Melioidosis: Emerging infection in Northern Sri Lanka

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Abstract
Melioidosis is an emerging infection, causing severe septic haemorrhagic illness from chronic infection, with a high mortality and morbidity. 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. Here we report two cases of melioidosis causing septic arthritis and pneumonia in old aged diabetic woman and multiple hepatic and lung abscesses in middle aged diabetic woman in Jaffna district.

Keywords: Melioidosis, Septic arthritis, Pneumonia, Abscess

Introduction
Melioidosis is a bacterial infection caused by Burkholderia pseudomallei, a Gram-negative, oxidase positive bacillus.1 The clinical presentation varies from an acute, fulminant septicemia with a high mortality to a chronic, localized infection.2 The isolation of B. pseudomallei in culture from clinical specimens is gold standard method for definitive diagnosis. However, the best clinical judgment and focused microbiological investigations are key factors for early diagnosis. Here we report two cases of melioidosis causing septic arthritis and pneumonia in old aged diabetic woman and multiple hepatic and lung abscesses in middle aged diabetic woman in Jaffna district.

Case Reports
Case 1: A 58 year old diabetic woman presented with a history of fever with constitutional symptoms for five days. She had productive cough with whitish coloured sputum for one month duration. She had a past history of hypertension and sarcoidosis. She was on regular clinic follow up and her diseases were controlled with her medication. On examination, she had eschar over left side cheek and moderate soft tender hepatomegaly. The lung examination revealed vesicular breathing with evidence of bilateral fine basal crepitations. Her pulse rate was 84 beats per minute, regular and blood pressure was 130/80 mmHg. Remaining examination was unremarkable. Her full blood count showed mild leucocytosis with predominant neutrophils, normochromic normocytic anaemia and thrombocytopenia. Her renal and liver profile showed elevated serum creatinine and hypoalbuminemia.

Initially, clinical diagnosis was made as typhus and was treated with course of doxycycline. Then she developed severe bilateral knee joint pain and swelling more on right side than left side during hospital stay. Bilateral knee joint with active inflammation was noted on examination involving right side more than left side. Her erythrocyte sedimentation rate (126 mmHg/1st hour) and C reactive protein (228) were elevated indicating an acute inflammatory process. The septic arthritis was suspected initially and orthopaedic opinion was sought to rule out septic arthritis. Empirically intravenous ceftriaxone and fluoxacillin therapy were initiated. The joint fluid analysis revealed polymorphleucocytosis and lymphocytosis with elevated protein level. The direct smear showed Gram (-) ve, oxidase (+) bacilli and Burkholderia pseudomallei was isolated from joint fluid culture. Melioidosis antibody titre was 5120. Definitive diagnosis was made as Melioidosis and was managed with intravenous ceftazidime 2g thrice daily and Cotrimaxazole 1920mg twice daily for two weeks. Her condition was deteriorated even with treatment and she developed pancytopenia during course of therapy and filgristin was commenced. However she died during 3rd week course of antibiotic treatment.

Case 2: A 49 year old diabetic woman presented with a history of fever and productive cough with whitish coloured sputum for one week duration. She also had right upper abdominal pain with watery diarrhoea for three days duration. She has involved actively in own cultivation. On examination, she had right side middle and lower zone crepitations and moderate soft tender hepatosplenomegaly. Her pulse rate was 100 beats per minute, regular and blood pressure was 120/80 mmHg. Remaining examination was unremarkable. Her full blood count showed mild leucocytosis with predominant neutrophils, normochromic normocytic anaemia and mild thrombocytopenia. Her initial blood
biochemical tests showed normal liver and renal functions except hypoalbuminemia with elevated inflammatory markers. Her ultrasound abdomen showed mild hepatomegaly and moderate splenomegaly. The chest X ray showed consolidation over middle zone of right lung.

