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Melioidosis, a Rare Cause of Infective Endocarditis: A Case Report

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Abstract

Burkholderia pseudomallei is an unusual causative organism of infective endocarditis. We present a case of Melioidosis mitral valve endocarditis with dissemination to the liver and kidney in a young woman with underlying SLE with lupus nephritis. Despite the delay in reaching a diagnosis, the patient was successfully treated with intravenous Ceftazidime and oral trimethoprim-sulfamethoxazole and was discharged well. The identification of the specific aetiologic organism is important for timely diagnosis as well as treatment of infective endocarditis.

Subject Areas

Melioidosis Infective Endocarditis

Keywords

Melioidosis, Infective Endocarditis, *Burkholderia pseudomallei*

1. Introduction

Melioidosis is an infection caused by intracellular gram-negative bacterium *Burkholderia pseudomallei*. It is an environmental saprophyte found in soils and fresh surface water in endemic regions, particularly in South-East Asia and Northern Australia [1]. Melioidosis causes a wide range of clinical manifestations, including pneumonia, septicemia and visceral abscesses with majority of patients having an underlying predisposing condition [2]. However, cardiac involvement is very rare. A diagnosis of Melioidosis requires a high level of clinical suspicion. Identification of specific causative organism in infective endocarditis is essential to ensure timely diagnosis and appropriate treatment. We report a rare case of infective endocarditis due to gentamicin-resistant strain of *B. pseu-*

domallei in a tertiary hospital in Malaysia that had been successfully treated.

2. Case Report

A 26-year-old woman from Pahang Malaysia, with a known case of systemic lupus erythematosus (SLE) with lupus nephritis, was presented with one-month history of intermittent fever, unproductive cough, significant loss of weight of 8 kg in 1 month and loss of appetite. She denied having night sweat, haemoptysis or failure symptoms. There was no feature suggestive of active SLE flare. 2 weeks prior to presentation, she had a visit to emergency outpatient clinic and had completed a 1 week course of oral amoxicillin-clavulanate to treat for community-acquired pneumonia.

On examination, she was cushingoid, febrile with a temperature of 38'C, blood pressure of 120/86 and pulse rate of 70 beats per minute. She was not tachypneic, her respiratory rate was 20 breaths per minute and her oxygen saturation was 98% when measured by pulse oximetry while breathing ambient air. She was noted to have bilateral subconjunctival haemorrhage. Her jugular venous pulse was normal and there was no pedal edema. On systemic examination, she had normal heart sounds with no murmur and her lungs were clear on auscultation. There was no evidence of vasculitic rash and no peripheral stigmata of infective endocarditis. The abdominal examination was otherwise unremarkable.

Initial blood investigations showed normochromic normocytic anaemia, with a normal platelet and total white cell count. Her inflammatory markers C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were elevated at 14.6 mg/dL and 41 mm/hr respectively. She had an acute renal injury with urea of 9.7 and creatinine of 146 umol/l and liver function test showed mildly elevated transaminases and alkaline phosphatase, bilirubin was normal. Her infective screening of Hepatitis B, Hepatitis C, HIV and rapid plasma reagin (RPR) was non reactive. Her liver autoantibody screening with Anti-mitochondrial antibody, anti-smooth muscle antibody, anti-liver-kidney microsomal antibody were all negative. Ultrasonography of the abdomen showed early liver parenchymal disease and bilateral renal parenchymal disease with no collection nor obstructive uropathy seen. A 24-hour urine protein was 0.13 g/day. Chest radiography showed right lower zone consolidation. A CT pulmonary angiogram revealed no pulmonary embolism, right middle to lower zone infective changes with mild right pleural effusion. Tuberculosis workup included samples from sputum as well as from bronchoalveolar lavage samples from bronchoscopy had ruled out tuberculosis.

Patient's initial blood culture was negative. Despite initial treatment for community acquired pneumonia with 5 days of IV amoxicillin-clavulanate, the patient continued to be febrile. On day 6 of admission, transthoracic echocardiography revealed a suspicious small vegetation at anterior mitral valve leaflet (AMVL) measuring 0.7 cm × 0.4 cm with moderate mitral regurgitation (MR). The vegetation was later confirmed by transoesophageal echocardiography which

showed AMVL vegetation 0.5 cm × 0.4 cm, with moderate mitral regurgitation and preserved ejection fraction. The patient's subsequent 3 sets of blood cultures taken on day 6 of admission had remained negative. Fungal blood cultures were negative. In addition, blood cultures for both HACEK and Brucella were negative, and brucella serology was negative.

