ESC European Society of Cardiology

European Heart Journal - Case Reports (2018) **2**, 1–4
doi:10.1093/ehjcr/yty055

CASE REPORT

Melioidosis: an unusual cause of infective endocarditis: a case report

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Received 29 September 2017; accepted 7 April 2018; online publish-ahead-of-print 2 May 2018

Introduction As a causal organism in infective endocarditis, *Burkholderia pseudomallei* is rare. *Burkholderia pseudomallei* is intrinsically resistant to aminoglycosides but a gentamicin-susceptible strain was discovered in Sarawak, Malaysian Borneo in 2010. We report the first occurrence of infective endocarditis due to the gentamicin-susceptible strain of *B. pseudomallei*.

Case presentation A 29-year-old man presented with pneumonia and melioidosis septicaemia. His condition was complicated with infective endocarditis and septic emboli to the brain. Despite difficulties in reaching a diagnosis, the patient was successfully treated using intravenous gentamicin and ceftazidime and was discharged well.

Discussion The role of gentamicin in the treatment of the gentamicin-susceptible strain of *B. pseudomallei* remains unclear.

Keywords Melioidosis • Infective endocarditis • Gentamicin • *Burkholderia pseudomallei* • Case report • Bintulu • Sarawak • Malaysia • Borneo • Gentamicin susceptible strain

Learning points

- *Burkholderia pseudomallei* is an unusual cause of infective endocarditis.
- *Burkholderia pseudomallei* is known to be resistant to many antibiotics, including aminoglycosides. A strain of *B. pseudomallei* that is gentamicin-susceptible was found in Sarawak in Malaysian Borneo in 2010.
- The standard intensive phase therapy using carbapenem or ceftazidime can be instituted together with intravenous gentamicin for its synergistic effect in the treatment of infective endocarditis caused by the gentamicin susceptible strain of *B. pseudomallei*.

Introduction

Melioidosis is caused by the bacterium *Burkholderia pseudomallei*. It is endemic in many regions in Southeast Asia and Northern Australia.[1] It is also increasingly reported in other tropical countries.[1] It has a high mortality rate due to its systemic involvement and intrinsic resistance to a myriad of antibiotics.[2] A novel strain of gentamicin-susceptible *B. pseudomallei* was recently reported to be predominantly found in the central region of Sarawak in Malaysian Borneo.[3]

Infective endocarditis causes significant morbidity and mortality.[4,5] Complications of infective endocarditis include thromboembolic events, which could be life-threatening. Treatment of infective endocarditis requires the administration of an effective intravenous (IV) antibiotic over a prolonged duration.[6] Common organisms identified for infective endocarditis are *Streptococci* and *Staphylococci*, both of which contributed to 80% of cases.[6]

We report the first occurrence of infective endocarditis due to the gentamicin-susceptible strain of *B. pseudomallei* in a tertiary hospital in central Sarawak of Malaysian Borneo.

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Timeline

Week	Day	Patient's progress	Culture site	Culture result
1	1	Septic shock secondary to pneumonia Stared intravenous (IV) ceftazidime and IV C-penicillin	Blood	*Burkholderia pseudomallei*
	3–4	Developed ventilator associated pneumonia	—	—
	6	Blood culture taken on first day confirmed for *B. pseudomallei*	Blood	*B. pseudomallei*
2	8	Weaned off inotrope	Respiratory tract	Multidrug-resistant *Acinetobacter baumanii*
	11	—	Respiratory tract	Multidrug-resistant *A. baumanii*
	12	—	Blood	*B. pseudomallei*
	14	Started on oral bactrim		
	24	—	Blood	No growth
3	25	Left side hemiplegia and pansystolic murmur Echocardiography and computed tomography of the brain done		
	26	—	Blood	No growth
	27	Weaned from ventilator support	Blood	No growth
5		Started on IV gentamicin		
7		Completed intensive phase of antibiotics and physiotherapy. Patient was discharged from hospital		
36		Last follow-up visit		

Case presentation

The patient, a regular and heavy consumer of alcohol, was a 29-year-old male lumberjack with no known medical illness. He had been having fever and cough for 2 weeks. He was brought to the hospital in a confused state after being reported missing from work for a few days.

The patient presented with septic shock, which was consistent with the definition of Sepsis-3.[7] He was in a very confused state and was talking irrelevantly. His Glasgow Coma Scale (GCS) registered E4V2M5. His temperature was 38.0°C, blood pressure was 85/42 mmHg, and his pulse rate was 135 b.p.m. He also had neck stiffness, bilateral upper and lower limbs power registered at least three, while his tone and reflexes were normal. He had normal heart sounds with no murmur and bilateral lung crepitations. The patient was given fluid resuscitation and required a vasopresssor for blood pressure support. He was also put on a mechanical ventilator before being admitted into the intensive care unit (ICU).

