained positive for *S. aureus* until day 36. Throughout this time, she was treated with multiple courses of antibiotics including clindamycin, imipenem and rifampicin. Despite multiple debridements and early intervention by the vascular surgeons, she underwent a right forefoot and a left mid-tibial amputation. Investigations for immunodeficiency and protein C deficiency were unremarkable.

Follow-up magnetic resonance imaging scans of the left femur demonstrated extensive osteomyelitis. This required further revision and prolonged treatment with antibiotics. At the present time, the child is clinically well.

Screening of household contacts for *S. aureus* carriage could not be performed because the parents and extended family were not resident in our local area.

**Abbreviations:** PF, purpura fulminans; PVL, Panton–Valentine leukocidin.
Discussion

PVL is a phage-encoded, 2-subunit exotoxin. This cytotoxin is formed from two synergistic proteins, LukS-PV and LukF-PV. In combination, an octameric protein is formed which results in pore formation in the cell membrane of leukocytes, allowing an influx of calcium. This effect appears to be concentration-dependent, with apoptosis occurring at low levels and necrosis at higher levels. The toxin is encoded by <5% of clinical isolates of S. aureus, almost half of which are meticillin-resistant (Morgan, 2005).

PVL-S. aureus is mainly associated with necrotic suppurative skin lesions, but it has also been isolated from patients with severe community-acquired necrotizing pneumonia with a mortality rate of 75% (Kravitz et al., 2005). The incidence of PVL-S. aureus infections is difficult to assess accurately. A recent study from the HPA confirmed that 1.6% of the isolates submitted to the laboratory carried the PVL genes (Holmes et al., 2005). Purpura fulminans (PF) is not a notifiable syndrome in the UK and there is a tendency to assume that PF is synonymous with meningococcal sepsis.

Due to the severity of PF and the growing appreciation that several organisms are associated with this syndrome, initial treatment should include broad-spectrum antibiotics (including adequate cover for meticillin-resistant S. aureus) (Morgan, 2005; Kravitz et al., 2005). In dealing with confirmed PVL-S. aureus infection, several studies have reported the value of combination therapy (McCartney et al., 2006) including two or more of vancomycin, clindamycin, linezolid, rifampicin or co-trimoxazole (Klein et al., 2003; Wargo & Eiland, 2005).

A recent report suggests that with appropriate treatment protocols the outcome of PF amongst children can be improved (Gürgey et al., 2005). In this recent series, 43% of the paediatric cases presented with a severe bacterial infection (seven cases), of which 57% (four cases) were secondary to sepsis caused by S. aureus. None of the isolates were tested for PVL. All of these patients survived, albeit with varying degrees of amputation.

There are conflicting thoughts with regard to the use of intravenous immunoglobulin (IVIG) in the treatment of PF due to PVL-S. aureus. There are in vitro data demonstrating neutralization of the PVL toxin (Gauduchon et al., 2004) but there are no comparative clinical studies. Several authors recommend the use of IVIG for its antitoxin properties (Morgan, 2005; Kravitz et al., 2005) although this mechanism has yet to be firmly established (Chambers, 2005).

This is the first report of PF secondary to PVL-meticillin-sensitive S. aureus sepsis in a child in the UK. It illustrates the dramatic evolution of infection caused by PVL. Our aim is to alert clinicians to consider PVL-S. aureus in conjunction with meningococcaemia when dealing with a clinical case of PF and respond promptly with appropriate therapeutic strategies, which may be a combination of antimicrobial, immunological and surgical methods. In our view, the initial choice of antimicrobials should be broad and include adequate anti-staphylococcal cover, including cover for meticillin-resistant S. aureus. These decisions should be made in conjunction with a microbiologist, pending the identification and susceptibility profiles of isolates. Screening for PVL genes in S. aureus isolates should be considered in patients with haemorrhagic necrotizing skin, soft tissue and pulmonary infections to inform clinicians on the appropriate management and prognosis.

Given the evidence of spread of PVL-S. aureus via skin-to-skin contact (Morgan, 2005), we suggest that in cases of serious, life-threatening disease, consideration must be given to screening of close contacts.

References


