CASE REPORT

Necrotising pneumonia caused by non-PVL *Staphylococcus aureus* with 2-year follow-up

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SUMMARY

Necrotising pneumonia (NP) is a rare but life-threatening complication of pulmonary infection. It is characterised by progressive necrosis of lung parenchyma with cavitating foci evident upon radiological investigation. This article reports the case of a 52-year-old woman, immunocompetent healthcare professional presenting to Accident and Emergency with NP and *Staphylococcus aureus* septicaemia. The cavitating lesion was not identified on initial chest X-ray leading to a delay in antimicrobial optimisation. However, the patient went on to achieve a full symptomatic recovery in 1 month and complete radiological recovery at 2-year follow-up. Long-term prognosis for adult cases of NP currently remains undocumented. This case serves as the first piece of published evidence documenting full physiological and radiological recovery following appropriate treatment of NP in an immunocompetent adult patient.

BACKGROUND

This case documents the long-term prognosis for an adult case of necrotising pneumonia (NP). This has only previously been recorded in children. As such, this case provides evidence that full parenchymal lung recovery and return to cardiorespiratory baseline is attainable in patients who survive initial infection. The case also highlights the importance of thorough review of radiological imaging, as a cavitating focus was overlooked on initial chest X-ray (CXR) but visible on subsequent CT imaging. Early identification of this lesion could have accelerated optimisation of antimicrobial therapy.

CASE PRESENTATION

A 52-year-old woman presented to Accident and Emergency with dyspnoea, chest pain and peripheral skin mottling. She described a 4-day history of headache, rigours, arthralgia, anorexia and a dry cough. The chest pain was left sided, intermittent and worse on deep inspiration. There was no radiation of the pain and no history of haemoptysis. Her shortness of breath was most pronounced when lying flat and had been gradually worsening over the previous 4 days.

The woman was previously fit and well. She had an asymptomatic congenital ventricular septal defect (VSD) and a history of mild hypercholesterolaemia with no other history of cardiovascular or respiratory disease and no known immunocompromise. She was non-diabetic and had no relevant family history. Her only regular medication was

simvastatin. She had no known drug allergies. The woman did not smoke, consumed minimal alcohol and worked as a consultant anaesthetist. She had recently returned from travel to Spain.

On examination she was tachypnoeic, feverish and tachycardic. Vital signs were: blood pressure 138/70 mm Hg; pulse rate 129/min; respiratory rate 24/min; temperature 39.0°C; O₂ saturation 99% on room air (figure 1). Upon auscultation of the chest, crepitations were detected in both lung bases, predominantly on the left-hand side, along with a pansystolic murmur loudest in the tricuspid region, consistent with her known VSD. Her calves were soft and non-tender with no sign of oedema. Peripheral mottling (livedo reticularis) was noted across the woman's trunk and legs. Gastrointestinal and neurological examinations were unremarkable.

INVESTIGATIONS

An initial arterial blood gas on room air showed: pH 7.49; pCO₂ 4.1 kPa; pO₂ 9.0 kPa; HCO₃⁻ 23.6 mmol/L; lactate 1.6 mmol/L; glucose 7.4 mmol/L. Full blood count was normal except for thrombocytopenia (platelets 93×10⁹/L). Renal and liver function tests were unremarkable. C-reactive protein (CRP) 214 mg/L; D-dimer 535 ng/mL. A CXR showed consolidation in the left lower lobe, left upper lobe and right lower lobe (figure 2).

DIFFERENTIAL DIAGNOSIS

On admission, the initial diagnosis was probable healthcare-associated pneumonia, given her profession. The differential diagnosis included: atypical pneumonia, avian influenza resulting from her recent travel to Spain and pulmonary embolism. Thirty-six hours after presentation, a Panton-Valentine leukocidin toxin-producing *Staphylococcus aureus* (PVL-SA) pneumonia was suspected.

TREATMENT

The patient was admitted to hospital and was given a first line of treatment including intravenous tazocin, clarithromycin oral alongside supportive therapies. Thirty-six hours after admission, her treatment plan was altered when microbiology confirmed *S. aureus* present in blood cultures. Intravenous flucloxacillin 2 g four times a day was given in place of her current antimicrobial regime.

The patient remained tachypnoeic, feverish and tachycardic. Blood results revealed biochemical deterioration: haemoglobin, 9.4 g/dL (110); white cell count, 9.1×10⁹/L (6.1); CRP, 265 mg/L (214).

