Panton–Valentine leucocidin *Staphylococcus aureus* necrotising pneumonia in a clinically well patient

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Introduction

Alongside its role in skin and soft tissue infections, Panton–Valentine leucocidin *Staphylococcus aureus* is occasionally associated with necrotising lower respiratory tract infections (Shallcross et al, 2013). Gillet et al (2002) proposed the classic picture of a patient with a lower respiratory tract infection caused by Panton–Valentine leucocidin *S. aureus*,

Case report

A previously healthy 35-year-old-man was admitted with progressive cough, pyrexia and shortness of breath following travel in India. He was not known to be immunocompromised, and his medical history only included smoking and a fracture to the distal phalanx of his hallux 1 month previously. On examination he was haemodynamically stable, with the only positive findings being pyrexia alongside crackles on auscultation in the right middle and lower lobes of his lungs.

Initial investigations showed a C-reactive protein level of 414 mg/litre and white cell count of 14.2×10^9/litre. The X-ray showed bilateral atypical consolidations (bilateral pleural effusions, confluent consolidation in the right middle and lower zones, and patchy consolidation in the left base and midzone; **Figure 1**).

Mindful of his travel history and radiological pattern of infection, a sputum acid-fast bacillus was sent; this, as well as legionella and mycoplasma testing, was negative. A viral screen, including HIV, was also negative. Owing to his travel history and concerns about the possibility of him having tuberculosis, he was nursed in a side room. After 72 hours of treatment with intravenous benzylpenicillin and oral clarithromycin, as per local guidelines for a severe community-acquired pneumonia, his symptoms were improving and discharge was considered. Although he was clinically well, his white cell count had increased to 17×10^9/litre and his C-reactive protein level had only marginally reduced to around 300 mg/litre.

Following positive sputum culture growing *S. aureus*, his antibiotics were changed to intravenous co-amoxiclav, and subsequently, following positive blood cultures also growing *S. aureus*, he was switched again to intravenous flucloxacillin. Further molecular analysis using polymerase chain reaction for *LukS-PV* and *LukF-PV* genes confirmed methicillin-sensitive Panton–Valentine leucocidin *S. aureus* in both his sputum and blood cultures; linezolid was added to his antibiotic regimen and Public Health England were contacted.

Subsequent computed tomography of the chest identified an 8.5 cm cavity in the right lower lobe containing fluid, gas and septations, alongside adjacent right lower lobe consolidation with cavitating foci (**Figure 2**). A transthoracic echo showed no valvular vegetations or defects, just a small pericardial effusion; an ultrasound of his abdomen was unremarkable. His previous toe fracture was reviewed; it was not painful, and there were no skin breaks, erythema or swelling.

Following concerns regarding a slow biochemical response, and considering literature proposing poor outcomes with beta-lactam antibiotics, flucloxacillin was stopped and teicoplanin and rifampicin were started, alongside linezolid. His inflammatory markers improved and he was discharged with long-term venous access to complete a 4-week course of intravenous teicoplanin, alongside existing oral antibiotics. Respiratory follow up with repeat imaging was arranged, and showed resolution of the observed infective changes. As his productive cough had reduced, Public Health England were happy for him to leave isolation following decolonisation, and decolonisation of his household and close contacts was arranged.

The patient was remarkably well throughout; he did not develop sepsis, remained in a ward-based setting and at no point required oxygen therapy.

