

# A fatal case of necrotising pneumonia due to community-associated methicillin-resistant *Staphylococcus aureus*

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## Clinical record

A 23-year-old woman presented to the emergency department with acute radicular lower back pain that became apparent when she was lifting books. She had normal blood pressure and 100% oxygen saturation breathing room air, but her heart rate was 110 beats/min and she had a temperature of 38.4°C. Inexplicably, she was discharged with a diagnosis of mechanical back pain. She presented again 2 days later with back pain, increasing shortness of breath, vomiting, myalgia, fever and sweating. She had also developed a dry cough and anterior pleuritic chest pain. There was an erythematous lesion on her left elbow. She and other family members had a history of recurrent furunculosis.

When examined on admission, the patient was tachycardic (heart rate, 160 beats/min), hypotensive (blood pressure, 80/50 mmHg) and hyperpnoeic (respiratory rate, 32 breaths/min), with an oxygen saturation of 100% on a non-rebreather mask with oxygen flow at 15 L/min. She was febrile, with a temperature of 38.2°C, and had a furuncle on her left elbow. She had tenderness in the right upper quadrant; the spleen was not palpable. There was midline and left paraspinal tenderness over T8/9. There was no tampon in situ.

Initial investigations showed a predominantly neutrophilic leukocytosis ( $18.4 \times 10^9$  cells/L [reference range (RR),  $3.5\text{--}11 \times 10^9$  cells/L]); coagulopathy (prothrombin time, 20 s [RR, 9–14 s]; activated partial thromboplastin time, 40 s [RR, 25–38 s]); thrombocytopenia (platelet count,  $59 \times 10^9$ /L [RR,  $140\text{--}400 \times 10^9$ /L]); renal dysfunction (urea level, 14.2 mmol/L [RR, 3–8 mmol/L]; creatinine level, 172  $\mu$ mol/L [RR, 50–100  $\mu$ mol/L]); and an elevated serum troponin I level (1.4  $\mu$ g/L [RR, <0.2  $\mu$ g/L]). A chest x-ray showed bilateral multilobar consolidation.

Initial therapy included large-volume fluid resuscitation, a noradrenaline infusion, intravenous hydrocortisone and empirical intravenous antibiotics (3.1 g ticarcillin/clavulanate, 400 mg gentamicin and 500 mg azithromycin, within 50 minutes of arrival). Subsequently 2 g dicloxacillin was administered intravenously.

The patient required intubation and mechanical ventilation 6 hours after admission, due to markedly deteriorating respiratory function. At this time, arterial blood gas results measured with the patient on 100% oxygen were: pH, 7.13 (RR, 7.35–7.45); partial pressure of carbon dioxide ( $P_{aCO_2}$ ), 52 mmHg (RR, 35–45 mmHg);  $P_{aO_2}$ , 237 mmHg (RR, 75–100 mmHg); base deficit, –12.3 mmol/L (RR, –3 to 3 mmol/L); and bicarbonate, 16 mmol/L (RR, 22–33 mmol/L). A computed tomography scan revealed multiple small areas of airspace opacification in a perivascular distribution, as well as bilateral extensive lower-lobe consolidation.

Nine hours after admission, in view of worsening shock, drotrecogin alpha (activated protein C) and vasopressin were commenced. Despite a high-dose infusion of noradrenaline and adrenaline, the patient's circulatory status continued to deteriorate.

*Staphylococcus* was grown from initial blood cultures after 14 hours, and intravenous vancomycin 1000 mg was administered. Sixteen hours after admission, the patient had an episode of ventricular tachycardia, which reverted to sinus rhythm after a single precordial thump. However, ventricular tachycardia recurred and progressed to asystole. The patient died 17 hours after presentation, despite resuscitation. Subsequently, methicillin-resistant *S. aureus* (MRSA) was grown from blood cultures, endotracheal aspirates, and furuncle swabs and biopsies. The organism was sensitive to erythromycin, clindamycin, gentamicin, tetracycline, ciprofloxacin and vancomycin.

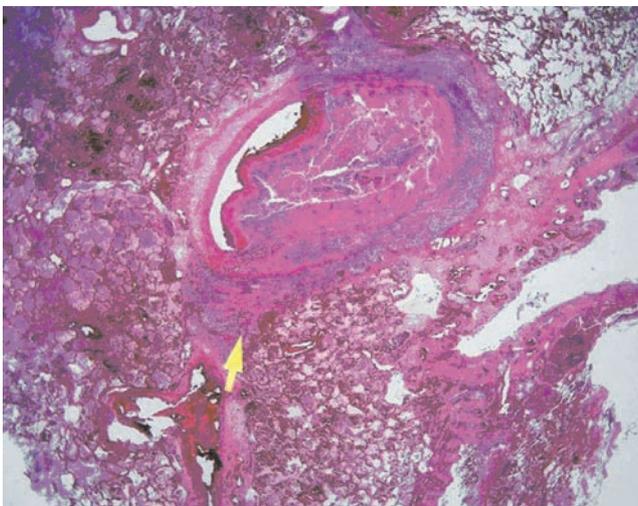
Isolates were typed using a real-time polymerase chain reaction method based on single nucleotide polymorphisms (SNP) of the core genome and the presence or absence of variable genes, including the gene for Pantone–Valentine leukocidin (*pvl*).<sup>1</sup> All isolates had an SNP and variable gene profile characteristic of the Queensland clone (ST93-MRSA-IV) of community-associated MRSA (CA-MRSA), including the presence of *pvl*.

