Man and woman flu

Introduction

This article presents two cases of *Staphylococcus aureus* pneumonia in young adults with evidence of preceding influenza B virus infection. One isolate carried the Panton-Valentine leucocidin (PVL) gene that has been associated with highly lethal necrotizing pneumonia in young immunocompetent patients (Gillet et al, 2002).

This provides a timely reminder of one of the complications of influenza, highlights the importance of starting empirical antibiotics active against *S. aureus* for influenza-associated pneumonia (e.g. during a flu pandemic) and discusses the association of the PVL gene with severe pneumonia.

Discussion

The case reports describe two cases of *S. aureus* pneumonia in young adults following infection with influenza B.

Secondary bacterial pneumonia complicating influenza infection is the commonest cause of death in young individuals during influenza pandemics. Priming of the respiratory epithelium by influenza virus infection predisposes the lung to attachment and infection with bacteria (Gillet et al, 2002). Signs and symptoms of pneumonia typically develop during the early convalescent period (4–5 days after onset of initial symptoms), often associated with a recrudescence of fever. Sometimes infection can blend in with the initial symptoms of flu and physicians must therefore be vigilant for possible bacterial super-infection at all times. Chest X-ray will normally show lobar consolidation but can show bilateral diffuse infiltrates and lobar consolidation, when bacterial and viral pneumonia occurs concurrently.

S. aureus pneumonia is a common complication of influenza infection, associated

Case Report 1

A 21-year-old woman was admitted to the authors' hospital with symptoms of breathlessness, pleuritic chest pain and haemoptysis having been unwell for 1 week with a flu-like illness. Clinical examination revealed a rapid respiratory rate (36/min), tachycardia (134 beats per minute), pyrexia (39°C), bibasal coarse crepitations and bronchial breathing. Investigations showed hypoxia (PO_2 12.4 on 100% oxygen), raised inflammatory markers (C-reactive protein 324 mg/litre), thrombocytopenia (platelets 144 x 10^9/litre), leucopenia (2 x 10^9/litre) and neutropenia (0.88 x 10^9/litre). Chest X-ray revealed bilateral air space shadowing (*Figure 1*). The patient was admitted to the high dependency unit and started on intravenous co-amoxiclav (1.2 g three times per day) and clarithromycin (500 mg twice daily). Blood cultures at 24 hours grew *Staphylococcus aureus* resistant to penicillin and fusidic acid. The patient was switched to intravenous flucloxacillin. Admission was complicated by the development of a small pleural effusion. The patient was managed with high flow oxygen therapy, did not require ventilatory support at any stage and was discharged home after 17 days. The patient received flucloxacillin for a total of 4 weeks. The *S. aureus* isolate carried enterotoxins G and I and the Panton-Valentine leucocidin gene. Throat swab was positive for influenza B by a molecular method.

Case Report 2

A 20-year-old non-smoking man presented to hospital with cough, haemoptysis and dyspnoea having been unwell for 1 week with flu-like symptoms. Examination revealed a fever (38°C), tachycardia (148 beats per minute), tachypnoea (respiratory rate 30 breaths/min) and diminished breath sounds bibasally. Investigations showed leucocytosis (white blood cell count 11.5x 10^9/litre), raised urea (11 mmol/litre) and creatinine (140 μmol/litre), raised C-reactive protein (282 mg/litre) and hypoxia (PO_2 8.1 Kpa). Chest radiograph showed bilateral patchy alveolar shadowing (*Figure 2*). He was treated with intravenous cefuroxime and clarithromycin and managed on the high dependency unit. He was treated with continuous positive airway pressure with a positive end expiratory pressure of 5 cmH_2O and 80% O_2 for 48 hours. Blood cultures grew *Staphylococcus aureus* resistant to penicillin and fusidic acid. The isolate carried enterotoxins A and H and was Panton-Valentine leucocidin negative. Throat swab was positive for influenza B by a molecular method. He was discharged from hospital after 7 days.

Figure 1. Chest X-ray from case 1 showing bilateral patchy alveolar shadowing and pleural effusion, more common with Panton-Valentine leucocidin-producing Staphylococcus aureus strains.

