

Nocardia asteroides pneumonia with bacteraemia

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TO THE EDITOR: A previously well 57-year-old man presented to the emergency department with a 3-day history of severe dyspnoea. Six weeks earlier he had noticed coryzal symptoms with subsequent lethargy, reduced appetite with weight loss, and a non-productive cough. He then developed ankle swelling and increasing abdominal girth. He had a background of excessive alcohol consumption, but had abstained for 10 years.

On examination, he was febrile and in respiratory distress, with a respiratory rate of 35 per minute, pulse rate of 130 bpm, and blood pressure of 130/85 mmHg. Chest auscultation revealed bilateral diffuse coarse crackles. The chest x-ray is shown in Box 1, and results of additional investigations in Box 2.

Despite treatment with broad-spectrum antibiotics (intravenous ceftriaxone, dicloxacillin and erythromycin), the patient's condition deteriorated rapidly, and he required intubation within 24 hours of presentation. Trap sputa contained abundant thin, partially acid-fast, beaded, branching filaments, suggesting *Nocardia asteroides*, which was later confirmed on culture using con-

ventional biochemical testing. Several blood cultures taken on admission also grew *N. asteroides*. All cultures for mycobacteria were negative. The patient was treated with intravenous trimethoprim-sulfamethoxazole for a total of 5 weeks and oral minocycline for 14 weeks. He spent 6 weeks in hospital.

Liver biopsy, performed because of persistently abnormal hepatic function at follow-up 8 weeks after hospital discharge, showed central fibrosis and non-

caseating granulomatous hepatitis (Box 3). The patient received no further treatment and remained well 18 months later, with almost normal hepatic function and a clear chest x-ray.

Nocardia bacteraemia is rare, although the incidence appears to be increasing in the immunosuppressed. *Nocardia* spp. are seldom isolated in blood cultures, with one study finding that blood was the source of only 8% of all *Nocardia* isolates.¹ Up to 30% of patients with *Nocardia* bacteraemia have coexistent infection with gram-negative bacteria.^{1,2} There has been one previous report of *Nocardia* pneumonia associated with positive blood cultures and liver disease. However, this patient had documented end-stage chronic liver disease at presentation, was taking prednisolone, and developed nocardiosis after prolonged hospitalisation with gram-negative sepsis.¹

Granulomatous reactions are well described in *Nocardia* infection. Although granulomatous hepatitis is also described in sarcoidosis, it is rare and usually presents with itch and obstructive abnormalities of liver function.⁴

In our patient, acute *N. asteroides* infection was the most likely cause of both the pulmonary infiltrate and the granulomatous hepatitis. Not only were results of modified acid-fast stains consistent with *Nocardia* spp., but cultures from multiple trap sputa and blood specimens also grew *N. asteroides*, sug-

2: Results of investigations

	Result	Reference range
At presentation		
<i>Arterial blood gases*</i>		
pH	7.37	7.35–7.45
pCO ₂ (mmHg)	43	35–45
pO ₂ (mmHg)	60	75–105
Bicarbonate (mmol/L)	24	24–31
Base excess	0	–3 to 3
<i>White cell count</i>		
Total (x 10 ⁹ /L)	31.5 [†]	4–11
Neutrophils (x 10 ⁹ /L)	30.2	2–7.5
Lymphocytes (x 10 ⁹ /L)	0.7	2–4
Follow-up at 8 weeks		
<i>Liver function tests‡</i>		
Bilirubin (μmol/L)	9	< 18
Alkaline phosphatase (U/L)	124	30–100
γ-Glutamyl transferase (U/L)	153	< 35
<i>Iron studies</i>		
Serum ferritin (μg/L)	446	30–400
Serum iron (μmol/L)	< 3	10–30
Transferrin (g/L)	1.9	2.0–3.5
Transferrin saturation	< 6%	15%–50%
Vitamin B ₁₂ (pmol/L)	376	> 126
<i>Immunological tests</i>		
HIV antibodies	Negative	
Hepatitis B and C [§]	Negative	
Autoantibody screen [¶]	Negative	
Complement C3 (g/L)	1.07	0.82–1.45
Complement C4 (g/L)	0.25	0.15–0.45

* Breathing 10 L/min oxygen.

† Occasional myelocytes, toxic granulation.

‡ Levels of alanine and aspartate aminotransferase were in the reference range.

§ Including hepatitis B surface antigen and hepatitis C antibody.

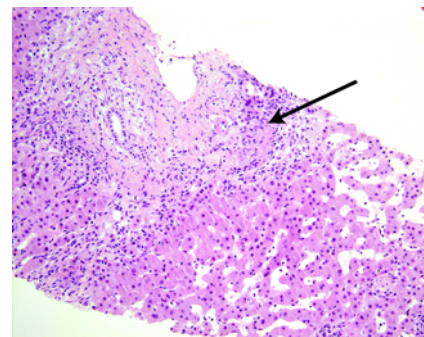
¶ Including antinuclear, extractable nuclear antigen, double-stranded DNA and antineutrophil cytoplasmic antibodies.

1: Chest x-ray of a patient with *Nocardia asteroides* pneumonia



Chest x-ray taken on admission to hospital, showing widespread non-symmetrical interstitial and airspace infiltrates.