Initially, clinical diagnosis was severe community acquired atypical pneumonia and was treated with course of intravenous meropenem and oral doxycycline for fourteen days duration. Her clinical condition was improved with therapy; evidenced by clinically, biochemically and radiologically and was discharged with oral antibiotics. One week later, she again admitted with fever with constitutional symptoms. On examination, she had moderate soft tender hepatosplenomegaly. Her full blood count showed normal white cell count and platelet with, normochromic normocytic anemia. Her initial blood biochemical tests showed normal liver and renal functions except hypoalbuminemia. Her erythrocyte sedimentation rate (126 mmHg/1st hour) and C reactive protein (246) were elevated indicating an acute inflammatory process. Her ultrasound abdomen showed focal liver lesion suggestive of abscess/metastasis. The chest X ray showed prominent paraaortic shadow with right side hilar lymphadenopathy. The 2D echocardiography showed no evidence of infective endocarditis. The mantoux test was normal. The sputum acid fast bacilli was negative. 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. The ultrasound guided fine needle aspiration of liver abscess was unsuccessful. The ELISA test of hepatic ameobiasis was negative. The liver abscess was suspected initially and was treated with oral metronidazole. However her clinical condition was not improved significantly. Based on clinical scenario combined with multiple liver and lung abscess unresponsive to conventional therapy, clinical diagnosis of melioidosis was made and empirical intravenous meropenem and oral doxycycline were initiated. Even, the repeated blood cultures were negative, her serum melioidosis antibody titre was 10240. Definitive diagnosis was made as melioidosis and was managed with same antibiotics for six weeks. Her condition was markedly improved with treatment and she discharged with course of oral antibiotic treatment for three month duration.

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 and a wide variety of animals.\(^2\) Melioidosis is 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.\(^4\)

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\(^5\). Eventhough Sri Lanka has been considered non endemic for melioidosis, there is increasing evidence for its emergence in the recent past.

Diabetes mellitus, alcohol use, chronic lung disease, chronic renal disease, malignancy, immunosuppression and thalassemia are the recognized risk factor.\(^6\) The diabetes was found a correlation of 76% of with Melioidosis.\(^6\) Diabetes mellitus was underlying risk factor for our two cases.

The clinical manifestations range from a severe septicaemic illness to chronic progressive infection associated with high morbidity and mortality.\(^7\) It causes various clinical like pneumoniae, septicaemia, arthritis, abscess. The systemic manifestation with pulmonary involvement is the commonest manifestation. Bone involvement has been reported in 16% cases.\(^7\) The septic arthritis followed by pulmonary involvement was observed in first case. The multiple foci of hepatic and lung abscesses was found in second case.

Isolation of the causative bacterium, Burkholderia pseudomallei, in culture is gold standard for the diagnosis. Isolation of Benzmbleria pseudomallei from joint aspirate culture and melioidosis antibody titre of 5120 were favoured the diagnosis of melioidosis in first case. However, blood culture was negative in second case inspite of high melioidosis antibody titre of 10240. These may be due to initiation of antibiotics prior to blood culture. Ceftazidime is the drug of choice in systemic melioidosis.\(^8\) Meropenem, Impenem or Augmentin are alternatives. However, the combination of Ceftazidime and Co-trimoxazole with or without doxycycline was the recommended treatment with successful outcome in systemic melioidosis.\(^8\) First case was managed with combination of Ceftazidime and Co-trimoxazole.

After six weeks of intravenous antibiotics, the patient should be continued usually on oral cotrimoxazole or doxycycline as maintenance therapy to prevent relapse.\(^8\) However she continued to deteriorate despite antibiotic therapy and supportive care. She deteriorated rapidly despite optimal medical management and supportive care and finally succumbed to the illness one week after the definitive diagnosis. Second case was managed with combination of intravenous meropenem and oral doxycycline for six
weeks. She was continued oral antibiotics as maintenance therapy to prevent relapse for three months. She improved clinically with the course of antibiotics therapy.

Studies have documented fatalities even after institution of therapy or due to late diagnosis. Delay in diagnosis due to the nonspecific nature of its presentation causes a major challenge to physicians. Delay in diagnosis has been a factor contributing to the high mortality.

Best clinical judgment and focused microbiological investigations are very important for early diagnosis. Therefore, it is important to identify different patterns of presentations of melioidosis; emerging infection in Northern Sri Lanka.

References