Queensland clone CA-MRSA was also isolated from nose swabs subsequently collected from three family members, two of whom had suffered from recurrent furunculosis.

Postmortem examination showed that the principal pathology lay in the lungs and myocardium. The lungs showed multiple foci of bronchopneumonia, many coalescing to form extensive areas of lobar pneumonia. However, the most striking feature seen on histology was involvement of the pulmonary vasculature by staphylococcal septicaemia. Staphylococci had invaded the walls of multiple blood vessels, producing a florid vasculitis with subsequent secondary thrombosis of the involved vessels (Figure). This process involved both large and small vessels to such an extent that a lethal degree of bilateral arterial thrombosis had developed. The larger thrombosed vessels were obvious at macroscopic examination of lung slices.

Multiple small thrombi were seen on microscopy. The myocardium showed focal abscesses containing staphylococcal colonies. Adjacent myocardial fibres showed necrosis, which correlated with the patient's raised troponin level. The other organs of the body were remarkably free of sepsis, the spleen was normal, and the spinal column showed no evidence of osteomyelitis. A furuncle on the left elbow was confirmed. ♦

## Histological section of the patient's lung at autopsy



The section shows confluent staphylococcal bronchopneumonia with invasion of vessels in the lungs, producing a florid vasculitis (arrow). Secondary thrombosis is occluding the pulmonary vascular system. (Haematoxylin–eosin stain; original magnification  $\times 100$ ) ♦

Virulent strains of methicillin-resistant *Staphylococcus aureus* (MRSA) have recently emerged in community settings around the world (including many parts of Australia)<sup>2</sup> and are causing community-acquired infection with increasing frequency.<sup>3</sup> Most of the virulent strains carry the genes for producing Pantone–Valentine leukocidin (PVL), a potent necrotising toxin. They most commonly cause primary skin and soft tissue infections such as furuncles and abscesses, but can also give rise to severe invasive conditions, including necrotising pneumonia.<sup>4</sup> While uncommon, necrotising pneumonia is associated with a high mortality rate.

In Australia, two major strains of PVL-positive, community-associated MRSA (CA-MRSA) are currently circulating: the Queensland (QLD) clone and the south-west Pacific (SWP) clone. Currently, these strains predominate among CA-MRSA in Queensland, New South Wales and the Australian Capital Territory, while in other states, PVL-negative strains are more common.<sup>2</sup>

Necrotising pneumonia due to PVL-positive *S. aureus* is often rapidly fatal, as in the case described here. A study by Gillet et al recorded a mortality rate of 37% within 48 hours of presentation.<sup>5</sup> A significant association with preceding furunculosis was also noted. Most cases occurred in otherwise healthy children and young adults. A recently reported fatal case of CA-MRSA necrotising pneumonia in an Indigenous person was also in a previously healthy young adult.<sup>6</sup> The patient in our case had a history of recurrent furunculosis and a furuncle on her elbow at presentation, both commonly caused by PVL-positive *S. aureus*. Two family members had also suffered from recurrent furunculosis. All isolates from the patient and from nose swabs of three family members belonged to the QLD clone.

QLD and SWP clones are frequently sensitive to numerous non- $\beta$ -lactam antimicrobials.<sup>2</sup> Agents such as clindamycin and cotrimoxazole may be used to treat mild-to-moderate CA-MRSA infections such as furunculosis, depending on the organism's susceptibility.<sup>7</sup> Agents that act against protein synthesis (and therefore toxin production) have a theoretical advantage in the treatment of toxin-related infectious syndromes, but good clinical studies in this area are lacking. The use of clindamycin for treating invasive CA-MRSA infections is supported by one retrospective study in children.<sup>8</sup> Linezolid, a new agent also active against protein synthesis, has been shown to be superior to vancomycin, but only in complicated skin and soft tissue infections.<sup>9</sup> Use of one of these agents, perhaps in combination with established anti-staphylococcal antibiotics, is worthy of prospective study. The current national recommendation for treating suspected MRSA pneumonia is to administer vancomycin together with a  $\beta$ -lactam antibiotic (dicloxacillin, flucloxacillin or cephalothin) until susceptibility data are known.<sup>7</sup>

The severity of this case and rapidity of progression make it unlikely that more appropriate antibiotic therapy would have led to survival. Indeed, azithromycin, which was administered soon after admission, is active against erythromycin-sensitive strains of *S. aureus*. Nevertheless, early optimum antimicrobial treatment will give the best chance of survival. The possibility of MRSA pneumonia should be considered in the context of severe community-acquired pneumonia, particularly in children or young adults, and especially if there is evidence of preceding staphylococcal infection, such as folliculitis or furunculosis.

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### Lessons from practice

- A history of recurrent furunculosis in a patient or in family members may precede severe *Staphylococcus aureus* sepsis, including necrotising pneumonia.
- Patients with recurrent infection due to *S. aureus* should be tested for persistent nasal carriage. Treatment aimed at eradication could be considered.
- The prevalence of virulent strains of community-associated methicillin-resistant *S. aureus* (CA-MRSA) is increasing in many parts of Australia. Knowledge of local prevalence would be valuable in guiding empirical treatment.
- In communities where CA-MRSA is prevalent, suspected severe sepsis due to *S. aureus* should be treated with a combination of vancomycin and one of dicloxacillin, flucloxacillin or cephalothin until culture and susceptibility results are available. ◆

### Competing interests

None identified.

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