

Case study

Epidemiological and Clinical profiles of Melioidosis in tertiary care centre in Northern Sri Lanka.

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.

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

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

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25 Sri Lanka including Jaffna, due to high foreign travelers to endemic areas (4). Diabetes
26 mellitus, chronic alcoholism, chronic obstructive airway disease, or chronic kidney
27 disease, cancer and steroid therapy are common risk factors (5). Here, we describe a
28 case series of melioidosis patients in Northern Sri Lanka and highlight the spectrum of
29 clinical manifestation. Informed consent was obtained from all patients in Jaffna district.

Comment [GP2]: Specify number of cases

30 Case Series

31 Case 1

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

Comment [GP3]: delete

42 Case 2

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

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

Comment [GP5]: correct

56 *Case 3*

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

64 *Case 4*

65 63 years old diabetic man presented with fever with constitutional symptoms, abdominal
66 pain, watery diarrhea and productive cough for two weeks duration. On examination, he
67 was pale, tachycardia. He had bilateral lower zone crepitations and moderate soft tender
68 hepatomegaly. His chest x ray showed bilateral patch shadow. His ultrasound abdomen
69 showed septated abscess in spleen. *Burkholderia pseudomallei* was isolated from blood
70 culture. Even on treatment with meropenem and clarithromycin, he developed septic shock,

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71 acute respiratory distress syndrome. However, the patient developed refractory sepsis,
72 required a ventilator and subsequently succumbed to sepsis with multiorgan dysfunction.

73 **Case 5**

74 57 years old poorly controlled diabetic man presented with fever with constitutional
75 symptoms, multiple skin abscess of left lower limb and back of chest and active
76 inflammation of left side knee joint. On examination, he was pale, tachycardia. He had
77 bilateral lower zone crepitations and septic arthritis of left side knee joint. The joint fluid
78 analysis revealed polymorpholeucocytosis predominant neutrophils with elevated
79 protein level and *Burkholderia pseudomallei* was isolated from blood culture. His chest x
80 ray showed bilateral patch shadow. His ultrasound of lower limbs showed deep seated
81 abscess in left side thigh and calf region. He underwent drainage of deep abscess and
82 knee joint aspiration. He developed septic shock and acute respiratory distress syndrome
83 and required a ventilator. Subsequently improved with meropenem and cotrimoxazole for
84 six weeks and was discharged with course of oral antibiotics. At 6 months of follow-
85 up, he had no signs of recurrence.

86 **Case 6**

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

Comment [GP9]: correcto to X-ray

Comment [GP10]: correct

94 **Case 7**

95 14years old healthy boy presented with fever with chills, rigors and productive cough for
96 2weeks duration.On examination,he was tachypnoea and tachycardia. He had lower
97 zone coarse crepitationsof rightside lung.His chest x ray showed lung abscess with fluid
98 level of right lung.His sputum culture ,sputum FB were negative.His serum melioidosis
99 antibody titre was 320.He was treated with intravenous meropenem and oral
100 cotrimaxazole for 6weeks duration and lung abscess had been completely regressed.

Comment [GP11]: separate in two words

Comment [GP12]: correct to X-ray

102 **Discussion**

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

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

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

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

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

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136 Meropenem is the drug of choice in systemic melioidosis (13). Co-
137 trimoxazole ,ceftazidime, imipenem or coamoxiclav are alternatives for systemic
138 melioidosis(14)The oral cotrimoxazole or doxycycline is used to prevent relapse (13) in
139 follow up. Intravenous meropenem and oral Co-trimoxazole or doxycycline were

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140 intensive therapy for six weeks and oral Co-trimoxazole or doxycycline was
141 maintenance therapy for most of our patients. Five patients improved with antibiotics
142 therapy.

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144 Late diagnosis has led to fatality in some cases even proper therapy in some studies
145 (14). The late diagnosis and poor availability of serological tests were contributing
146 factors for death of our one patient. Nonspecific presentation leading delayed diagnosis
147 causes a great clinical challenge to clinicians and leads to the high mortality and
148 morbidity of patients.

149 **Conclusion**

150 The proper clinical assessment and availability of microbiological cultures are key role
151 for early detection of cases of melioidosis. Best clinical judgment and focused
152 microbiological investigations are very important for early diagnosis. Poor awareness of
153 melioidosis among health care personnel was probably contributed to the high case
154 fatality rate. Therefore, it is important to recognize patterns of melioidosis to prevent
155 mortality and morbidity in Northern Sri Lanka.

156 **Ethics approval and consent to participate**

157 The informed written consent was obtained from the participants for publication of
158 journal.

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160 **Competing interests**

161 The authors declare that they have no competing interests.

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

Characteristics	Case						
	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	Pneumonia	Lung abscess	Splenic abscess	Pneumonia	Pneumonia	Splenic abscess	Lung abscess
Presentation	Septic arthritis	Liver abscess		Splenic abscess	Septic arthritis Cutaneous & Deep 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
Antibiotics sensitivity	CZM, MER	MER CTX	CZM MER	MER CTX	CZM MER	CZM MER	

	CTX	DOX	CTX	IMI	CTX	CTX	
			DOX		DOX	DOX	
Outcome	Died	Survived	Survived	Died	Survived	Survived	Survived

234 **Abbreviations:**DM;diabetesmellitus,ESR:Erthrocyte sedimentation rate,CRP:C reactive

235 protein,USS:Ultrasoundscan,CSZ:Ceftazidime,MER:Meropenem,CTX:

236 Cotrimaxazole,DOX:Doxycyline.

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