Renal failure associated with *Legionella pneumophila* infection

Introduction

Acute renal failure is a known complication of *Legionella pneumophila* infection. A review of the English literature since the Legionnaires' disease epidemic of 1976 yielded 63 cases (Tsai et al, 1979; Lin et al, 1995; Verhaeverbeke et al, 1995; Kaufman et al, 2002). The pathophysiology underlying renal involvement in Legionnaires' disease still remains obscure. Legionnaires' disease has an overall mortality of about 15%, but this increases to 53% in the subset of patients with associated renal failure (Shah et al, 1992).

The authors describe a case of Legionnaires' disease complicated by severe acute renal failure, which was successfully treated with antibiotics and a short course of haemodialysis.

Case Report

A 61-year-old African-American male with a past medical history of hypertension and osteoarthritis was brought to the emergency department for severe dyspnoea and agitation for the past few hours. Family members gave a history of fever, myalgias, anorexia, nausea and a non-productive cough of 3–4 days duration. He also had a several day history of shortness of breath and right-sided pleuritic chest pain. He had a 40-pack a year tobacco history and consumed 1–2 beers every day. He had had no alcohol in the past 4 days. His home medications included amlodipine and ibuprofen. He was currently unemployed. In the emergency department, vitals signs included a temperature of 38.8°C, pulse rate of 118 beats per minute, respiratory rate of 24 breaths per minute, blood pressure of 122/68 mmHg with no orthostatic signs and an oxygen saturation of 89% on 4 litres oxygen by nasal cannula. Physical examination was unremarkable except for intermittent agitation and crackles on auscultation of the right middle and lower lung zones.

Laboratory values at admission were as follows: sodium =129 mmol/litre, bicarbonate = 23 mmol/litre, blood urea nitrogen = 30.7 mmol/litre, creatinine = 910.5 μmol/litre, total bilirubin = 80.4 μmol/litre with an unconjugated fraction of 53 μmol/litre, alkaline phosphatase = 110 U/litre, alanine transaminase = 147 U/litre, aspartate aminotransferase = 234 U/litre, creatine kinase = 7533 U/litre with muscle-brain fraction of 7.48 U/litre, haemoglobin = 129 g/litre, white blood cell count = 10100/mm^3 with 43% bands, platelet count = 200 000/mm^3, other labs including serum calcium, magnesium, chloride, potassium, phosphate, amylase and lipase were within the normal range. Serum and urine toxicological screens were negative. Electrocardiogram revealed normal sinus rhythm with left ventricular hypertrophy by voltage criteria. Urine dipstick was positive for large amount of blood. Urine microscopy showed 110 red blood cells per high power field. A chest roentgenogram showed a right lower lobe infiltrate.

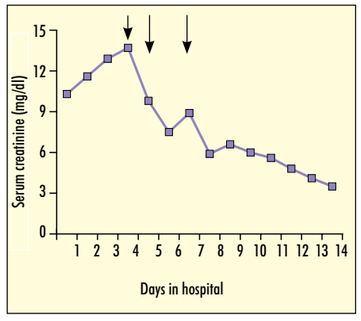
Upon admission, the patient's hypoxaemia worsened and he required bi-level positive airway pressure for ventilation. With a presumptive diagnosis of aspiration pneumonia *vs* community-acquired pneumonia, piperacillin-tazobactam and azithromycin were instituted. In view of the agitation and the patient's history of alcohol use, he was placed on alcohol withdrawal precautions. Renal service was consulted the following morning for his non-oliguric acute renal failure (urine output = 600 ml over the previous 24 hours). The baseline renal function of this patient was not known. With evidence of multiple organ system involvement including the lungs, liver and kidney, an extensive work-up for vasculitides as well as an infectious aetiology was initiated. Serum complement levels (C3, C4, and CH 50) were within the normal range. Assays for anti-nuclear antibody, anti-double-stranded DNA antibody, anti-neutrophilic cytoplasmic antibodies, anti-glomerular basement membrane antibody as well as serological tests for hepatitis B and C were all negative. Renal failure worsened over the next 3 days and the patient required hemodialysis three times over the next 4 days (*Figure 1*). While all tests including sputum, urine and blood cultures remained negative, the urinary antigen for *Legionella pneumophila* serogroup 1 was positive. Piperacillin-tazobactam was discontinued and azithromycin was continued to complete a 21-day course. Serum creatinine at discharge was 300.5 μmol/litre. The patient was subsequently lost to follow-up.

