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Melioidosis – a case series from south India

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Summary Melioidosis is sporadically reported from various parts of India. We present a case series from south India, highlighting the varied manifestations of the disease. Seven cases of culture-proven melioidosis are presented in whom *Burkholderia pseudomallei* were isolated from aspirate or blood. Melioidosis had a varied presentation involving multiple abscesses in the soft tissues, liver, spleen, mediastinum and the subdural space. It presented as either acute fulminant sepsis or followed a chronic indolent course, mimicking tuberculosis. Most cases had predisposing risk factors such as diabetes and chronic alcoholism.

1. Introduction

Melioidosis is an infectious disease caused by the Gram-negative soil-dwelling bacillus *Burkholderia pseudomallei*.[1] The disease is endemic to Southeast Asia and northern Australia, with sporadic case reports being reported in India; and multiple cases have been reported in Vellore and Pune, India.[1–4] Several risk factors for developing melioidosis have been described, including diabetes, excessive alcohol consumption and chronic renal disease.[1] In this report, we describe a case series of melioidosis patients presenting during 2001–2007 in south India and highlight the spectrum of clinical manifestation. Informed consent was obtained from all patients.

2. Case series

2.1. Case 1

A 49-year-old-male presented with fever and headache of 1 month. He had received anti-tubercular therapy (ATT) prior to admission. He had anaemia, tender swellings over the ankle, wrist and temporal region. The clinical investigations performed are shown in Table 1. He had loculated right-sided pleural effusion. Ultrasonography showed hepatomegaly. Bronchial lavage and blood culture showed *Pseudomonas aeruginosa*. Aspirate from the subcutaneous swellings grew *B. pseudomallei*. He was treated with amoxicillin–clavulanate for 4 months. At 6 months of follow-up he had no signs of recurrence.

2.2. Case 2

A 45-year-old female presented with fever, pain in knees and left hip, jaundice of 8 weeks and recent onset of breathlessness. Examination revealed jaundice, hepatosplenomegaly and pleural effusion. The Mantoux test was positive. Ultrasonography showed hepatomegaly with abscesses in the spleen. She had chronic osteomyelitis of the left hip. Culture of the splenic aspirate and blood revealed *B. pseudomallei*. The patient was treated with sequestrectomy, parenteral ceftazidime and amoxicillin–clavulanate for 6 weeks followed by oral amoxicillin–clavulanate and cotrimoxazole for 6 months. At 6 months of follow-up, the hip pain had subsided, she had gained 22 kg weight and the splenomegaly had completely regressed.

2.3. Case 3

A 43-year-old male presented with fever and abdominal pain for 1 year. He had received empirical ATT elsewhere. He had pallor and hepatosplenomegaly. The Mantoux test was positive. Multiple hepatic and splenic abscesses were seen on ultrasonography. Culture of the splenic aspirate disclosed *B. pseudomallei*. He was treated with amoxicillin–clavulanate for 6 months. As there was only partial clearance of the abscess, he underwent splenectomy. The spleen measured 19×12×10 cm, with multiple abscesses.

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Table 1 General characteristics and investigation results of cases

Characteristic	Case						
	1	2	3	4	5	6	7
Age (years)	49	45	40	65	27	54	42
Sex	Male	Female	Male	Male	Female	Male	Male
Occupation	Agriculturist	Housewife	Government service	Contractor	Housewife	Government service	Fisherman
Presenting month	September	May	June	July	June	January	August
Risk factors	Diabetes, alcoholic	Diabetes, alcoholic	Diabetes, alcoholic	Diabetes, alcoholic	AIDS	Diabetes, alcoholic, COPD	Diabetes
Hb < 10 g/dl	+	+	+	–	–	–	–
Leucocytosis	+	+	+	–	–	+	+
ESR > 100 mm/h	+	+	+	+	+	–	–
ALP > 300 U/l	+	+	+	+	–	–	–
Mantoux test	–	+	+	–	–	–	–
Chest X-ray	Pleural effusion, pneumonia	Bilateral pleural effusion	Normal	Normal	Bilateral pneumonia, pleural effusion	Mediastinal widening	Normal
USG abdomen	Hepatomegaly	Hepatosplenomegaly, splenic abscess	Hepatic and splenic abscesses	Hepato-splenomegaly, hepatic abscess	Hepatosplenomegaly	Normal	Splenomegaly
Antibiotic sensitivity	AC, PIP, CZM, CEF, CP, MER	AC, CTX, CZM, DOX	AC, CTX	AC, CIP, CTX, AMI, CZM	AC, CEF[2]	AC, CTX, CFX	AC, CHL, PIP, CZM
Outcome	Survived	Survived	Survived	Died	Died	Lost to follow-up	Survived

ALP: alkaline phosphatase; AMI: amikacin; AC: amoxicillin–clavulanate; CZM: ceftazidime; CEF: cefepime; CFX: cefotaxime; CHL: chloramphenicol; CIP: ciprofloxacin; COPD: chronic obstructive pulmonary disease; CP: cefadroxil–perazone; CTX: cotrimoxazole; DOX: doxycycline; ESR: erythrocyte sedimentation rate; MER: meropenum; PIP: piperacillin; USG: ultrasonography.

Histopathology showed stellate necrotizing granulomas, stellate abscesses with central coagulation necrosis, and foreign body giant cells. There was no recurrence at the 2-year follow-up.

