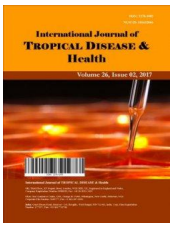

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Case Review of Melioidosis in a Tertiary Care Centre from Northern Sri Lanka

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Authors' contributions

This work was carried out in collaboration between all authors. Authors SP and JP designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors SP and TK managed the literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Melioidosis is sporadically reported from various parts of Sri Lanka. It is a major recent endemic in Northern Sri Lanka. The causative organism *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 an array of clinical presentation involving multiple abscesses in the skin, liver, spleen, mediastinum and septic arthritis. It presented as either an acute fulminant septicemia with a high mortality or a chronic localized infection. Most cases had predisposing risk factors such as diabetes, chronic kidney disease and occupational risk.

Keywords: Melioidosis; Burkholderia pseudomallei; septic arthritis; pneumonia; abscess; diabetes; Northern; Sri Lanka.

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ABBREVIATIONS

DM: Diabetes Mellitus, ESR: Erthrocyte Sedimentation Rate, CRP: C Reactive Protein, USS: Ultrasoundscan, CSZ: Ceftazidime, MER: Meropenem, CTX: Cotrimaxazole, DOX: Doxycyline.

1. INTRODUCTION

Melioidosis is an 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 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, several cases of melioidosis have been reported in Sri Lanka, probably due to an increase in international travel 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 seven cases of melioidosis patients from a single center of Northern Sri Lanka highlighting the spectrum of clinical manifestation. Informed consent was obtained from all patients in Jaffna district.

2. CASE SERIES

2.1 Case 1

A 58 years old diabetic woman presented with fever, constitutional symptoms, severe bilateral knee joint pain and swelling. On examination, she had moderate soft tender hepatomegaly and bilateral fine basal crepitations. Knee joints were inflamed bilaterally with 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 detoriated and she died due to septic shock with multi-organ dysfunction during 3rd week in course of therapy.

2.2 Case 2

A 49 year old diabetic woman presented with fever and productive cough with whitish coloured sputum for one week duration. She was involved actively in cultivation. On examination, she had right 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 lymphadeonopathy and two focal lesions measuring 2.2 & 1.5 cm and 2.4 & 1.5 cm in segment 5 and 6 of liver suggestive of lung and hepatic abscess. Even though, 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 a course of oral antibiotic. At 6 months of follow-up she had no signs of recurrence.

2.3 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 was unremarkable. The contrast enhanced computerized tomography of abdomen revealed septated abscess measuring size of 3.6 cm & 4.8 cm 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, she had gained weight and the splenomegaly had completely regressed.

2.4 Case 4

A 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 and tachycardic. He had bilateral lower zone crepitations and moderate soft tender hepatomegaly. His chest X ray showed bilateral patchy shadow. The ultrasound of abdomen showed septated abscess in the spleen. *Burkholderia pseudomallei* was isolated from blood culture. While on treatment with meropenem and clarithromycin, he developed septic shock and acute respiratory distress syndrome. Later he developed refractory sepsis, required a ventilatory support and subsequently succumbed to sepsis with multiorgan dysfunction.

Table 1. The epidemiological, clinical, investigation and treatment profile of patients with melioidosis in a tertiary care centre, Northern Sri Lanka

Characteristics	Case						
	1	**2**	**3**	**4**	**5**	**6**	**7**
Year	2015	2016	2016	2016	2016	2017	2017
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	-	_	-	+	+	_	-
Meliodosis antibody	5120	10,240	10,240	N/A	N/A	640	320
Antibiotics sensitivity	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

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

2.6 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 was 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 6weeks duration. At 6 months of follow-up, she had gained weight and the splenomegaly had completely regressed.

2.7 Case 7

14 years old healthy boy presented with fever with chills, rigors and productive cough for two weeks duration. On examination, he had tachypnoea and tachycardia. Lower zone coarse crepitations noted on right side of the lung. His chest X ray showed lung abscess with a fluid level of right lung. Sputum culture, sputum for AFB was 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.

3. DISCUSSION

Burkhloderia pseudomallei is an important emerging pathogen in Sri Lanka. It may be acute or chronic pyogenic infection capable of causing various clinical manifestations like pneumoniae, septicaemia, arthritis, abscess etc. and is associated with high morbidity and mortality [2]. It is usually geographically restricted to tropical and subtropical areas of Australia and Southeast Asian countries [6]. Isolated cases have also been reported from eastern and northeastern parts of Sri Lanka. 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% 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 pneumonia, 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 pseudo mallei* in culture from blood or serous fluids [6]. However, prior antibiotics therapy leads to negative blood culture in our patient. The serological test is useful for diagnosis of meliodosis in culture negative cases [12]. The serological test was positive among most of the cases and culture from blood or joint fluid was positive in certain cases in our study.

The current convention is to view the treatment of melioidosis as comprising two phases: The acute phase is aimed to stop patients from dying of overwhelming sepsis. The eradication phase is aimed to kill any residual bacteria and to minimize the risk of the infection relapsing. There have been several attempts to formulate clinical guidelines for melioidosis [13,14]. The key recommendations were use of ceftazidime or a carbapenem antibiotic for initial treatment of acute infection over 2-4 weeks and a combination of co-trimoxazole and doxycycline for eradication over a 12-20 week period [13,14]. More recently, those recommendations were updated by an Australian group noted for clinical trials on melioidosis therapy [15]. International consensus recommendations for the treatment and prophylaxis of melioidosis were developed by an expert group that met in Australia in 2010 [16].

Meropenem is the drug of choice in complicated melioidiosis and ceftazidime is drug of choice in uncomplicated melioidosis [16]. Co-trimoxazole, imipenem or coamoxiclav are alternatives for systemic melioidosis in acute phase [17]. The oral cotrimoxazole or coamoxiclav is recommended therapy for eradication phase [16]. Doxycycline is also used as alternative to prevent relapse [18] in follow up. Intravenous meropenem and oral co-trimoxazole or doxycycline were intensive therapy for six weeks and oral co-trimoxazole or doxycycline was maintaence therapy for most of our patients. Five patients improved with antibiotics therapy.

Late diagnosis has led to fatality in some studies, even proper therapy has been initiated [18]. One case was probably missed due to lack of clinical awareness and correct microbiological diagnosis. A high index of suspicion is needed for diagnosis due to its varied clinical presentations. Nonspecific presentation and delayed diagnosis cause a great clinical challenge to clinicians and lead to the high mortality and morbidity of patients. At the same time, the case series highlight the need for improved microbiology services in patient care management. We were able to successfully treat the case by institution of correct antimicrobials based on microbiology feedback.

4. CONCLUSION

The proper clinical assessment and availability of microbiological cultures play 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 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.

CONSENT

The informed written consent was obtained from the participants for publication of the case reports to the journal.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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