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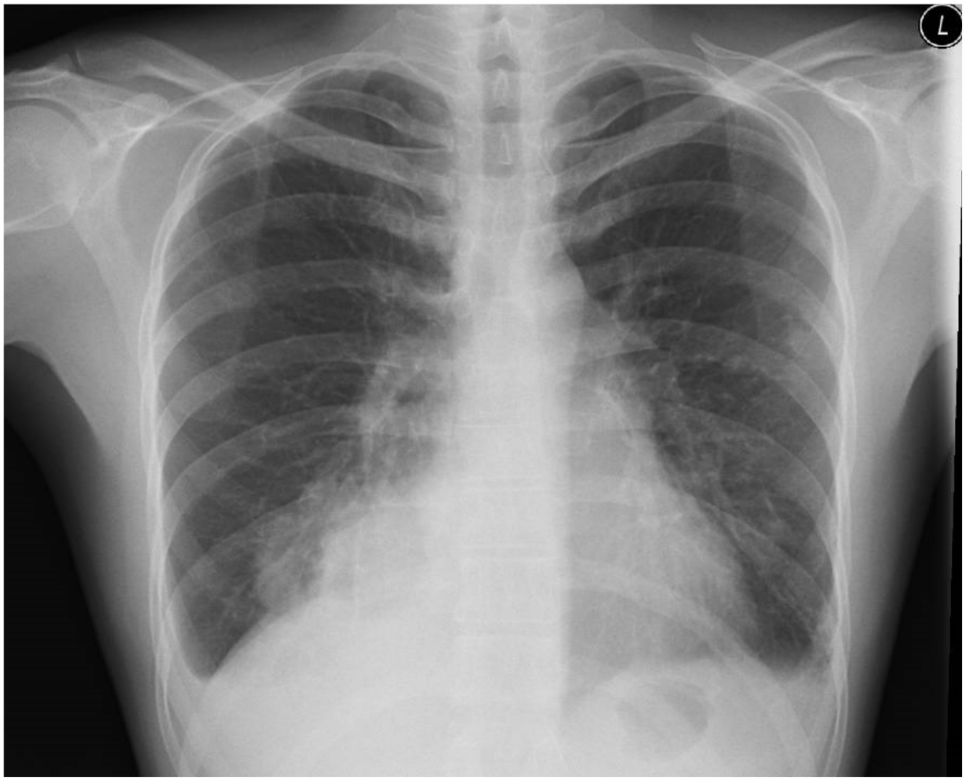

Figure 1. Admission chest X-ray.

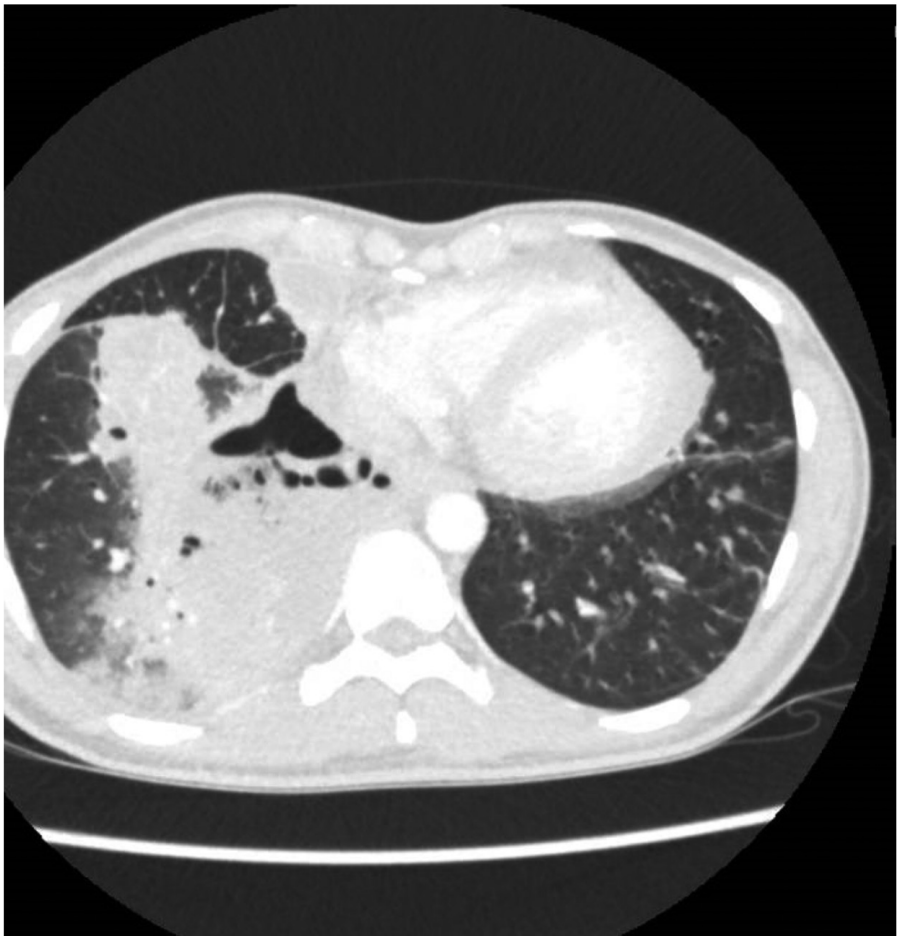

Figure 2. Computed tomography of the chest.

describing a previously well, young patient with multi-lobar consolidation and resultant rapidly deteriorating respiratory function, following a flu-like prodrome. Often fatal, Panton–Valentine leucocidin *S. aureus* lower respiratory tract infections are commonly associated with haemoptysis and overwhelming sepsis (Gillet et al, 2002; Kreienbuehl et al, 2011).

