Burkholderia pseudomallei sepsis presenting with pericardial effusion and tamponade

Bart L De Keulenaer, Simon R Van Hooland, Prabha R Damodaran, Bart J Currie, Bruce P Powell and Ian R Jenkins

ABSTRACT

Severe septicaemia secondary to melioidosis carries a high mortality. Although melioidosis can involve most tissues and organs, pericardial involvement is rare. We report a 40-year-old woman with melioidosis with pericardial involvement but no contiguous pulmonary involvement. She developed acute pericardial tamponade but was successfully treated with surgery and medical therapy. This is the first case in Australia or New Zealand of melioid sepsis presenting with pericarditis and subsequent cardiac tamponade. We review the literature on cardiac involvement in melioidosis.

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Clinical record

A 40-year-old Indigenous woman presented to the emergency department with a 2-week history of general malaise, fever, grade II dyspnoea and a productive cough with white sputum. She had been treated for 5 days before presentation with intramuscular procaine penicillin (1.5 g daily).

Her history included poorly controlled type 2 diabetes, hypertension, smoking and alcohol misuse. Her medications were ramipril (5 mg daily), metformin (500 mg three times daily), gliclazide (80 mg daily) and aspirin (300 mg daily).

Physical examination revealed a temperature of 38.8°C, pulse rate of 98 beats per min, blood pressure of 101/65 mmHg, respiratory rate of 24 breaths per min, and O_2 saturation when breathing room air of 90%. Lung auscultation revealed decreased air entry at the left base without crackles or wheezing. Results of heart and abdominal examination were unremarkable.

Laboratory tests revealed a white blood cell count of 9.9×10^9/L (reference range [RR], $4–11 \times 10^9$), and serum concentrations of C-reactive protein, 238 mg/L (RR, 0–8 mg/L); creatinine, 77 μmol/L (RR, 50–110 μmol/L); urea, 2.7 mmol/L (RR, 3.0–8.0 mmol/L); albumin, 31 g/L (RR, 35–45 g/L); γ-glutamyltransferase, 136 U/L (RR, 0–40 U/L), and alkaline phosphatase, 160 U/L (RR, 39–117 U/L).

An electrocardiogram (ECG) showed T-wave flattening inferolaterally. Chest x-ray showed marked cardiomegaly suggesting pericardial effusion, without any obvious consolidation (Figure 1). Computed tomography (CT) of the chest confirmed a large pericardial effusion (Figure 2), and CT of the abdomen did not reveal hepatic, splenic or renal abscesses. Unfortunately, the radiographic findings were initially not seen by the medical team.

The patient was admitted and treated for a community-acquired lower respiratory tract infection, with gentamicin (350 mg daily) and intravenous ceftriaxone (1 g daily).

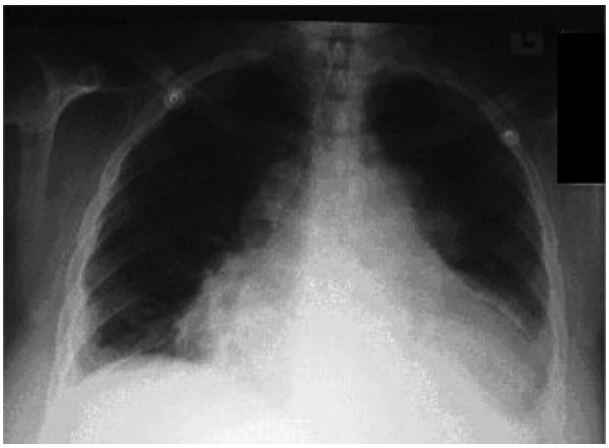
Blood cultures showed no growth but, on Day 6 of the admission, cultures of sputum taken on admission revealed *Burkholderia pseudomallei*. Serological testing for melioidosis by indirect haemagglutination revealed an antibody titre of 1 : 160. Throat swabs were negative for melioidosis. Antibiotic therapy was changed to intravenous meropenem (1 g three times daily) and oral trimethoprim–sulfamethoxazole (320/1600 mg twice daily).

On Day 5 of the admission, the patient developed haemodynamic instability, and an ECG showed a large global pericardial effusion with collapse of the right atrial free wall consistent with early tamponade.