3: Liver biopsy in a patient with *Nocardia asteroides* pneumonia



Core biopsy of liver, showing a granuloma within the central portal triad (arrow); the portal ducts are expanded and fibrosed with a patchy lymphocytic infiltrate (original magnification x 40; haematoxylin and eosin stain).

gesting a large load of this organism. No other organisms were isolated despite prolonged incubation of cultures, and the patient recovered after specific treatment directed at *Nocardia* spp. Furthermore, he remained well with no further treatment at 18-month follow-up, with near-normal hepatic function and no new abnormalities.

We conclude that *N. asteroides* infection can present as a fulminant community-acquired pneumonia with bacteraemia in the absence of immunosuppression or coexistent infection. Our case illustrates the potential hepatic sequelae of *Nocardia* bacteraemia.

Competing interests: None identified.

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Rhabdomyolysis secondary to interaction of fusidic acid and simvastatin

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TO THE EDITOR: A 71-year-old man was admitted to hospital in 2002 with nausea, abdominal discomfort and myalgia. He was dehydrated and had mild right upper quadrant tenderness. No muscle tenderness was noted.

Five weeks previously, an infected right femoropopliteal gortex graft had been surgically removed. Methicillin-resistant *Staphylococcus aureus* was present on culture. Therapy with fusidic acid (250 mg three times daily) and rifampicin (600 mg daily) had been commenced, and the patient's condition improved. Fusidic acid therapy was continued because of unsatisfactory wound healing. On presentation he had been taking fusidic acid for 4 weeks. He had been taking simvastatin (40 mg nightly) for 8 years.

The patient had a history of generalised vascular disease and multiple

bypass procedures. He had a background of paroxysmal atrial fibrillation, myocardial infarction, left ventricular failure, hypertension, hypercholesterolaemia and chronic airways limitation. His other medications were metoprolol, irbesartan, frusemide, warfarin, paracetamol and narcotic analgesics.

Test results showed the following biochemical concentrations: aspartate transaminase, 1618 U/L (normal range, <40 U/L); alanine transaminase 657 U/L (normal range [NR], <35 U/L); alkaline phosphatase 133 U/L (NR, 25-100 U/L); total bilirubin, 29 µmol/L (NR, <20 µmol/L); γ-glutamyltransferase, 37 U/L (NR, <50 U/L); urea, 24.7 mmol/L (NR, 3.0-8.0 mmol/L); creatinine, 0.35 mmol/L (compared with previous creatinine concentration of 0.11 mmol/L [NR, 0.06-0.12 mmol/L]).

Drug hepatitis, secondary to fusidic acid was suspected, and therapy with this drug was ceased.

The following day, the patient's clinical status declined, with generalised muscle pains and weakness, significantly impairing his mobility. The serum creatine kinase concentration was elevated at 66 710 U/L (normal range, 60-220 U/L), with a normal troponin I concentration. Myoglobinuria (567 200 ng/mL) was detected.

Simvastatin therapy was ceased, and there was prompt clinical improvement, with recovery of renal function and a gradual fall in the concentration of serum creatine kinase. On discharge 14 days after admission, his serum creatine kinase concentration was 1153 U/L and creatinine concentration was 0.12 mmol/L. Transaminase concentration readings fell rapidly in line with the creatine kinase concentration, suggesting they were of muscular rather than hepatic origin.

Three other cases of rhabdomyolysis have been reported as a result of interaction between an HMG CoA-reductase inhibitor and fusidic acid,¹⁻³ but there have been no previous reports from Australia.

Fusidic acid, like simvastatin, undergoes extensive first-pass metabolism in the liver (over 98%). Simvastatin is metabolised via the cytochrome P3A4 enzyme system. It is known that, if given concomitantly with inhibitors of this system (eg, macrolides and azole deriv-

atives), statin concentrations can become elevated and lead to an increased likelihood of adverse effects.⁴ Fusidic acid is not known to be an inhibitor of this system (Peter Hobbs, Manager of Medical Affairs, CSL Limited [manufacturers of fucidin], personal communication), although our case is suggestive of such an interaction.

This case demonstrates the interaction of fusidic acid with simvastatin resulting in rhabdomyolysis. The extensive use of statin therapy in patients with vascular disease makes it important for doctors to be aware of this interaction when prescribing fusidic acid.

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Influenza outbreak related to air travel

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TO THE EDITOR: Modern air travel lends itself to aerosol transmission of viral infection. Infected individuals in modern aircraft represent a significant risk for other travellers during long journeys.

In September 1999, a person with an influenza-like illness joined other workers returning by aircraft to an isolated mine in north-western Australia. He was identified as unwell by a mine supervisor in the airport lounge but was allowed to board the BAe 146 aircraft (a 75-seat passenger jet aircraft). The flight lasted 3 hours 20 minutes. On landing in the evening, most workers were transported to their quarters in a 10-minute bus trip, but some, including the affected worker, travelled independently. They then went to their individual rooms.

The next day, the affected worker reported sick immediately on going to his work site and did not work for 4 days. The other workers undertook 12-