Discussion

In the 1976 epidemic of Legionnaires' disease, moderate azotaemia was reported to be common; proteinuria was reported in 20% and microscopic haematuria in 10% of patients (Fraser et al, 1977). Of the 123 patients who were hospitalized during this epidemic in Philadelphia, 11% developed frank renal failure; 21% of the patients with renal failure required haemodialysis and 78% of them died (Tsai et al, 1979).

Nishitazumizu et al reviewed 45cases of Legionnaires' disease associated with acute renal failure; of these, 16% of patients had rhabdomyolysis, 55% patients required haemodialysis and 51% patients died. Renal pathology was available in 26patients of whom six had acute tubular necrosis, five had acute tubulo-interstitial nephritis, two had acute pyelonephritis and one each had membranous glomerulonephritis and rapidly progressive glomerulonephritis (Nishitarumizu et al, 2000). It has been suggested that rhabdomyolysis could be either a result of direct muscle injury by *Legionella* spp. or caused by a circulating endotoxin (Hall et al, 1983). Thus, the cause of acute renal failure in this patient population could be multifactorial including acute tubular necrosis secondary to myoglobinuria or shock with or without sepsis, circulating endotoxin, acute interstitial nephritis and rarely from direct bacterial involvement of the kidneys (Weiseburger et al, 1981).

Figure 1. Changes in serum creatinine levels during the patient's stay in the hospital. Arrows indicate days on which haemodialysis was performed.



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The patient in the current case was not clinically in shock at any time during the course of the illness, the degree of rhabdomyolysis was not severe enough to account for his acute renal failure and there was no evidence of bacteraemia. The aetiology of acute renal failure in this patient is therefore uncertain and without a renal biopsy, one can only speculate that acute interstitial nephritis and direct bacterial invasion of the kidney are two likely possibilities. However, this case and other similar cases reported in the past highlight the association between *Legionella pneumophila* infection and acute renal failure.

The higher mortality associated with renal failure in Legionnaires' disease emphasizes the need to suspect *Legionella* spp. as an aetiological agent in patients with multiple organ system involvement and therefore make an early diagnosis; prompt treatment including antibiotics and haemodialysis as needed are keys to avoid fatal outcomes. **BJHM**

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Dishonesty will out

The year 2006 has already seen two highly publicised medical research frauds. Jon Sudbø, a Norwegian doctor, was lead author in a study showing that non-steroidal anti-inflammatory drugs protected smokers against oral cancer. The media picked up the story when it was published in the *Lancet* in 2005, suggesting that smokers pop an ibuprofen each time they take a drag. It turns out that Sudbø falsified all 900 patients, fooling his 12 co-authors, the journal's referees, and the readers. It's a lot of work to study 900 patients, but it's actually quite a lot of work to invent them too. He would deserve a prize, but he did it so incompetently that 250 of his sample of 908 shared the same birthday. It's like those bank robbers who push a note across to the cashier on which they've written, 'Put all the money in the bag', failing to notice that they've written the note on a piece of paper that includes their address.

But, if he hadn't been so incompetent, he might never have been found out. Lots of smokers would have popped their pills (perhaps: smokers are not known for following health advice). Then, eventually, someone would have done a follow-up case-control study with a contradictory outcome. But so what? We are bombarded daily by suggestions of what is or isn't good for us. No one would have looked suspiciously at Sudbø's earlier study; the epidemiological literature is littered with contradictions.

The other fraud is more important and more incomprehensible. Hwang Woo-sook became the darling of South Korea and a hero to research biologists when his team published a paper in *Science* describing how they had produced 11 distinct human stem-cell lines from only about 180 cloned human eggs. This efficiency was staggeringly better than any previous work.

It wasn't long before unease surfaced. Not 180 but 1100 eggs, said some. There were rumours that the eggs had been obtained unethically from junior researchers, and illegally (in South Korea) from paid donors. This produced much huffing and puffing, which might have blown over if the science had been valid – but it was as much a fraud as Sudbø's. Hwang claims he knew nothing of it, and blames his team. Hwang made a public statement to the effect that his team was thinking only about the greater glory of South Korea. But how could any scientist think for one moment that pretending to clone a human cell would not be found out? The therapeutic potential (an important word, that: potential) is so great that laboratories would be frantic to replicate. Sudbø might have got away with it, but Hwang never stood a chance.

Fortunately, neither of these frauds in any way involved the UK. Otherwise we'd have had more navel-gazing from the government keen to regulate research so that no misdemeanour was possible. They would, of course, succeed; because much more regulation will stop research altogether.

Hwang's best chance lies with the Raelian Movement, the cult who believe humans were created by aliens and who announced a human clone a couple of years ago. It seems that Clonaid, the US firm owned by the cult, have offered him a job. **BJHM**

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