2.4. Case 4

A 65-year-old male presented with fever of 15 d, sudden onset hemiplegia and altered sensorium of 1 d. He was pale and had neck stiffness. Ultrasonography of the abdomen showed hepatosplenomegaly with multiple liver abscesses of up to 3.6×2.9 cm in size. A magnetic resonance image of the brain showed a small bilateral subdural collection. Examination of the cerebrospinal fluid revealed neutrophilic pleocytosis with normal protein and sugar. The patient required mechanical ventilation when the liver abscess ruptured into the lungs. Aspirate from the liver grew *B. pseudomallei*. The patient was treated with meropenem and amoxicillin–clavulanate. He developed septic shock, bilateral lung consolidation and pleural effusion. After 2 weeks of therapy the liver abscess reduced in size, the subdural collection disappeared, and the patient could be weaned off the ventilator. Parenteral amoxicillin–clavulanate was continued. However, the patient developed aspiration pneumonia, required a ventilator and subsequently succumbed to fungal sepsis.

2.5. Case 5

A 27-year-old female with AIDS was receiving highly active antiretroviral therapy and presented with 1 week of fever and abdominal pain. She was febrile, had tachycardia and tachypnoea. She had pallor, icterus, hepatosplenomegaly and bilateral diffuse inspiratory crackles. She was hypoxic. A chest X-ray showed bilateral consolidation with right pleural effusion. Ultrasonography showed hepatosplenomegaly. Blood culture grew *B. pseudomallei*. Even on treatment with ceftazidime and amoxicillin–clavulanate, she developed septic shock, acute respiratory distress syndrome and died.

2.6. Case 6

A 54-year-old male diabetic patient was found to have soft tissue mass in the mediastinum on routine screening with a chest X-ray. He had facial puffiness and dilated veins of the left upper limb. A computed tomography scan revealed necrotic mediastinal lymph node with compression of the superior vena cava. Bronchoscopy was normal. Aspiration of the mediastinal node showed caseous material and was negative for malignancy. Culture of the aspirate grew *B. pseudomallei*. The patient was treated with ceftazidime followed by oral amoxicillin–clavulanate and cotrimoxazole. However, the patient was lost to follow-up.

2.7. Case 7

A 42-year-old male presented with fever of 10 d and splenomegaly. The blood culture grew *B. pseudomallei*. The patient was treated with ceftazidime for 2 weeks followed by amoxicillin–clavulanate and cotrimoxazole for

14 weeks. The patient remained symptom free at 6 months of follow-up.

3. Discussion

Pathologists Whitmore and Krishnaswami isolated *B. pseudomallei*, the causative organism of melioidosis in 1911 at Rangoon. The disease is more common in individuals with diabetes, chronic alcoholism, immunodeficiency, chronic respiratory illness or chronic renal failure.[5] In this report, all cases, except for one, presented during the rainy season between May and September. This finding is in agreement with previous studies.[5] Melioidosis can present as skin ulcers, abscesses in liver, spleen, kidney, adrenals, parotid, brain, muscle and soft tissue. It can also present as septic arthritis, osteomyelitis, pleural effusion, emphysema, pericardial effusion, and encephalomyelitis. Sometimes, only bacteraemia without any focus may be present. The incidence of bacteraemic melioidosis has been reported to be between 46% and 60%, with an overall mortality rate ranging from 19% to 46%.[5] The infection is under-diagnosed in India, probably due to a low index of suspicion among clinicians and clinical microbiologists.

Burkholderia pseudomallei on Gram staining is Gram negative and tends to stain darkly at the ends giving a 'safety pin' appearance. Definitive diagnosis of melioidosis requires a positive culture of *B. pseudomallei*. Three of our patients (cases 2, 5 and 7) had a positive blood culture, and in the remaining patients the organism was isolated from the pus. *Burkholderia pseudomallei* is a non-fastidious organism that is biochemically a non-fermenter. It may be easily mistaken for *Pseudomonas* spp. of no clinical significance since they share several common phenotypic characteristics. It is recommended that all isolates of non-fermenting Gram-negative bacilli (NFGNB) be discriminated using biochemical tests.[3] Both antigen- and DNA-detection techniques are being used in endemic regions but these are not yet commercially available. Positive indirect haemagglutination test is useful in supporting the possibility of melioidosis.[5]

Melioidosis can present as acute fulminant sepsis with a high mortality or follow a chronic indolent course. Clinically the chronic form of the disease may mimic tuberculosis. The Mantoux test may be positive, as it was in 2 cases (cases 2 and 3). Histopathology may show granulomas, which were evident in case 3, and bacteria, which are rarely demonstrable in tissue section. The pus of melioidosis may be mistaken for caseous necrosis of tuberculosis.[4] Diagnostic confusion with tuberculosis can occur, especially in areas where there is a high incidence of both diseases. In this series, two cases received empirical ATT before the diagnosis.

The organism responsible for melioidosis, *B. pseudomallei*, is most often sensitive to amoxicillin–clavulanate, ceftazidime, cotrimoxazole and carbapenems. Two patients (cases 1 and 7) were cured with a 4-month course of amoxicillin–clavulanate and cotrimoxazole, and another patient (case 3) required a splenectomy before a complete cure was achieved. Superadded fungal infection was fatal in case 4 while fulminant pseudomallei septicaemia was fatal in a retro-positive patient. Adherence to long-term multidrug therapy is important in achieving a cure and follow-up is required to identify any relapse. Melioidosis is probably much more prevalent than what is reported in India, and awareness and a high index of suspicion amongst clinicians and microbiologists will aid in early diagnosis and appropriate therapy.

Authors' contributions: SK, RSK, ASB and GKV were involved in patient care and carried out the clinical assessment; IB and CM carried out identification of the organism; SK and VS collected data and reviewed the literature; SK and VS drafted the manuscript and GKV critically revised it. All authors read and approved the final manuscript. SK is guarantor of the paper.

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Ethics approval: Ethical approval was obtained from the Institutional Ethical Committee, Kasturba Medical College, Manipal, Karnataka, India and the patients' assessment and treatment were done in accordance with the clinical practice guidelines of Institutional Ethical Committee.

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