As such, she was empirically started on IV Ceftriaxone to treat culture-negative infective endocarditis. However, despite 10 days of IV Ceftriaxone, patient was still having intermittent temperature spike. On day 16 of admission, her condition deteriorated when she developed sudden respiratory distress with bronchospasm and was tachycardic. She required non-invasive ventilatory support for 1 day under Intensive Care Unit. A repeated chest radiography showed no worsening of previous consolidation and a repeated transthoracic echocardiography showed similar vegetation as seen previously. In view of persistent high-grade temperature and worsening respiratory symptoms, antibiotic was escalated to IV Meropenem.

Patient responded well to IV Meropenem with resolution of fever and was able to wean off oxygen after 3 days. Following negative blood culture results, IV Meropenem was de-escalated to IV Ceftriaxone after having completed for 5 days. Unfortunately, however, she started to be febrile again upon de-escalation to IV Ceftriaxone. Thus antibiotic was then switched back to IV Meropenem was given for 1 week duration. Another blood culture taken during this time finally yielded *Burkholderia pseudomallei*, on day 23 of admission. As part of screening for dissemination of melioidosis bacteremia, computed tomography (CT) of thoracic, abdomen and pelvis points to hematogenous spread with intra-abdominal foci—segment VII hypodense liver lesion (0.7 × 0.7 cm and 0.6 × 0.6 cm) and left renal hypodense lesions (Two ill defined non enhancing hypodense lesions in mid-pole of left kidney, largest measuring 0.5 cm × 0.8 cm) which could represent early abscess formation. Due to small sizes of lesions, no drainage was done.

For the intensive phase therapy of melioidosis, she was started on IV Ceftazidime for a total duration of 6 weeks. Taking into account of deep seated collection in liver and kidney, a combination therapy is recommended according to local Malaysian guidelines. Hence she was concomitantly started on adjuvant therapy with oral trimethoprim-sulfamethoxazole (TMP-SMX) which was subsequently continued as monotherapy in the eradication phase therapy for melioidosis to complete for a total 3 months.

During 4th week of admission, patient developed active flare of SLE with haematological involvement as substantiated by leukopenia, lymphopenia, warm autoimmune haemolytic anaemia (AIHA) with positive direct anti-human globulin test monospecific anti-IgG and high reticulocytosis. Anti-double-stranded DNA was positive with elevated titre of 107 IU/mL and low complements level C3 and C4. She was given IV Immunoglobulin for 5 days for warm AIHA with a tapering dose of prednisolone.

During her hospital stay, her fever resolved and her cough and appetite improved. Patient had achieved blood culture clearance after 1 week of IV Meropenem. A repeated transthoracic echocardiography at the end of 4 weeks of intensive phase therapy showed no evidence of vegetation. At the end of 4th weeks of treatment, infective markers had also markedly improved with resolution of acute kidney injury and transaminitis. To follow up, a repeated transthoracic echocardiography at the cardiology centre after 8 weeks of treatment revealed no vegetation. A contrasted enhanced CT abdomen after 11 weeks of treatment showed residual liver lesion with resolving segment VII liver lesion and unchanged renal hypodense lesion.

The patient was discharged with oral co-trimoxazole monotherapy in the eradication phase therapy for melioidosis to complete for 3 months. She was given cardiology follow-up and an outpatient scheduled review along with a follow-up contrasted CT abdomen to look for resolution of microabscesses.

3. Discussion

Melioidosis is an infection caused by the facultative intracellular gram-negative bacterium *Burkholderia pseudomallei*. It is an environmental saprophyte found in wet soils in endemic regions [1]. Melioidosis is endemic in both Northern Australia and Southeast Asian countries particularly in Malaysia [3]. In Malaysia, Melioidosis has a high annual incidence rate in Pahang, a state which is active in agriculture [4] [5]. Our patient resides in Kampung Kuala Lipis, a rural area in Pahang Malaysia with rich land of agricultural farms. Her family also manages fruit farms. The environmental occupational exposure to soils suggests possible aerosol transmission.

