Fatal *Burkholderia pseudomallei* septicaemia

Kaushalya Jayasekara[1], **Shalinie Perera**[2] and **Anula Wijesundere**[3]

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Introduction

Melioidosis, the infection caused by the saprophytic bacterium *Burkholderia pseudomallei*, is endemic in south-east Asia and northern Australia [1]. Sporadic cases have been reported from the Indian subcontinent and it is an emerging infection in India [2]. A low prevalence of antibodies against melioidosis among hospital-associated groups in Colombo had been reported in 1976 [3], as well as a report of melioidosis abscess after travel to Sri Lanka in 1999 [4]. Septicaemic melioidosis represents the most severe form of this infection, with a high mortality. We report here the first laboratory confirmed patient with *Burkholderia pseudomallei* infection in Sri Lanka, who had septicaemic melioidosis leading to multi-organ dysfunction.

Case report

A 48-year old man was admitted to Sri Jayewardenepura General Hospital with right hip joint pain for 2 days and fever with rigors since the previous night. He had been treated for *Salmonella* arthritis of the right hip joint 3 weeks ago based on a Widal test titre of *Salmonella typhi* 'H' 1/320, 'O' 1/80 and 'AH' 1/320. He was a type 2 diabetic on oral hypoglycaemics.

On examination, he was febrile, unwell and had right hip joint tenderness restricting movement. His pulse was 110/min and blood pressure 110/70 mmHg. The liver was tender and enlarged to 4 cm below the right costal margin. Blood was taken for culture, and he was given intravenous cefotaxime and cloxacillin. Initial investigations showed: haemoglobin 8.9 g/dL, SGOT 41 IU/L, SGPT 107 IU/L, total bilirubin 68 µmol/L with direct fraction 39.1 µmol/L, alkaline phosphatase 1112 U/L, serum creatinine 127 µmol/L, serum sodium 125.9 mmol/L and potassium 5.7 mmol/L. Initial blood cultures were negative. The white count was 16.1×10^9/L with neutrophils 82%.

The fever persisted and the patient deteriorated in spite of treatment. By the fifth day, he had myocarditis confirmed by echocardiography, worsening dyspnoea with diffuse lung crepitations, and increasing hepatomegaly. Transabdominal ultrasonography demonstrated no other abnormality except hepatomegaly, and hip joint radiographs were normal. Blood for malaria antigens and serology for hepatitis A and B, mycoplasma and HIV were negative. The chest radiograph showed diffuse alveolar opacities. The direct smear of sputum for acid fast bacilli was positive. Blood culture isolate revealed a Gram negative organism resembling *Burkholderia pseudomallei*. A diagnosis of pulmonary tuberculosis and Gram negative sepsis was made.

He was managed in the intensive care unit with intravenous meropenam, ceftazidime, cotrimoxazole and antituberculous treatment. Blood culture isolate was identified as *Burkholderia pseudomallei* on the ninth day. He developed bilateral sixth cranial nerve palsy and subsequently, respiratory exhaustion needing mechanical ventilation. There was an initial response to the antibiotics and sputum direct smear was negative for acid fast bacilli after two weeks of antituberculous therapy. However, the response was short-lived and he deteriorated despite optimal supportive care and addition of intravenous co-amoxiclav. He succumbed on the 36th day of intensive care.

Culture of blood in commercially prepared blood culture medium, containing brain-heart infusion broth with sodium polyanithol sulphonate (SPS), yielded smooth grey non-haemolytic colonies on blood agar and non-lactose fermenting smooth colonies on MacConkey agar. The colonies had large and small variants on both media, which became dry and wrinkled after overnight incubation. There was no growth on anaerobic blood agar.

On Gram stain of the colonies, the organisms were Gram negative bacilli which showed the characteristic bipolar staining. The oxidase and bile aesculin tests were positive. Antibiotic susceptibility done by the NCCLS method revealed that the isolate was sensitive to amoxicillin-clavulanic acid, ceftazidime, cefotaxime and imipenam, and resistant to all aminoglycosides, ampicillin, cotrimoxazole and ciprofloxacin. The API 20 NE panel was used to identify the organism which was confirmed to be *Burkholderia pseudomallei*, with good identity to genus level.

Discussion

The true distribution of melioidosis probably extends beyond south-east Asia and Australia, as seen by case reports from India, central Africa, South America and the Caribbean. It is under-diagnosed in many of these regions due to the lack of laboratory facilities necessary

[1]*Registrar,* [2]*Microbiologist, and* [3]*Physician, Sri Jayewardenepura General Hospital (Teaching), Nugegoda, Sri Lanka.*
Correspondence: KJ, *e-mail: <kaushalyahkj@yahoo.com>* *(Competing interests: none declared). Received 25 March 2005 and accepted 28 May 2005.*

to confirm the diagnosis. *Burkholderia pseudomallei*, being an environmental saprophyte readily isolated from soil and surface water, particularly from rice paddy, is likely to exist in Sri Lanka, but has probably gone undiagnosed.

The infection is primarily acquired via the inoculation of compromised surface tissues by contaminated soil and water. The timing and location of cases had been generally correlated with rainfall or associated with post-cyclonic flooding [1]. Melioidosis severe enough to be seen in hospital is an opportunistic disease, as over 70% of patients have underlying predisposition to the infection [5], such as diabetes (37%), excessive alcohol intake (39%), chronic lung disease (27%), and chronic renal disease (10%) [6].

The clinical spectrum of melioidosis is broad and the infections may be acute or chronic, and localised or disseminated. In a series of 252 confirmed melioidosis patients from northern Australia, pneumonia accounted for 50% of presentations and other presentations included genitourinary infections (37%), skin abscesses (13%) and osteomyelitis/septic arthritis (4%) [6].

B pseudomallei is intrinsically resistant to many antibiotics, including aminoglycosides and early β-lactams, and is often sensitive *in vitro* to extended-spectrum cephalosporins (e.g. ceftazidime), imipenam and co-amoxiclav. However, despite administration of ceftazidime or carbapenems, mortality up to 86% has been shown among those with septic shock [6]. Its capsule and a type III protein secretion apparatus enable *B pseudomallei* to survive intracellular killing and facilitate intercellular spread, contributing to the refractory and persistent nature of infection [7].

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