She underwent a thoracotomy to create a pericardial window. The pericardial fluid was negative for acid-fast bacilli, with a lactate dehydrogenase concentration of 2415 U/L (reference range, 200–400 U/L), mildly inflammatory bloodstained fluid on microscopy, and a leukocyte count of 600×10^6/L (30% neutrophils and 70% mononuclear cells). The fluid was negative for *B. pseudomallei* on Gram stain but positive on culture. Examination of the pericardial tissue revealed gram-negative rods but no acid-fast rods. Histological examination showed fibrinous pericarditis with no signs of malignancy.

The patient's immediate postoperative course was complicated by severe septic shock requiring vasopressor therapy, and acute respiratory distress syndrome requiring high inspired oxygen concentrations and granulocyte colony-stimulating factor (G-CSF). Her condition responded well to treatment, and she was extubated on Day 7 after surgery, and discharged to the ward on Day 9, when the antibiotic therapy was narrowed to ceftazidime (continuous infusion of 6 g per 24 h) and continuing oral trimethoprim–sulfamethoxazole. Her stay was further complicated by a left pleural effusion and fever, which resolved with drainage of the effusion. She developed neutropenia secondary to the

Figure 1. Chest x-ray at presentation



Chest x-ray showed marked cardiomegaly, marked prominence of the left hilar region, minor blunting of both costophrenic angles and some patchy changes in the right mid-zone and the retrocardiac region.

trimethoprim–sulfamethoxazole therapy, which resolved after the therapy was changed to doxycycline (100 mg twice daily).

Her condition improved gradually, and she was discharged from hospital on Day 29 with continuing intravenous ceftazidime via a peripherally inserted central catheter through the hospital-in-the-home service. She received a total of 6 weeks of intravenous antibiotics after the last positive culture (obtained intra-operatively). Doxycycline was continued for a further 4 months after discharge from hospital-in-the-home. A transthoracic echocardiogram during this period showed a trivial remnant pericardial effusion, with normal left systolic function and no evidence of constriction.

Discussion

Melioidosis is caused by *B. pseudomallei*, a facultative intracellular gram-negative bacterium found in soil and fresh surface water in endemic areas. It is an important cause of sepsis in South-East Asia and northern Australia.[1]

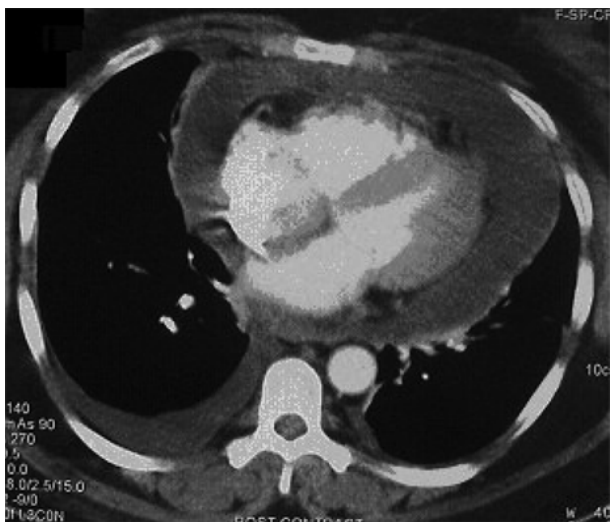
The incubation period of melioidosis ranges from 1 to 21 days (mean, 9 days). Early literature suggested that inhalation was a route of infection (eg, inhalation of dust from helicopter blades by soldiers in Vietnam[2]). It is now generally accepted that the predominant route is percutaneous inoculation during exposure to wet season soils or contaminated water.[3] Person-to-person spread is considered very rare. Diabetes and excessive alcohol ingestion are risk factors for melioidosis — both present in our patient.

Clinical manifestations vary widely, from subclinical infection, through local skin and lung infection, to bacteraemic spread to any organ and fulminant septic shock, the latter having a high mortality (up to 86%). As illustrated by a study in the Northern Territory,[4] the most common clinical presentation is pneumonia, which accounts for half the cases.

Melioidosis with pericardial involvement is rare. In the NT study, pericardial involvement was mentioned in two of 252 cases of melioidosis (< 1%) collected over 10 years.[4] In a prospective study in Darwin, pericarditis was a major complicating factor in three of 390 culture-positive cases of melioidosis, including one fatal case. To our knowledge, three other case reports have been published on this rare manifestation.[5-7] In two of these patients, the primary source was a concomitant lung abscess in the right upper lobe.[5,6] In one of these, *B. pseudomallei* was not isolated from the pericardial fluid.[5] In the other, the lung abscess ruptured into the pericardial cavity causing pericarditis and a pericardial effusion.[6] The third, most recent, patient had pericarditis complicated by cardiac tamponade, with no other infectious focus.[7] Our patient represents the second reported case of melioid pericarditis not associated with a lung abscess.