Majority of the melioidosis cases are presented with bacteraemia, with pneumonia being the commonest presentation. Internal organ abscesses with multi organ involvement were common [2]. Cardiac involvement is very rare. In a 5 year retrospective review of cases of melioidosis in Malaysia, only 1 out of 33 cases (3%) had heart vegetation [6]. In the Darwin prospective melioidosis study from tropical Australia reported only 4 of 540 cases (<1%) had pericarditis [3]. As well, melioidosis pericardial effusion was reported in around 1% - 3% of the total cases in previous studies [7]. Majority of patients had underlying predisposing condition, most notably diabetes mellitus. Other recognized risk factors include hazardous alcohol use, chronic lung disease and chronic renal disease, malignancy and immunosuppression [2]. Though rare, *B. pseudomallei* has been reported to be the cause of infective endocarditis [8] [9] [10].

It is not unusual for the initial absence of bacteremia as in systematic review of endocarditis in Melioidosis, only 83% had positive blood culture for microbiological diagnosis while the remaining patient was diagnosed via liver aspirate sample [11]. One of the major factors of blood culture-negative endocarditis has been reported to be associated with previous antibiotic treatment [12] [13]. In our case, the initial empiric therapy with orally given amoxicillin-clavulanate is certainly inadequate as an intensive phase therapy for melioidosis, nor does Cef-

triaxone which was given later on provide any coverage for the treatment of Melioidosis [3]. However, this may have been responsible for the absence of growth of *B. pseudomallei* in the first few sample of blood culture. Although inadequate microbiological technique such as inadequate volume in blood culture samples might be another contributing factor. It was only after 23 days of admission that blood culture finally yielded *B. pseudomallei* which subsequently enabled adequate intensive phase antibiotic treatment to be commenced.

In a systematic review to assess cardiac involvement in patients with culture proven *B. pseudomallei* infection, all left-sided valvular vegetation were treated with a ceftazidime or a carbapenem ± TMP-SMX as part of induction therapy, followed by eradication therapy with TMP-SMX [11]. *B. pseudomallei* are intrinsically resistant to penicillin, ampicillin, first- and second-generation cephalosporins, gentamicin, and many third-generation cephalosporins [4]. Nevertheless, gentamicin-susceptible *B. pseudomallei* strain has been reported. A strain of gentamicin-susceptible *B. pseudomallei* was found in Sarawak of Malaysian Borneo in 2010. Another case of disseminated melioidosis complicated with infective endocarditis due to gentamicin-susceptible *B. pseudomallei* was also reported in 2018 in Sarawak of Malaysian Borneo where gentamicin were added for synergistic effect in the intensive phase treatment of melioidosis [8]. As such, in gentamicin-susceptible *B. pseudomallei* there is role for synergism with combination of ceftazidime and short term aminoglycosides. In our patient, *B. pseudomallei* was resistant to gentamicin based on disk diffusion test. Gentamicin was not used for the initial empirical treatment for culture negative infective endocarditis for the benefit of renal sparing as this patient had acute kidney injury with underlying lupus nephritis.

To date, there are no guidelines on the treatment of melioidosis infective endocarditis. In our patient, she was started on 6 weeks of intensive phase antibiotics for the treatment of melioidosis, which is also consistent with the duration of treatment of infective endocarditis. The importance of identification of the specific aetiologic organism of infective endocarditis is also highlighted in this case, in order for appropriate antibiotic therapy to be started.

4. Conclusions

This case illustrates a rare case of Melioidosis native valve endocarditis complicated with dissemination to the liver and kidney in a young woman with underlying SLE with lupus nephritis, who was initially presented with pyrexia of unknown origin, and was subsequently treated as culture negative endocarditis before isolation of the causative organism. Delayed isolation in blood culture was probably due to previous antibiotic treatment and inadequate blood culture technique.

The identification of the specific aetiologic organism is important in the treatment of infective endocarditis. The intensive phase of melioidosis treatment must be consistent with the duration of treatment of infective endocarditis, guided by the patient's clinical response.

