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CASE REPORT **INTENSIVE CARE**

Fulminant septic shock from melioidosis and leptospirosis co-infections

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Abstract

Melioidosis and leptospirosis are common tropical infectious diseases, but confirmed co-infection by both is rare. We describe a fulminant case of *Burkholderia pseudomallei* and l*eptospira* co-infection in a 29-year-old Malay lady with underlying uncontrolled type 2 diabetes mellitus, who had no obvious exposure to either organism. Despite close monitoring and aggressive treatment in the Intensive Care Unit (ICU), this patient eventually succumbed to death from the disease progression. As co-infections of melioidosis and leptospirosis can lead to a high mortality, suspicion of the diagnosis must always be raised especially in diabetic patients from endemic area, who present with sepsis of unknown origin, to allow for prompt initiation of appropriate treatment.

Key words: Leptospirosis; Melioidosis; Co-infection; Sepsis; Septic shock

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1. Introduction

Melioidosis is caused by facultative intracellular gram-negative bacillus, *Burkholderia pseudomallei.* It is a common infection in Malaysia since 1913, and is recognized with high incidence in the northern Malaysia.[1] Leptospirosis is a zoonotic disease that is caused by highly motile, spiral-shaped aerobic spirochetes that belong to the genus leptospira. Both organisms can infect via percutaneous inoculation, inhalation, and ingestion from the contaminated environment. A misdiagnosis or a delayed diagnosis may happen as both diseases portray a wide spectrum of clinical features. Most common clinical manifestations of melioidosis are pneumonia and localized skin infection, but the presentations can be diversified due to hematogenous spread of the organisms. Over half of the patients have bacteremia and up to a quarter to have sepsis on presentation.[2] On the other hand, a clinically apparent leptospirosis can present with non-specific febrile illness that is associated with myalgia, headache, and conjunctival suffusion.[3] However, the course of leptospirosis can be complicated with acute kidney injury and acute respiratory distress syndrome. Melioidosis and leptospirosis can cause mortality up to

50% respectively and the co-infection by both may cause higher mortality.[4]

In this report, we aim to share our rare experience in managing a case of confirmed co-infections with melioidosis and leptospirosis in the intensive care unit (ICU), so that the readers may be able to diagnose and start prompt management of this lethal condition.

2. Case report

A 29-year-old Malay lady with underlying uncontrolled type 2 diabetes mellitus, hypertension, and history of craniopharyngioma, post-debulking surgery complicated with panhypopituitarism, presented to our Emergency Department during rainy season with intermittent fever and colicky central abdominal pain for three days prior to admission. On the day of admission, she developed jaundice and passed tea-colored urine. Of note, there was no history of recreational activities, rat infestation, or participation in agricultural work.

On examination, she was conscious but appeared lethargic and dehydrated. She was febrile with temperature of 38.6°C. The hemodynamic and oxygenation status was initially unremarkable. Palpation of her abdomen revealed tenderness over the right hypochondriac region and presence of hepatomegaly. Significant findings from her baseline blood investigations were elevated inflammatory markers, including the total white blood cells count (with predominant neutrophilia), erythrocyte sedimentation rate and C-reactive protein. Her baseline hepatic profile showed elevated aspartate aminotransferase, while her baseline renal profile was normal. Bedside abdominal ultrasonography only showed the presence of hepatomegaly with features of fatty liver, with no evidence of neither biliary dilatation nor obstruction.

In the ward, the patient was treated for possible intraabdominal sepsis with cefoperazone and metronidazole IV. On day 5 of admission, her temperature spiked to 39.2°C and she developed type 1 respiratory failure with metabolic acidosis. She was subsequently referred to the ICU team for respiratory support. In the ICU, she was initially put on a trial of non-invasive ventilation and required vasopressor support with noradrenaline infusion @ 0.01 µg/kg/h. The antibiotic was escalated to meropenem 1 gm IV 8 hourly. However, the patient's condition continued to deteriorate; she was intubated on the second day in the ICU because of reducing conscious level and worsening hypoxemia with metabolic acidosis.

A list of investigations was ordered in the ICU to ascertain the exact diagnosis, but these were initially remarkable. However, on day 10 of ICU admission, her leptospirosis microscopic agglutination test and melioidosis serology were both reported positive with the latter showing IgM > 1:80. Hence, the primary diagnosis was revised to septic shock secondary to melioidosis and leptospirosis co-infections. Subsequently, the patient developed acute kidney injury requiring regular hemodialysis, and this was further complicated with poor neurological recovery and prolonged ventilation requiring tracheostomy. Despite intensive monitoring and aggressive intervention, the patient succumbed to death from septic shock complicated with multi-organ failure on day 49 of ICU admission.

3. Discussion

Both melioidosis and leptospirosis are endemic in Kelantan, which is in northern Malaysia.[1,5] From review of the literature, this is the fourth report of leptospirosis and melioidosis co-infections.[6–8] Our case is however, distinctive as the initial non-specific clinical presentation of the patient failed to raise the suspicion of the possibility of neither melioidosis nor leptospirosis. This led to a delayed administration of appropriate antibiotic treatment. In this case, intravenous meropenem 1 gm was only started after 7 days from the onset of fever. It is possible that much delayed diagnosis and initiation of antibiotic treatment may have caused bacteremia and subsequently septic shock which worsened the prognosis.

The case fatality for confirmed leptospirosis co-infected with melioidosis was reported as high as 70%.[4] The clinical symptoms suggestive of leptospirosis such as myalgia, headache, conjunctival suffusion, nausea and vomiting were not present in this case. In addition, the severe form of leptospirosis, which is complicated with severe pulmonary hemorrhagic syndrome was not seen.[3] Furthermore, none of the common manifestations of melioidosis were seen is this patient such as pneumonia, multiple abscesses, septic arthritis, and encephalomyelitis.[9] The suspicion was only raised when the patient's condition was declining despite initiation of a broad-spectrum antibiotic treatment. Moreover, the absence of typical risk factors associated with melioidosis acquisition other than diabetes mellitus possibly added to the failure to suspect the disease.

We hypothesized that the co-infections in this case could be due to environmental factors. The mode of transmission of melioidosis was most likely due to inhalation rather than cutaneous transmission as the patient had no significant cutaneous contact with fresh water and soil exposures and did not display any skin lesions. This can especially occur during rainy season, in which the strong wind with heavy rainfall could have contaminated the soil and the infected aerosolized dust may spread, predisposing the patient to acquire melioidosis through inhalation.

To sum up, the lesson that we learnt is that the suspicion of melioidosis as a diagnosis must always be raised in patients with underlying diabetes mellitus who present with fever, as the mortality can be immensely high, up to 65%.[10] At the same time, the diagnosis of leptospirosis must be ruled in as co-infections are possible although rare which could further raise the already heightened mortality risk with mono-infection. Thus, treating clinicians should maintain a high index of suspicion of melioidosis and leptospirosis co-infections in high-risk patients such as those with diabetes mellitus from endemic area, who present with sepsis of unknown origin. This is important to expedite the administration of appropriate antibiotic treatment and hence, to reduce the likelihood of progression to severe disease and prevent mortality.

4. Conflict of interest

None declared by the authors.

5. Patient's consent

Written consent was obtained from the patient to publish this case report.

6. Authors' contribution

LKY: Conducted the case, literature review, manuscript writing
WFMWS: Supervision of the case, review of the manuscript, manuscript editing
MZM, MRH, HZA: Supervision of the case, review of the manuscript

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