The route of infection in our patient was not entirely clear. As the symptoms on admission suggested a respiratory infection, and *B. pseudomallei* was cultured from sputum, it is possible that there was a primary lung infection with secondary bacteraemic spread to the pericardium, even though blood cultures showed no growth.

Figure 2. Computed tomography scan at presentation



Computed tomography showed very marked pericardial effusion and bilateral minor pleural effusions (larger on the right than on the left), and no inflammatory changes in either lung field.

Another possibility is bacteraemia following percutaneous inoculation, with subsequent lung and pericardial infection.

In our patient, the correct diagnosis was made 5 days after admission. The delay was probably because of the absence of the major clinical manifestations of acute pericarditis (chest pain, pericardial friction rub and widespread ST segment elevation on ECG),[8] and the high likelihood of a lung infection on clinical grounds.

When impending cardiac tamponade was diagnosed, the patient underwent surgical drainage without a prior attempt at pericardiocentesis. Postoperatively there was a moderate left pleural effusion, due to persistent production of pericardial fluid and drainage into the left pleural space. Cultures of the pleural fluid were negative for *B. pseudomallei*. The patient reported by Majid,[6] in whom pericardiocentesis failed due to the accumulation of pericardial pus and loculi, was also treated successfully with surgery.

Based on experience in the Royal Darwin Hospital,[9,10] we added G-CSF to the patient's treatment while she was in the ICU. After ICU discharge, she underwent repeat transthoracic echocardiography, which showed that no constrictive component had developed, in contrast to the expectation in tuberculous pericarditis. Her sputum, pericardial fluid and tissue were negative for acid-fast bacilli. Although corticosteroids are recommended in tuberculous pericarditis, in addition to antituberculous therapy,[11] there is no evidence supporting their use in melioidosis pericarditis.

Our patient made an excellent recovery. Therapy for the duration she received is expected to eradicate the infection, leaving no long-term complications.

Treatment of septicaemia secondary to melioidosis comprises an initial short course of intravenous antibiotics (for at least 10 days) and a prolonged eradication phase of oral antibiotics lasting up to 20 weeks.[3] For the initial intensive phase, ceftazidime plus trimethoprim–sulfamethaxole or imipenem–meropenem has been recommended. Oral treatment comprises a four-drug combination of chloramphenicol, doxycycline, trimethoprim and sulfamethoxazole. Chloramphenicol is usually given for 8 weeks, while doxycycline and trimethoprim–sulfamethaxole are continued for 20 weeks.

The response to treatment is often slow despite high-dose parenteral antibiotics. Blood cultures are usually negative by the end of the first week of oral antibiotics, whereas sputum and draining abscesses can remain culture-positive for up to a month, even in infections that are responding to treatment. The relapse rate, even after such long antibiotic therapy, is about 10%, rising to 30% if treatment is limited to 8 weeks.[3] The cure rate is higher in children than in adults.

Pericardial tamponade is one of the many possible manifestations of melioidosis. This rare manifestation should be suspected when pericarditis is diagnosed in a patient who has risk factors for melioidosis and lives, or has travelled, in an endemic area. Furthermore, melioidosis and its protean manifestations need to be considered in any patient living in, or travelling from, a melioidosis-endemic region who is admitted to an ICU with severe sepsis.

It is very likely that, with increasing travel to endemic areas and availability of diagnostic microbiology, melioidosis will be diagnosed more often over the next decade.

Author details

Bart L De Keulenaer, Intensive Care Specialist[1]
Simon R Van Hooland, Registrar[1]
Prabha R Damodaran, Registrar[1]
Bart J Currie, Professor of Medicine,[2] and Head[3]
Bruce P Powell, Senior Registrar[1]
Ian R Jenkins, Intensive Care Specialist[1]
1 Intensive Care Unit, Fremantle Hospital, Fremantle, WA.
2 Northern Territory Clinical School, Flinders University and Royal Darwin Hospital, Darwin, NT.
3 Infectious Diseases Division, Menzies School of Health Research, Charles Darwin University, Darwin, NT.
Correspondence: bdekeul@hotmail.com

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