



EPIDEMIOLOGICAL AND CLINICAL PROFILES OF MELIOIDOSIS IN TERTIARY CARE CENTRE IN NORTHERN SRI LANKA.

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ABSTRACT

Melioidosis is sporadically reported from various parts of Sri Lanka. It is major recent endemic in Northern Sri Lanka. It is caused by *Burkholderia pseudomallei*, a Gram-negative, oxidase positive bacillus. The first case of melioidosis was reported in a European tea broker in 1927 in Sri Lanka. We present a case series of seven patients of culture or serologically proven melioidosis from Northern Sri Lanka, highlighting the different clinical manifestations of the disease. Melioidosis had a varied presentation involving multiple abscesses in the skin, liver, spleen, mediastinum and septic arthritis. It presented as either an acute fulminant septicaemia with a high mortality to a chronic localized infection. Most cases had predisposing risk factors such as diabetes and occupational risk.

KEYWORDS

melioidosis, *Burkholderia pseudomallei*, septic arthritis, pneumonia, abscess, diabetes, northern, Sri Lanka.

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Introduction

Melioidosis is acute or chronic pyogenic infection, caused by bacterium *Burkholderia pseudomallei* from soil (1). It occurs following inoculation of skin and causes illness in humans and animals. It is an endemic in tropical and subtropical areas of South East Asia (2). The first case of melioidosis was reported in a European tea broker in Sri Lanka in 1927 (3). Recently, many cases of melioidosis were reported in Sri Lanka including Jaffna, due to high foreign travelers to endemic areas (4). Diabetes mellitus, chronic alcoholism, chronic obstructive airway disease, or chronic kidney disease, cancer and steroid therapy are common risk factors (5). Here, we describe a case series of melioidosis patients in Northern Sri Lanka and highlight the spectrum of clinical manifestation. Informed consent was obtained from all patients in Jaffna district.

Case Series

Case 1

A 58 years old diabetic woman presented with fever with constitutional symptoms, severe bilateral knee joint pain and swelling. On examination, she had moderate soft tender hepatomegaly and bilateral fine basal crepitations. Bilateral knee joint with active inflammation was noted right side more than left side. The clinical investigations performed are shown in Table 1. The joint fluid analysis revealed polymorpholeucocytosis predominant lymphocytosis with elevated protein level and *Burkholderia pseudomallei* was isolated from joint fluid culture. Melioidosis antibody titre was 5120 and was managed with intravenous ceftazidime and Cotrimaxazole for two weeks. Her condition was deteriorated and died due to septic shock with multiorgan dysfunction during 3rd week course of therapy.

Case 2

A 49 year old diabetic woman presented with fever and productive cough with whitish coloured sputum for one week duration. She has involved actively involved cultivation. On examination, she had righted side middle and lower zone crepitations and moderate soft tender hepatosplenomegaly. The clinical investigations performed are shown in Table 1. Her ultrasound abdomen showed focal liver lesion

suggestive of abscess/metastasis. The contrast enhanced computerized tomography of chest and abdomen revealed large lesion with peripheral echogenicity with right hilar lymphadenopathy and two focal lesions measuring 2.2&1.5cm and 2.4&1.5cm in segment 5 and 6 of liver suggestive of lung and hepatic abscess. Even, the repeated blood cultures were negative, her serum melioidosis antibody titre was 10,240. She was treated with intravenous meropenem and oral doxycycline for six weeks and was discharged with course of oral antibiotics. At 6 months of follow-up he had no signs of recurrence.

Case 3

A 27-year-old female presented with fever with constitutional symptoms for three weeks duration. She was febrile, pale and had tachycardia and tachypnoea. Her systemic examination is unremarkable. The contrast enhanced computerized tomography of abdomen revealed septated abscess measuring size of 3.6 & 4.8cm size +in spleen. Her serum melioidosis antibody titre was 10,240. She was treated with intravenous meropenem and oral doxycycline. At 6 months of follow-up, the hip pain had subsided, she had gained weight and the splenomegaly had completely regressed.

