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Challenges in Managing Melioidosis with Fulminant Sepsis: A Case Report

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Abstract **Case Report**

Managing melioidosis with fulminant sepsis is difficult and challenging. We describe the case of a 30-year-old man with clinical presentation of non-specific septicemic shock with multi organ impairment and severe respiratory distress. The causative organism, Burkholderia pseudomallei was only identified on day 4 of ICU admission. Imaging investigation revealed multiple lung and splenic abscesses. This led to delay in the diagnosis and initiating specific antimicrobial therapy which arise from difficulties in clinical recognition and laboratory diagnosis. Our patient was managed in the ICU for 23 days with intensive antimicrobial therapy. As for now, we should increase the awareness of melioidosis in treating our patients and realize its burden to our community and hoping that a better diagnostic test will arise and helps us in achieving early confirmatory diagnosis and guide for better therapeutic efficacy and survival of the patients.

Keywords: Melioidosis, Burkholderia pseudomallei, fulminant sepsis, microbiological diagnosis.

INTRODUCTION

Having a nicknamed “the great mimicker” [1], melioidosis is a challenging infectious disease caused by the environmental Gram-negative bacterium *Burkholderia pseudomallei*. With the current fatality rate of 10-50% [1], it is estimated that 5-28% [1] of the survival will experience recurrent of infection due to recrudescence (recurrent) of the original strain that was not completely cleared and remain in a dormant state, or reinfection with a different strain following a recent exposure of bacterium *Burkholderia pseudomallei* [1].

Melioidosis is an interesting infection in terms of its pathogenesis, and the outcome of its host-pathogen interaction can range from asymptomatic seroconversion to rapidly fatal septicemic shock and mortality. However, delays in the treatment of acute melioidosis are significantly common due to difficulties in clinical recognition and delayed in laboratory diagnosis which often leads to poor outcome. This is further aggravated by under-diagnosis and under-reporting especially in developing countries. With an early detection and proper antimicrobial therapy consisting of an initial intensive and the subsequent eradication phase, the outcome of acute melioidosis can significantly be improved.

CASE REPORT

We report the case of a 30-year-old gentleman with no known medical problem who work at school canteen. He presented to our district hospital with two days history of rapid breathing associated with persistent high-grade fever and cough with blood-stained sputum. He had history of fishing one day prior to developing these symptoms. On examination, he was in severe respiratory distress with evidence of poor oxygenation, and auscultation of the lungs revealed bibasal crepitations up to midzone. ABG showed PaO2 of 30.8 mmHg, PaCO2 of 42.1mmHg with pH of 7.4 and lactate level of 4.3 mmol/L. He was immediately intubated and referred to our intensive care for further resuscitation and management with the differential diagnosis of septicemic shock secondary to severe pneumonia with moderate adult respiratory distress syndrome (ARDS). He was also investigated for leptospirosis and severe acute respiratory infection (SARI) for Covid-19.

In ICU, he was managed with a high ventilator setting and broad-spectrum antibiotic of ceftazidime 2 gm tds. After 72 hours of ICU stay, the broad-spectrum antibiotic was escalated to meropenem 1g tds in view of worsening organ's function. Investigation taken during his admission to ICU was negative for leptospirosis and Covid-19 infection. Despite above management, the patient was persistently febrile with worsening septic parameters and was unable to wean down the ventilator settings. Imaging investigation revealed severe pneumonia with multiple lung abscesses (CT scan of thorax) and multiple collection of micro abscesses in the spleen (ultrasound of abdomen). Blood culture taken prior to admission to ICU revealed *Burkholderia pseudomallei* on Day 4 of his ICU admission. The antibiotic was further escalated with addition of intravenous Bactrim 160 mg bd and intravenous fluconazole 400 mg daily. Intravenous meropenem was continue for 4 weeks. The septic parameters were gradually improved, and the patient was able to wean off from mechanical ventilation after 23 days of ICU admission.

DISCUSSION

Our case report demonstrated a similar and consistent clinical pattern and presentation of acute melioidosis as described in previous case reports from South and Southeast Asia. More importantly our case report had a similar clinical pattern of acute melioidosis as described in a recent review of case reports in Malaysia from 1975 to 2015 [3]. However, despite with the advancement of medical technology, we are still facing with the same problems in managing acute melioidosis which are severe bacteremia acute melioidosis with an early onset of fulminant septic shock within 24-48 hours of admission and delayed in finding a confirmatory diagnosis of acute melioidosis warranting a prompt empirical broad spectrum antibiotics in suspicious cases, delaying the use of narrow spectrum antibiotics that targeting for organism *Burkholderia pseudomallei*.