Discussion

The exact pathogenesis of Panton–Valentine leucocidin *S. aureus* in sepsis is unknown, although animal studies highlighted a role for neutrophil migration and leukocyte lysis within lung tissues, likely contributing to lung parenchymal necrosis (Diep et al, 2010, 2013). The Panton–Valentine leucocidin toxin has a key role in the development of necrotising pneumonia, a pneumonic complication in which severe infection causes cavitation and breakdown of lung parenchyma (Jung et al, 2008; Tsai and Ku, 2012). A systematic review of Panton–Valentine leucocidin *S. aureus* case studies predicted a 41% mortality rate, with 87% of cases displaying multi-lobar involvement (Kreienbuehl et al, 2011).

While this patient presented in a similar manner to previously published cases, with an initial flu-like prodrome and multi-lobar consolidation with cavitation, many classical features were lacking, including rapidly deteriorating respiratory function and overwhelming sepsis. In this case, biochemical response to infection was not achieved until the addition of linezolid and rifampicin. This is consistent with previous studies that proposed that beta-lactam activity is not helpful and that disease control is only achieved with the addition of rifampicin, linezolid and/or clindamycin (Kreienbuehl et al, 2011). Beta-lactams, with drug levels below minimum inhibitory concentrations, may increase toxin stimulation and release secondary to cell wall lysis, poor tissue penetration into necrotic tissue and diminished activity in anaerobic conditions. Therefore, the Health Protection Agency guidelines on treatment of Panton–Valentine leucocidin *S. aureus* suggest a combination of clindamycin, linezolid and rifampicin, although there is no clear consensus on this, with the most recent guidelines published in 2008 (Health Protection Agency, 2008).

The key question is whether this patient would have deteriorated without appropriate antibiotics for Panton–Valentine leucocidin *S. aureus*, highlighting the importance of performing sputum and blood cultures. For patients who deteriorate requiring intensive care support, adjunctive therapy with intravenous immunoglobulin can be considered, with the aim of neutralising exotoxins and superantigens. However, evidence surrounding this is limited, with just a small number of case studies (Francis et al, 2005; Micek et al, 2005; Health Protection Agency, 2008). Given its virulence, testing for Panton–Valentine leucocidin toxin is recommended for all patients with positive *S. aureus* blood cultures or clinical suspicion in UK hospitals. Detection of Panton–Valentine leucocidin-producing bacterial strains is achieved through polymerase chain reaction testing for *LukS-PV* and *LukF-PV* genes (Health Protection Agency, 2008; Haider and Wright, 2013; Health Protection Scotland, 2014). In the current case, decolonisation of the patient and his household contacts was carried out by Public Health England. However, there is no high-quality

Learning points

- Consider Panton–Valentine leucocidin in all patients with *Staphylococcus aureus* lower respiratory tract infection, not only in unwell patients.
- Clinical features often suggestive of Panton–Valentine leucocidin *S. aureus* infection include a previously well, young patient with multi-lobar consolidation, haemoptysis and overwhelming sepsis, following a flu-like prodrome.
- Beta lactams alone may not be sufficient and specialist microbiology input should be sought regarding the addition of rifampicin, linezolid and/or clindamycin.
- Sputum and blood cultures are important in the diagnostic work-up – in the current case, the patient may have deteriorated without appropriate antibiotics for Panton–Valentine leucocidin *S. aureus*.

evidence that decolonisation was effective in reducing infection or eradicating carriage of Panton–Valentine leucocidin *S. aureus* (Lynch et al, 2022).

This case highlights the need to consider Panton–Valentine leucocidin in all patients with *S. aureus* lower respiratory tract infection, not just those who are unwell, as without treatment the risk of late deterioration may contribute to its significant morbidity.

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