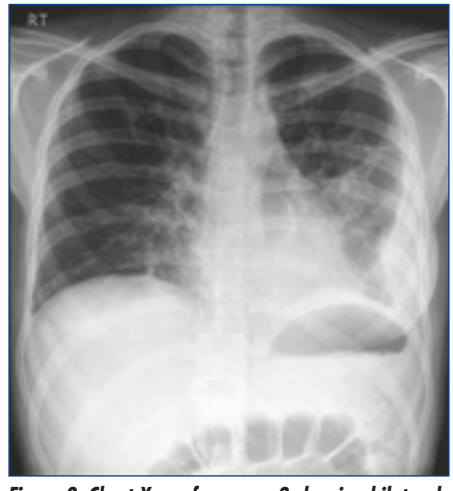
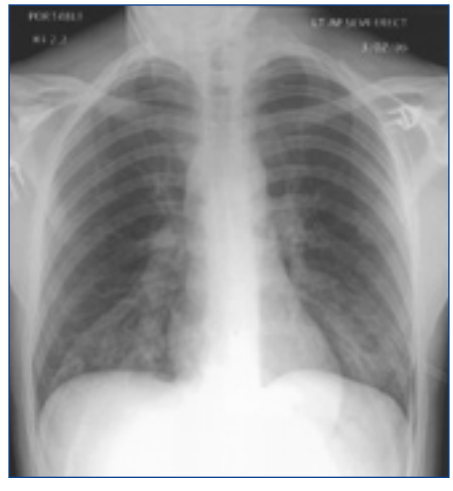


Figure 2. Chest X-ray from case 2 showing bilateral patchy alveolar shadowing.



Dr Brendan Healy *is Specialist Registrar in Microbiology and* **Dr Rosemary Barnes** *is Reader and Honorary Consultant in Medical Microbiology in the Microbiology Department, National Public Health Laboratory Service, University Hospital of Wales, Cardiff CF14 4XW,* **Dr Ben Hope-Gill** *is Consultant in Respiratory and General Medicine and* **Dr Sangeetha Ramanujam** *is Senior House Officer in Respiratory and General Medicine, Llandough Hospital, Cardiff and* **Dr Kesh Baboolal** *is Consultant in Nephrology and General Medicine, University Hospital of Wales, Cardiff*

Correspondence to: Dr B Healy

with a poor prognosis (Nicholson, 2000). *S. aureus* was the commonest pathogen isolated during the 1957 pandemic (Nicholson, 2000) and the second commonest pathogen isolated during the 1968 pandemic (Schwarzmann et al, 1971). During influenza pandemics the incidence of *S. aureus* pneumonia increases markedly above background level (Schwarzmann et al, 1971).

The *S. aureus* isolated from case one expressed the PVL gene. This has been associated with highly lethal necrotizing pneumonia in young immunocompetent adults (Gillet et al, 2002) and has been postulated as a possible cause of the huge death toll during the 1918 pandemic (Gillet et al, 2002). It is often associated with a preceding flu-like illness (Gillet et al, 2002). Haemoptysis, pleural effusions, leucopenia, decreased survival rate at 48 hours and increased lethality rate in patients with no underlying diseases are all more common in pneumonia as a result of PVL-carrying *S. aureus* strains (Gillet et al, 2002). PVL-carrying *S. aureus* has also been associated with outbreaks of community-acquired methicillin-resistant *S. aureus* infections around the world (Diep et al, 2004).

During an influenza pandemic patients at high risk of complications or secondary infection should be considered for antibiotics in the presence of lower respiratory tract features (British Infection Society et al, 2006). Empiric treatment of suspected bacterial superinfection should provide activity against *Streptococcus pneumoniae*, *S. aureus*, *Haemophilus influenzae* and beta-haemolytic streptococci (groups A, C and G) with antibiotics such as co-amoxiclav, cefuroxime or a respiratory quinolone (Mandell et al, 2003). In PVL-associated severe pneumonia additional options include addition of antibiotics to 'switch off toxin production' (e.g. clindamycin) and immunoglobulin if toxic shock develops (Wargo and Eiland, 2005).