Burkholderia pseudomallei is an opportunistic pathogen, with the characteristic of facultative intracellular and motile saprophyte (an organism that obtains energy from decaying organic matter) that possesses a remarkable intrinsic array of virulence factors and broad antimicrobial drug resistance[2]. Estimated global burden [4] of melioidosis in human is around 165,000 cases per year worldwide, of which 89,000 (54%) are estimated to be fatal acute melioidosis. The predicted mortality from melioidosis is equivalent to that of measles (95,000 individuals per year) and higher than that for leptospirosis (50,000 individuals per year) and dengue infection (12,500 individuals per year) [4]. Diabetes mellitus remain a significant risk factor for melioidosis. Other known risk factors for melioidosis include exposure to soil or water, male sex, age of >45 years, excess alcohol consumption and liver disease, chronic renal disease, chronic lung disease, and thalassemia (which probably related to neutrophil dysfunction due to iron overload), prolonged steroid use and immunosuppression [5]. However, greater than 80% of pediatric patients, and almost 20% of adult patients have no recognized risk factors. Melioidosis in adults with no risk factors are commonly occurs in patients who have been exposed to a high bacterial load [6].

Our case report demonstrated few challenges in managing acute melioidosis. Presented with life-threatening fulminant sepsis with multiple organs failure, our patient was initially treated for septic shock secondary to severe pneumonia with moderate ARDS with the possible cause of leptospirosis. The diagnosis of acute melioidosis was made only after 4 days of ICU care with the growth of *Burkholderia pseudomallei* in blood culture taken on the first day of ICU admission. Clinical presentation, severity, and outcome of acute melioidosis are significantly affected by the presence or absence of risk factors, the route of infection and the bacterial load and strains, and importantly, the presence or absence of specific non-ubiquitous *Burkholderia pseudomallei* virulence genes [7]. However, making a diagnosis on clinical ground alone is difficult and required local epidemiological data and clinical experience. At the end, laboratory tests, specifically microbiological diagnosis are still required to confirm the clinical diagnosis of melioidosis.

Culture of body fluids remains the mainstay of microbiological diagnosis for melioidosis and blood culture are the most important culture as bacteremia is common in acute melioidosis. Other body fluid samples that should be cultured include pus from abscesses and sputum in patients who presented with melioidosis associated pneumonia. However, as with our case report, *Burkholderia pseudomallei* growth much more slowly (up to 4 days) than many other organisms in the most routine laboratory media and with a low sensitivity (60%) [8], repeating cultures should be seriously considered in patients with strong indications or differential diagnosis of melioidosis. Logically, direct detection of *Burkholderia pseudomallei* in clinical sample could provide a quick confirmation of the diagnosis of melioidosis, however, examination through light microscopy had a significant lacks of sensitivity and specificity [9] and time consuming, especially when involving a very critically ill patient. Even the PCR assays are not routinely used for clinical used due to its sensitivity issues [10], and more importantly are not cost-effective in providing the timely confirmation of diagnosis for accurate therapeutic decisions in critically ill patients. Serological diagnosis of melioidosis is also difficult due to the poorly characterized antigens and more importantly had never been internationally standardized [11]. Moreover, with the high background seropositivity

rates in the healthy population in some endemic area, this investigation may lead to a misdiagnosis of melioidosis in every patient.

To our knowledge, survival of the patients with fulminant septic melioidosis depend on the early diagnosis and early starting of antimicrobial therapy which are specific *to Burkholderia pseudomallei*. Based on a 2010 expert workshop [12], antimicrobial therapy for melioidosis consisted of the initial intensive phase and followed by subsequent eradication phase. Intravenous ceftazidime or meropenem remains as the preferred choice of antimicrobial in the initial intensive phase [2], with a minimum duration of 10-14 days. However, longer phase for intensive therapy is required for critically ill patients including those with deep-seated collections or organ abscess as in our patient. Subsequent eradication phase with oral antibiotics is recommended to prevent recrudescence or recurrent of the melioidosis or relapse of the patient. The eradication phase should last for more than 3 months after the end of the initial intensive therapy. Trimethoprim-sulfamethoxazole is the preferred antimicrobial agent for eradication therapy, with co-amoxiclav or doxycycline remain as the second choice of antimicrobial agent [2].

Clinical management of acute melioidosis still remains a significant challenge with a high fatality rate. This is due to delay in the diagnosis and initiating specific antimicrobial therapy which arise from difficulties in clinical recognition and laboratory diagnosis. As for now, we should increase the awareness of melioidosis among our patients and realize its burden to our community and hoping that a better diagnostic test will arise and helps us in achieving early confirmation of diagnosis and finally will enable for better therapeutic efficacy and survival of the patients.

CONCLUSIONS

Managing melioidosis with fulminant sepsis is difficult and challenging. This is because to make a diagnosis on clinical ground alone is difficult and require local epidemiological data and clinical experience. However, delay in the diagnosis and initiating specific antimicrobial therapy which arise from difficulties in clinical recognition and laboratory diagnosis will lead to a serious fatality. As for now, we should increase the awareness of melioidosis among our patients and realize its burden to our community and hoping that a better diagnostic test will arise and helps us in achieving early confirmation of diagnosis.

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Compliance with ethics guidelines

Mohd Nazri Ali, Abdul Karim Othman declare that they have no conflict of interest. Patient anonymity was preserved. Funding: No funding sources. Ethical approval: Not required. Malaysia National Medical Research Register ID: NMRR-21-994-60054

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