Initial blood investigations showed anaemia and thrombocytopenia with normal total white cells and renal function. Ultrasonography examination showed the presence of splenic microabscesses and chest radiograph showed bilateral lung fields consolidation. Computed tomography (CT) of the brain was normal and lumbar puncture examination of the cerebrospinal fluid on admission showed no signs of inflammation or infection.

The patient's blood culture taken on admission grew *B. pseudomallei*. This was confirmed by a real-time polymerase chain reaction assay targeting the type III secretion system (TTS1).[8] This *B. pseudomallei* isolate appeared to be gentamicin-susceptible by the Kirby–Bauer disk diffusion susceptibility test (*Table 1*). He remained bacteraemic with positive blood cultures on Day 6 and 12 of admission yielding *B. pseudomallei* with the same antibiogram pattern. Subsequent blood cultures on Day 24, 26 and 27 of admission had no growth.

The patient was administered IV noradrenaline upon admission. The highest dose used was 0.27 mcg/kg/min on Day 4 of admission, and he was subsequently weaned off after a week. Upon admission, he was empirically given IV ceftazidime and IV C-penicillin. On Day 4 of admission, antibiotics were escalated to IV imipenem in view of the patient's persistent high-grade temperature and leukopenia. He required ventilatory support on a high setting for 2 weeks. During the second week of intensive phase therapy with IV antibiotics, he was started on oral trimethoprim-sulfamethoxazole (co-trimoxazole). His condition was complicated with ventilator-associated pneumonia. Culture of endotracheal secretions grew a multidrug resistant *Acinetobacter baumanii*, which was treated successfully with high dose IV ampicilin-sulbactamfor 14 days. He also developed sepsis-induced supraventricular tachycardia which resolved spontaneously.

In the third week of admission, there was a new onset of left-sided hemiparesis (muscle power 1/5) and pansystolic murmur with thrills at the apex of the heart. A repeat CT of the brain showed a right corona radiata infarct with a high parietal petechia haemorrhage (*Figure 1*). An echocardiogram showed a thickened mitral valve with an oscillating mass at the posterior mitral valve leaflet suggestive of vegetation (*Figure 2*) with a moderate eccentric mitral regurgitation.

The intensive phase therapy for melioidosis was extended to 6 weeks using IV ceftazidime, and we added IV gentamicin at the dose of 60 mg, 8-hourly for 14 days. He was also given concurrent oral co-trimoxazole, which was subsequently continued as monotherapy in the eradication phase therapy for melioidosis.

He was discharged after 12 weeks of admission with minimal residual left sided weakness (Modified Rankin Score of 2). The patient was able to perform all activities of daily living independently with intact cognitive function. He was subsequently transferred to a cardiac referral centre for definitive management. He remained well during follow-up in the cardiac centre at nine months from initial presentation. Echocardiogram showed that the vegetation on mitral valve had resolved with residual moderate mitral regurgitation and left ventricular ejection fraction of 66.5%. He remained in Modified Rankin Score of 2.

Discussion

Majority of the melioidosis cases are presented with bacteraemia and pneumonia is a common presentation.[2] Cardiac involvement is very rare. A prospective study on melioidosis in Darwin reported pericarditis in only 4 out of 540 cases.[2] As well, melioidosis pericardial effusion was reported in around 1–3% of the total cases in previous studies.[9,10] A defective native heart valve, however, is a predisposition for infective endocarditis.[6] And *B. pseudomallei* was recently found to cause infective endocarditis.[4,5]

This case illustrates that of a young man, with no known medical illness, who presented with disseminated melioidosis but, which was complicated with infective endocarditis and cerebral infarct. The diagnosis of infective endocarditis was unexpected because the patient was initially sedated and ventilated. Infective endocarditis was only discovered upon cessation of sedative medications, when he was found to have hemiparesis. A possible septic embolus was suspected. This led to the discovery of the prolapsed mitral valve, which had a vegetation.

Table 1 **Antibiogram of *B. pseudomallei* isolate based on disk diffusion test**

Antibiotics tested	Disk diffusion result
Ampicilin	Sensitive
Ceftazidime	Sensitive
Ciprofloxacin	Sensitive
Trimethoprim-sulfamethoxazole	Sensitive
Imipenem	Sensitive
Meropenem	Sensitive
Tetracycline	Sensitive
Gentamicin	Sensitive

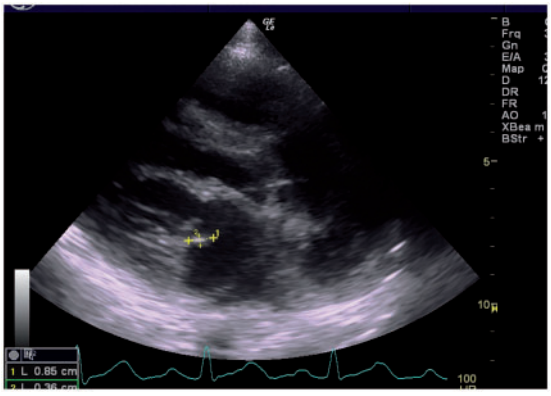

Figure 2 Echocardiogram of parasternal long-axis view showed an oscillating mass of 0.3 cm × 0.8 cm attached to posterior mitral leaflet suggestive of vegetation.