With pandemic influenza imminent, the authors predict an increase in previously fit young adults presenting with serious bacterial pneumonia caused by *S. aureus* (including PVL-producing strains), *S. pneumoniae*, and beta-haemolytic streptococci. They recommend early aggressive empirical therapy with anti-staphylococcal and streptococcal agents to reduce morbidity and mortality, and vigilance for PVL-producing *S. aureus* strains as they affect management. **BJHM**

British Infection Society, British Thoracic Society and Health Protection Agency in collaboration with the Department of Health (2006) *Pandemic flu. Clinical Management of patients with an influenza like illness during an influenza pandemic.* http://www.brit-thoracic.org.uk/c2/uploads/pandemicflu.pdf

Diep BA, Sensabaugh GF, Somboona NS, Carleton HA, Pedreau-Remington F (2004) Widespread skin and soft tissue infections due to two methicillin resistant *Staphylococcus aureus* strains harbouring the genes for Panton-Valentine Leucocidin. *J Clin Micro* **42**(5): 2080–4

Gillet Y, Issartel B, Vanhems P et al (2002) Association between *Staphylococcus aureus* strains carrying gene for Panton-Valentine Leucocidin and highly lethal necrotising pneumonia in young immunocompetent patients. *Lancet* **359:** 753–9

Mandell LA, Bartlett JG, Dowell SF, File TM, Musher DM, Whitney C (2003) Update of practice guidelines for the management of community acquired pneumonia in immunocompetent adults. *Clin Infect Dis* **37:** 1405–33

Nicholson KG (2000) Human influenza. In: Nicholson K, Webster R, Hay A, eds. *Textbook of Influenza.* 2nd edn. Blackwell, Oxford

Schwarzmann SW, Adler JL, Sullivan RJ, Marine WM (1971) Bacterial pneumonia during the Hong Kong influenza epidemic of 1968-69. *Arch Intern Med* **127**(6): 1037–41

Wargo KA, Eiland EH (2005) Appropriate antimicrobial therapy for community acquired methicillin resistant *Staphylococcus aureus* carrying the Panton-Valentine Leucocidin genes. *Clin Infect Dis* **40:** 1376–7

Another fishy tale

If you want your research to get into the public's view, do something with oily fish. The newspapers warned in October that premature labour was more likely if pregnant women ate oily fish. The report on the BBC's website lists linked stories. One, from 2003, was that the risk of premature labour was reduced if pregnant women ate oily fish. The media are interested only in facts: pure, simple, and devoid of context.

Not having read either paper that spawned the contradictory stories, I don't know which, if either, is the more reliable. Science deals not in truths, but in hypotheses that are supported or rejected. As a generalization, it is not possible to support both hypotheses relating oily fish to premature labour, but different study designs, populations or confounding factors in the studies may make contradictory hypotheses supportable under different circumstances. The only sensible advice for pregnant women is, as ever, to eat a varied diet.

It's not surprising that the public get confused: Google returns 41 000 hits on oily fish and BBC. The first blow was in September 1999, as 'Toxin worry for oily fish' lead the government to advise us to eat oily fish once per week. Move on to January 2001 and 'Eating fish "cuts strokes"'. In October 2002 researchers complained 'Public ignorant of oily fish guidance'. All I can say is that I'm not surprised and it's not got any easier since.

March 2003 saw 'Oily fish "helps lupus patients"', and I think I caught a story that it's also good for arthritis. May 2004 and 'A mother-to-be who eats fish during the later stages of pregnancy is less likely to have a very small baby, research suggests'. Note those last words: research suggests. A suggestion is only a suggestion. The year 2004 was full of oily fish benefits – in June came 'Doctors could better predict which patients are likely to have a heart attack by testing blood for fish fats', and in July 'Fish prevents deadly heart rhythms'. 'Fish oil hope for breast cancer' burst upon us in June 2005, and 'Oily fish makes "babies brainier"' in January 2006.

It now seems that mums-to-be will go into labour prematurely; but will their babies still be brainier and less likely to be very small? Is the risk worth the gain?

But the really bad news was in March 2006 when the BBC reported that 'There is no evidence of a clear benefit to heart health from fats commonly found in oily fish'.

I have never done epidemiological observational research but I know that it is bedevilled by confounding factors. In one well-funded study men with prostate cancer were asked how many cream crackers they were eating 5 years before. I don't imagine they remembered how many mackerel they were eating either. **BJHM**

Dr Neville Goodman *is Consultant Anaesthetist at Southmead Hospital, Bristol*