Case 4

63 years old diabetic man presented with fever with constitutional symptoms, abdominal pain, watery diarrhea and productive cough for two weeks duration. On examination, he was pale, tachycardia. He had bilateral lower zone crepitations and moderate soft tender hepatomegaly. His chest x ray showed bilateral patch shadow. His ultrasound abdomen showed septated abscess in spleen. *Burkholderia pseudomallei* was isolated from blood culture. Even on treatment with meropenem and clathromycin, he developed septic shock, acute respiratory distress syndrome. However, the patient developed refractory sepsis, required a ventilator and subsequently succumbed to sepsis with multiorgan dysfunction.

Case 5

57 years old poorly controlled diabetic man presented with fever with constitutional symptoms, multiple skin abscess of left lower limb and

back of chest and active inflammation of left side knee joint. On examination, he was pale, tachycardia. He had bilateral lower zone crepitations and septic arthritis of left side knee joint. The joint fluid analysis revealed polymorpholeucocytosis predominant neutrophils with elevated protein level and Burkholderia pseudomallei was isolated from blood culture. His chest x ray showed bilateral patch shadow. His ultrasound of lower limbs showed deep seated abscess in left side thigh and calf region. He underwent drainage of deep abscess and knee joint aspiration. He developed septic shock and acute respiratory distress syndrome and required a ventilator. subsequently improved with meropenem and cotrimoxazole for six weeks and was discharged with course of oral antibiotics. At 6 months of follow-up, he had no signs of recurrence.

Case 6

A 34 year old female presented with fever with constitutional symptoms for three weeks duration. The contrast enhanced computerized tomography of abdomen revealed 21 cm size of spleen. The infectious, retroviral, septic and autoimmune screening were negative. Blood picture showed normocytic normochromic anemia and thrombocytopenia. Her serum melioidosis antibody titre was 640. She was treated with intravenous meropenem and oral cotrimoxazole for 6 weeks duration. At 6 months of follow-up, she had gained weight and the splenomegaly had completely regressed.

Case 7

14 years old healthy boy presented with fever with chills, rigors and productive cough for 2 weeks duration. On examination, he was tachypnoea and tachycardia. He had lower zone coarse crepitations of right side lung. His chest x ray showed lung abscess with fluid level of right lung. His sputum culture, sputum FB were negative. His serum melioidosis antibody titre was 320. He was treated with intravenous meropenem and oral cotrimoxazole for 6 weeks duration and lung abscess had been completely regressed.

Discussion

Melioidosis is caused by the soil-associated bacterium *Burkholderia pseudomallei* (1). It is a pyogenic infection presenting as acutely or chronic infection. It usually follows percutaneous inoculation and causes disease in humans (2). It is an endemic in tropical and subtropical zones of South East Asia and Northern Australia. The first case of melioidosis was reported in a European tea broker in 1927 in Sri Lanka (3). Recently, several cases of melioidosis have been reported in Sri Lanka, probably due to an increase in international travel to endemic areas (6). The first case of melioidosis was reported in Jaffna in 2013 (7). Subsequently two cases were reported in 2016 (8).

The known endemic distribution of *B. pseudomallei* is expanding well beyond the traditional melioidosis-endemic regions of Southeast Asia and northern Australia, with recent case reports of melioidosis from the Americas, Madagascar, Mauritius, India and elsewhere in south Asia, China and Taiwan (2). Even though Sri Lanka has been considered non endemic for melioidosis, there is increasing evidence for its emergence in the recent past.

Diabetes mellitus, chronic alcoholism, chronic obstructive airway disease, or chronic kidney disease, cancer and steroid therapy are common risk factors (5). The diabetes found a correlation of 76% of with Melioidosis (9). Diabetes mellitus was underlying risk factor among three cases.