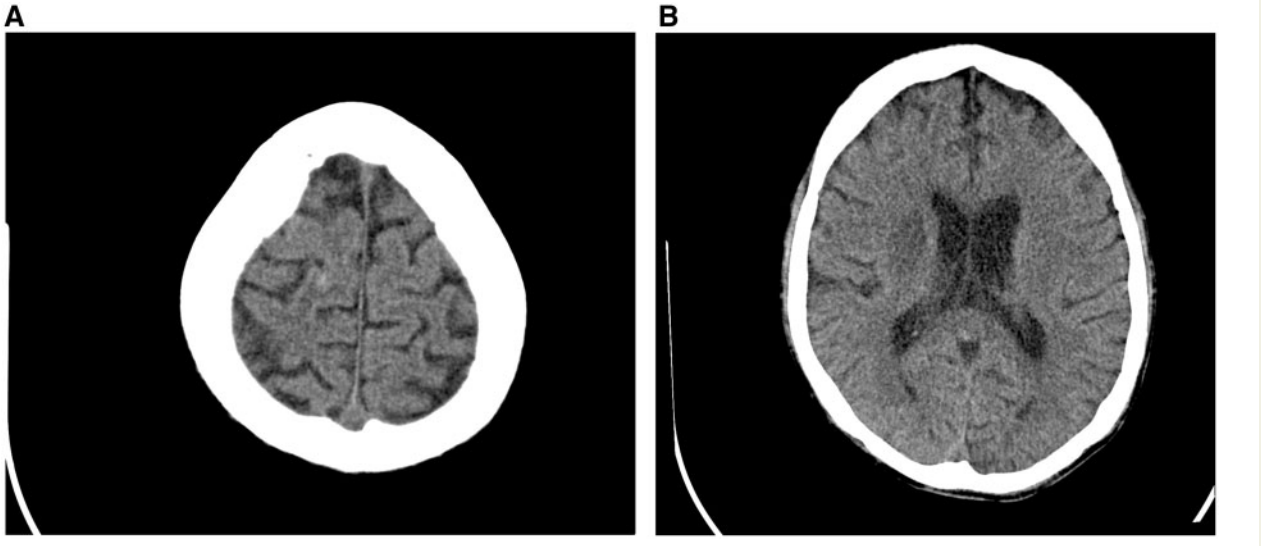

Figure 1 (*A*) Axial plain computed tomography brain shows there is a small hyperdense punctate haemorrhage at right high parietal region. (*B*) Axial plain computed tomography brain shows ill-defined hypodense area at right basal ganglia in keeping with infarction.

Infective endocarditis was complicated with septic emboli to the brain. This resulted in cerebral infarct and haemorrhages as seen in this case.

Gentamicin is not used for treatment of melioidosis because *B. pseudomallei* is intrinsically resistant to penicillin, first and second-generation cephalosporin, aminoglycosides, and macrolides.[3,11] However, this patient was infected by the gentamicin-susceptible *B. pseudomallei* strain. Therefore, we decided to use the combination of ceftazidime and gentamicin for the treatment of infective endocarditis in this patient. This was based on the experience of the synergistic effect of cephalosporins and aminoglycosides in the treatment of infective endocarditis. There are currently no guidelines on the treatment of melioidosis infective endocarditis. The identification of the specific aetiologic organism of infective endocarditis was important for the appropriate antibiotic therapy. In managing this case, we used 6 weeks of intensive phase antibiotics in the treatment of melioidosis, which was also consistent with the duration of treatment of infective endocarditis.

Conclusion

Melioidosis infective endocarditis is rare and reaching a diagnosis can be difficult. The intensive phase of melioidosis treatment must coincide with the duration of treatment of infective endocarditis. This would require clinical judgement, which would be guided by the patient's clinical response and blood culture results. The use of gentamicin in the intensive phase of treatment for the gentamicin-susceptible *B. pseudomallei* strain requires further study.

Acknowledgements

We are grateful to Dr Chua Hock Hin and Prof. Bart Currie for their advice and input in managing this case. We thank Dr Andrew Aeria for language editing. We also acknowledge the contributions of our colleagues from the ICU, medical, laboratory, and radiology teams in the management of this case.

Funding

This work is supported partly by the Ministry of Higher Education under the Research Acculturation Collaborative Effort Grant Scheme [RACE/b(2)/1246/2015(02))] and partly by our own operational funds.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

Authors' contributions: T.S. was responsible for patient management and this case write-up. T.B. provided radiology support, i.e. selecting images and providing related explanations. Y.P. was responsible for laboratory confirmation of the isolates. T.S., Y.P. and J.W. jointly prepared and compiled the facts of this case.

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