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Figure 1 Observations and blood results for the woman during her hospital admission. CRP, C-reactive protein; WCC, white cell count.

Due to the clinical suspicion of a PVL-SA, rifampicin oral 300 mg twice a day and intravenous clindamycin 1.2g four times a day were added, both of which the *S. aureus* was sensitive to. Cefoxitin sensitivity showed the organism to be methicillin sensitive.

Figure 2 A plain chest radiograph taken on the first day of the woman's admission. Bilateral lower lobe consolidation is noted as well as the overlooked cavitating lesion (arrow).

Figure 3 CT scans showing the cavitating focus missed on chest radiograph (A) and an additional cavitating focus (B). Complete resolution of these foci is evident 2 years later (C, D).

A D test for inducible clindamycin resistance was not performed at this stage due to the organism's sensitivity to erythromycin.

By her third day in hospital, the patient began to improve both clinically and biochemically. However, she began to experience hemoptysis and her temperature continued to spike intermittently to 40°C. Her chest examination revealed normal breath sounds and no adventitious sounds. However, a repeat CXR showed further consolidation despite her clinical improvement. Flucloxacillin was stopped upon microbiology advice. *Legionella* and pneumococcal urine antigen tests and an HIV test were all found to be negative. A transthoracic echocardiogram showed no cardiac vegetations.

On day 4, a CT scan of her chest, abdomen and pelvis was conducted to investigate for a source of her persistent fever. The CT chest depicted multifocal consolidation with an upper lobe predominance (figure 3). An area of cavitation was noted in the right upper lobe along with a further focus partially cavitating consolidation peripherally in the left upper lobe. This consolidation demonstrated hypodense areas consistent with liquefactive necrosis. Small pleural effusions were seen with no features to suggest pleural infection. Abdominopelvic organs were all within normal limits with no evidence of abscess formation. The rifampicin dose was doubled due to a strong suspicion of PVL-SA in light of the cavitating foci.

The patient continued to recover clinically and biochemically. One week after admission, she was not feverish and saturating 96% on room air. As she was clinically stable, she was discharged home to continue domiciliary intravenous antibiotic therapy, returning to the hospital for cannula changes and blood monitoring as needed.

OUTCOME AND FOLLOW-UP

The patient completed her course of antibiotics at home. She described continuing tachycardia and dyspnoea lasting approximately 10 days after her therapy was completed and during this time she could only mobilise for roughly 50 yards at a time. Two weeks after discharge she was followed-up in clinic and

informed that the infection had been found to be non-PVL-SA by PCR test. Following this period, she recovered swiftly, returning to her cardiovascular and respiratory baseline within a month of discharge.

Roughly 2 years later, she developed a lower respiratory tract infection with a cough, productive sputum and clearly audible wheeze. Given no history of previous respiratory symptoms or pathology prior to her NP, she was concerned that she may have developed bronchiectasis or asthma and thus sought a further respiratory opinion. Upon respiratory follow-up, she had a normal clinical examination with no suggestion of asthma or bronchiectasis, normal spirometry with no obstructive or restrictive abnormalities, and her CT chest showed a complete resolution of her previously documented areas of cavitation with no evidence of bronchiectasis (figure 3).

She now has a normal exercise tolerance and states that she has no residual respiratory symptoms following her NP.

DISCUSSION

NP is a potentially life-threatening complication of pulmonary infection. It is characterised by progressive necrosis of lung parenchyma with cavitating foci evident upon radiological investigation. The presenting symptoms of this case mirror those most commonly associated with NP: fever, chest pain, dyspnoea and cough.¹ Clinically, NP can ultimately progress into respiratory failure, sepsis and death.

The aetiology of NP is identified in fewer than 50% of cases.² The most common of these are *S. aureus*, *Streptococcus pneumoniae* and *Klebsiella pneumoniae*.¹ In children, *S. pneumoniae* is found most frequently.³ However, over recent years, there has been a rise in NP caused by other pathogens.^{4–6} The patient in this case was infected by *S. aureus*. However, unusually, the *S. aureus* was not PVL-SA, known for causing rapidly progressive necrosis. This lies contrary to the predominance of PVL-SA in children.⁷

Diagnosis of NP is based on radiological imaging. Contrast-enhanced CT is the gold standard. CXR can be used, particularly to monitor treatment efficacy. A recent study examining adult patients who developed radiologically detected necrotising changes through pneumococcal infection found no significant prevalence differences in age, gender, race or the prevalence of other comorbidities.⁸ Necrotising changes were noted on 0% and 4.4% of initial reading of CXRs and CT scans of patients with pneumococcal pneumonia. However, on re-examination of these same scans, the observation of necrotising changes rose to 2.3% and 11.0% respectively, highlighting a significant proportion of changes that were initially overlooked.