Conflicts of Interest

The authors declare there are no competing interests.

References

[1] White, N.J. (2003) Melioidosis. *The Lancet*, **361**, 1715-1722. https://doi.org/10.1016/S0140-6736(03)13374-0

[2] Currie, B.J., Ward, L. and Cheng, A.C. (2010) The Epidemiology and Clinical Spectrum of Melioidosis: 540 Cases from the 20 Year Darwin Prospective Study. *PLOS Neglected Tropical Diseases*, **4**, e900. https://doi.org/10.1371/journal.pntd.0000900

[3] Cheng, A.C. and Currie, B.J. (2005) Melioidosis: Epidemiology, Pathophysiology, and Management. *Clinical Microbiology Reviews*, **18**, Article 383. https://doi.org/10.1128/CMR.18.2.383-416.2005

[4] Nathan, S., Chieng, S., Kingsley, P.V., Mohan, A., Podin, Y., Ooi, M.H., Mariappan, V., Vellasamy, K.M., Vadivelu, J., Daim, S. and How, S.H. (2018) Melioidosis in Malaysia: Incidence, Clinical Challenges, and Advances in Understanding Pathogenesis. *Tropical Medicine and Infectious Disease*, **3**, Article 25. https://doi.org/10.3390/tropicalmed3010025

[5] How, S.H., Ng, T.H., Jamalludin, A.R., Tee, H.P., Kuan, Y.C., Alex, F., Sc, M., Aminudin, C.A., Sapari, S. and Quazi, M. (2009) Pahang Melioidosis Registry. *The Medical Journal of Malaysia*, **64**, 27-30.

[6] Pagalavan, L. (2005) Melioidosis: The Johor Bahru Experience. *Medical Journal of Malaysia*, **60**, 599-605.

[7] Kingsley, P.V., Leader, M., Nagodawithana, N.S., Tipre, M. and Sathiakumar, N. (2016) Melioidosis in Malaysia: A Review of Case Reports. *PLOS Neglected Tropical Diseases*, **10**, e0005182. https://doi.org/10.1371/journal.pntd.0005182

[8] Sia, T., Podin, Y., Chuah, T.B. and Wong, J.S. (2018) Melioidosis: An Unusual Cause of Infective Endocarditis: A Case Report. *European Heart Journal-Case Reports*, **2**, yty055. https://doi.org/10.1093/ehjcr/yty055

[9] Schultze, D., Müller, B., Bruderer, T., Dollenmaier, G., Riehm, J.M. and Boggian, K. (2012) A Traveller Presenting with Severe Melioidosis Complicated by a Pericardial Effusion: A Case Report. *BMC Infectious Diseases*, **12**, Article No. 242. https://doi.org/10.1186/1471-2334-12-242

[10] Subramony, H., Gunasekaran, S. and Paul, P.V.K. (2019) Disseminated Melioidosis with Native Valve Endocarditis: A Case Report. *European Heart Journal-Case Reports*, **3**, ytz097. https://doi.org/10.1093/ehjcr/ytz097

[11] Velusamy, R. and Muhi, S. (2020) Melioidosis and the Heart: A Systematic Review. *Tropical Medicine and Infectious Disease*, **5**, Article 121. https://doi.org/10.3390/tropicalmed5030121

[12] Zamorano, J., Sanz, J., Almería, C., Rodrigo, J.L., Samedi, M., Herrera, D., Aubele, A., Mataix, L., Serra, V., Moreno, R. and Sánchez-Harguindei, L. (2003) Differences between Endocarditis with True Negative Blood Cultures and Those with Previous Antibiotic Treatment. *Journal of Heart Valve Disease*, **12**, 256-260.

[13] Lamas, C.C., Fournier, P.E., Zappa, M., Brandão, T.J., Januário-da-Silva, C.A., Correia, M.G., Barbosa, G.I., Golebiovski, W.F., Weksler, C., Lepidi, H. and Raoult, D. (2016) Diagnosis of Blood Culture-Negative Endocarditis and Clinical Comparison between Blood Culture-Negative and Blood Culture-Positive Cases. *Infection*, **44**, 459-466. https://doi.org/10.1007/s15010-015-0863-x