The clinical presentation varies from a septicemia to chronic infection associated with high morbidity and mortality (2). It causes different clinical manifestations such as pneumoniae, septicemia, arthritis and abscess. The lung involvement is the commonest clinical manifestation. Lung was involved among five cases in the form of either lung abscess or pneumonia. Bone disease was reported in 16% of cases (10). septic arthritis was the clinical manifestation in two cases. The cutaneous or deep seated or visceral abscess is also reported as common clinical manifestation (11). There were four cases of abscess reported in our cases.

The gold standard diagnostic investigation is isolation of *Burkholderia pseudomallei* in culture from blood or serous fluids (6). However, prior antibiotics therapy lead to negative blood culture in our patient. In culture negative case, serological diagnosis is mandatory for diagnosis of melioidosis (12). The serological diagnosis was important stool among our cases and culture from blood or joint fluid was positive in certain cases.

Meropenem is the drug of choice in systemic melioidosis (13). Cotrimoxazole, ceftazidime, imipenem or ceftazidime are alternatives for systemic melioidosis (14). The oral cotrimoxazole or doxycycline is used to prevent relapse (13) in follow up. Intravenous meropenem and oral Cotrimoxazole or doxycycline were intensive therapy for six weeks and oral Cotrimoxazole or doxycycline was maintenance therapy for most of our patients. Five patients improved with antibiotics therapy.

Late diagnosis has led to fatality in some cases even proper therapy in some studies (14). The late diagnosis and poor availability of serological tests were contributing factors for death of our one patient. Nonspecific presentation leading delayed diagnosis causes a great clinical challenge to clinicians and leads to the high mortality and morbidity of patients. The proper clinical assessment and availability of microbiological cultures are key role for early detection of cases of melioidosis. Best clinical judgment and focused microbiological investigations are very important for early diagnosis. Poor awareness of melioidosis among health care personnel was probably contributed to the high case fatality rate. Therefore, it is important to recognize patterns of melioidosis to prevent mortality and morbidity in Northern Sri Lanka.

Table 1: Clinical profile Melioidosis; Single centre experience from Northern Sri Lanka.

Characteristics	1	2	3	4	5	6	7
Age (years)	58	49	28	63	57	34	14
Sex	Female	Female	Female	Male	Male	Female	Male
Occupation	Housewife	Housewife	Financial Assistant	Farmer	Farmer	Housewife	Student
Risk factors	-	DM	-	DM	DM	-	-
Clinical Presentation	Pneumonia Septic arthritis	Lung abscess Liver abscess	Splenic abscess	Pneumonia Splenic abscess	Pneumonia Septic arthritis Cutaneous & Deep abscess	Splenic abscess	Lung abscess
Hb (10g/dL)	+	+	+	+	+	+	-
Leucocytosis	+	+	+	+	+	+	+
ESR	126	126	60	110	130	112	100
CRP	228	246	93	336	280	207	90
Chest X ray	Pneumonia	Pneumonia, Lung abscess	-	Pneumonia	Pneumonia	-	Lung abscess
USS Abdomen	Hepatomegaly	Hepatomegaly Liver abscess Splenomegaly	Splenic abscess	Splenic abscess	-	Splenomegaly	-
Blood Cultures	-	-	-	+	+	-	-
Melioidosis antibody	5120	10,240	10,240	N/A	N/A	640	320
Antibiotic	CZM, MER CTX	MER CTX DOX	CZM MER CTX DOX	MER CTX IMI	CZM MER CTX DOX	CZM MER CTX DOX	-
Outcome	Died	Survived	Survived	Died	Survived	Survived	Survived

Abbreviations: DM: diabetes mellitus, ESR: Erythrocyte sedimentation rate, CRP: C-reactive

protein,USS:Ultrasoundscan,CSZ:Ceftazidime,MER:Meropenem, CTX: Cotrimaxazole,DOX:Doxyclyline.