Upon re-examining this patient's CXR, taken on her first day of admission, a lesion is visible that matches the dimensions and anatomical location of the later discovered cavitating focus. As per British Thoracic Society guidelines published in 2015, antibiotic therapy should 'include the addition of a combination of intravenous linezolid 600 mg bd, intravenous clindamycin 1.2 g qds and intravenous rifampicin 600 mg bd to the initial empirical antibiotic regimen.'⁹ With early recognition, the patient's treatment could have been reviewed and treatment for NP considered earlier in her admission. The CT chest could also have been arranged sooner to assess disease extent and severity. Therefore, careful examination of imaging is critical, especially in patients who appear to display a miscorrelation between radiological and clinical appearances.

Currently, there is no single best way to treat NP; however, a multidisciplinary approach appears to offer the best prognosis.¹⁰

Patient's perspective

- ▶ I called into work on Monday morning certain that I had the 'real flu'. Trying to think why I had skipped my 'flu jab' earlier that winter. Too busy? But certain I would feel better, I took my paracetamol and ibuprofen and waited. By Wednesday I felt suddenly much worse not better, my chest was painful and breathing was becoming an issue. I took a bath and remember looking down in a very distracted way at the mottling on my legs, thinking, 'oh dear, I think I'm septic, perhaps I'd better go to hospital now.' The pyrexia and sepsis were taking away my reasoning.
- ▶ I remember the hallucinations as my temperature hit 39.4. I remember being frightened. I remember the junior doctors being very excited when my blood cultures came back positive for *Staph aureus*. We had a strange doctor-to-doctor conversation as they had never taken care of someone with necrotising pneumonia and announced 'We know what you've got!' And I thought 'yes, but I'm the patient, I'm not excited, I'm exhausted.'
- ▶ I remember my consultant telling me clearly that I would be 'fine' and he would see me after the weekend and also to remember his words when I Googled necrotising *Staph aureus* pneumonia on my smartphone, which I did 10 s after he left the room. So there I was reading papers on my own mortality risk being quietly shocked. But I remembered his words and the tone of his voice. I hung onto the safe feeling he gave me as I struggled through the next 2 days. This doctor gave me more than facts and evidence. He communicated hope and trust.
- ▶ Glad to be here. I'll never miss a 'flu jab' again.

Learning points

- ▶ Necrotising pneumonia (NP) can occur in immunocompetent patients. It is associated with significant morbidity and mortality and thus should be considered as part of a differential diagnosis for sepsis with evidence of pulmonary infection.
- ▶ Symptomatic and radiological recovery along with a return to cardiorespiratory baseline is possible in adult NP.
- ▶ Early suspicion of NP and reimaging or review of initial imaging should be considered in patients who display a miscorrelation between radiological and clinical appearances.
- ▶ Microbiology-informed antimicrobial therapy is key to treating NP and reducing morbidity and mortality.

Adequate antimicrobial therapy has shown to hold significant benefit for patients with NP, often providing a total cure.¹¹ At present, there are no clear guidelines regarding the duration of antibiotic therapy required for NP, time interval until follow-up, or follow-up investigations such as CXR or CT scan. Additional treatment such as mechanical ventilation, closed pleural drainage and surgical intervention may also be required.^{10 12 13}

The long-term prognosis for NP in adults remains poorly understood. In children, good clinical and radiological recovery has been observed.^{3 7 11 14} However, in adults, emphasis has been placed upon rare presentations and fatal complications of NP.^{5 12 15 16} The only study documenting postdischarge prognosis briefly mentions that of six patients followed-up after NP, three held normal full-time work or study, two had part-time activities

and one was unable to work.¹² This limited body of data sheds little light on the resolution of lung lesions and symptomatic improvement. Therefore, this case serves as the first piece of published evidence that full clinical and radiological recovery is attainable following appropriate treatment of NP in an immuno-competent patient. Further case series or studies are required to identify the long-term clinical and radiological outcome of this severe and potentially life-threatening form of pneumonia.

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