References

1. Cheng AC, Currie BI. Melioidosis: Epidemiology, Pathophysiology and Management. *Clin Microbiol Rev.* 2005; 18: 383-416. <https://www.ncbi.nlm.nih.gov/pubmed/15831829>
2. Dance, D. A. Melioidosis as an emerging global problem. *Acta Trop* 2000; 74, 115-119. <https://www.ncbi.nlm.nih.gov/pubmed/10674638>
3. Denny CR. Melioidosis in a European. *Cey J Sci* 1927; 2: 37-40. <https://www.cabdirect.org/cabdirect/abstract/19272701945>
4. Corea E, Dharshan de Silva A, Thevanesam V Melioidosis in Sri Lanka. *Trop. Med. Infect. Dis.* 2018, 3, 22 <https://www.mdpi.com/2414-6366/3/1/22>
5. Leelarasamee A.Epidemiology of melioidosis. *J. Infect. Dis. Antimicrob. Agents* 1986; 3: 84-93. <https://pdfs.semanticscholar.org/0b1f/2ecd363d68b5256a1a2d20b14034375b7b07.pdf>
6. Corea E, Thevanesam V, Perera S, Jayasinghe I, Ekanayake A, Masakorala J, Inglis T. Melioidosis in Sri Lanka: an emerging infection. *Sri Lankan J Infect Dis* 2012;1: 2-8. <https://sljid.sljol.info/articles/10.4038/sljid.v2i1.3801/>
7. Caldera, A.S.; Kumanan, T.; Corea, E. A rare cause of septic arthritis: Melioidosis. *Trop. Doct.* 2013; 43:164-6. <https://www.ncbi.nlm.nih.gov/pubmed/24067292>
8. Pirasath S, Selvaratnam G, Kumanan T, Pradeepan J, Mubarak FN. Melioidosis: Emerging infection in northern Sri Lanka. *Int. J. Med. Microbiol. Trop. Dis.* 2016, 2, 112-4. <http://repo.jfn.ac.lk/med/bitstream/701/1467/1/Dr.Ku.pdf>
9. Vidyalakshmi K, Shrikala B, Bharathi B, Suchitra U. Melioidosis: An under-diagnosed entity in western coastal India: A clinico-microbiological analysis. *Ind J Med Microbiol.* 2007;25: 245-8. <https://www.ncbi.nlm.nih.gov/pubmed/17901643>
10. Mukhopadhyay C, Chawla K, Krishna S, Nagalakshmi N, Rao SP, Bairy I. Emergence of *Burkholderia pseudomallei* and pandrug-resistant non-fermenters from southern Karnataka, India. *Trop Med Hygiene* 2008;102:S12-7. <http://www.mdpi.com/2414-6366/3/2/51/s1>
11. Mathurageethan, M.; Kahathuduwa, C.N.; Badanasinghe, N.; Corea, E.; Fernando, R. Melioidosis associated with chronic osteomyelitis and visceral organ abscesses. *Sri Lanka J. Surg.* 2014; 32:41-42. <https://sljs.sljol.info/articles/10.4038/sljs.v32i2.7358/>
12. Alexander, A.D.; Huxsoll, D.L.; Warner, A.R.; Shepler, V.; Dorsey, A. Serological diagnosis of human melioidosis with indirect haemagglutination and complement fixation tests. *Appl. Microbiol.* 1970; 20: 825-33. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC377056/>
13. Sookpranee M, Boonma P, Sudaengrat W, Bhuripanyo K, Punyagupta S. Multicenter prospective randomized trial comparing ceftazidime plus co-trimoxazole with chloramphenicol plus doxycycline and co-trimoxazole for treatment of severe melioidosis. *Antimicrobial Agents Chemo.* 1992; 36: 158-62. <https://www.ncbi.nlm.nih.gov/pubmed/1590682>
14. Cheng AC, Fisher DA, Anstey NM. [Outcomes of Patients with Melioidosis Treated with Meropenem. *Antimicrob Agents Chemother.* 2004; 48 \(5\): 1763-65. https://www.ncbi.nlm.nih.gov/pubmed/15105132](https://www.ncbi.nlm.nih.gov/pubmed/15105132)