Case Report

Infective endocarditis - an uncommon presentation of disseminated melioidosis: a case report

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Abstract

Melioidosis is a potentially fatal bacterial infection involving multiple organ systems and is increasingly being reported in Sri Lanka in recent times. The clinical presentation of the disease varies from localized cutaneous infections to sepsis and death. Involvement of the heart in melioidosis is rare and only a few cases have been described so far in the world literature.

Herein we report a case of infective endocarditis in a 53-year-old man with poorly controlled type 2 diabetes mellitus for 5 years duration, who presented with intermittent low-grade fever along with loss of appetite, and malaise for 5 months duration. Examination revealed tachycardia, generalized abdominal tenderness, and coarse crackles on the left lower lobe of the lung. No peripheral stigmata of infective endocarditis or murmur were present. Blood cultures were positive for *Burkholderia pseudomallei*. 2D echocardiography was performed to exclude infective endocarditis as a cause of prolonged fever which showed a healed vegetation on the mitral valve and contrast-enhanced computerized tomography revealed renal, liver, and lung abscesses with splenic infarctions. A diagnosis of disseminated melioidosis was made. He was successfully treated with three weeks of initial intensive therapy with intravenous meropenem and oral sulfamethoxazole-trimethoprim (TMP-SMX) followed by subsequent three-month eradication therapy with TMP-SMX. Disseminated melioidosis can manifest as infective endocarditis hence a high index of clinical suspicion along with 2D echocardiography and other relevant investigations are crucial for the diagnosis. Initiation of intensive therapy with meropenem in combination with TMP-SMX as an adjunct can be lifesaving.

Keywords: Infective endocarditis, Melioidosis, Multiple abscesses, *Burkholderia pseudomallei*

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Introduction

Melioidosis is a potentially fatal infectious disease caused by a gram-negative aerobic bacterium, *Burkholderia pseudomallei*, which is mostly found in rice fields, in contaminated soil, water, and plants [1]. It is transmitted predominantly through percutaneous inoculation, and less commonly by inhalation or ingestion [2]. These are facultative intracellular pathogens that possess various mechanisms to evade the host immune system and enable cell-to-cell bacterial spread and biofilm production [3].

Human melioidosis occurs predominantly in endemic regions including Northern Australia, Thailand, Southeast Asia, South Asia, the Indian sub-continent, Sri Lanka, and China [1]. An increasing number of cases have been reported in Sri Lanka in recent times through the national surveillance for melioidosis, and a significant number of patients present with systemic infection with multiple foci [4,5]. Yet, the disease burden in Sri Lanka related to Melioidosis is still underrated.

Infective endocarditis (IE) is an entity with great morbidity and mortality, which requires prolonged intravenous antibiotic therapy [6-8]. Although melioidosis can involve any organ in the body, IE caused by *Burkholderia pseudomallei* is rare and so far, only a few case reports have been published in world literature [6-8].

Case presentation

A 53-year-old male with poorly controlled type 2 diabetes mellitus for 5 years duration, with no macro or microvascular complications detected as of now, presented to the emergency department with a five month history of intermittent low-grade fever without chills & rigors. He also complained of generalized malaise, loss of appetite, and a significant loss of weight. Along with the intermittent, bilateral asymmetrical inflammatory type of joint pains of moderate severity predominantly involving large joints (knee/ankle). He denied any symptoms suggestive of a respiratory, urinary, or gastrointestinal infection preceding the onset of the above symptoms. His travel history was unremarkable but he was employed as a supervisor for road construction work for the past 7 years duration, hence he had significant exposure to dust. His first presentation to medical services for the above symptoms was 2 weeks back where he presented to a peripheral hospital and there he was evaluated extensively for pyrexia of unknown origin. During those investigations, he was found to have hyperbilirubinemia therefore an ultrasound scan of the abdomen was performed which revealed a splenic vein thrombosis with features suggestive of early chronic liver cell disease. He denied a history of alcohol abuse, ingestion of hepatotoxic drugs or a history of blood transfusions which could have accounted for the above findings.

On admission, he was afebrile with features of moderate dehydration. Mild conjunctival pallor was present but was not icteric. No generalized lymphadenopathy or peripheral stigmata of infective endocarditis was noted. No ankle oedema was present. His pulse rate was 128 beats/ minute and the volume and character of the pulse were normal. His blood pressure was 108/76 mmHg. Heart sounds were normal with no audible murmurs. There was generalized abdominal tenderness without organomegaly. He had a respiratory rate of 32 per minute with coarse crepitations in the left lower lobe of the lung. The rest of the systemic examination was unremarkable.

His laboratory investigations revealed high inflammatory markers with neutrophil leukocytosis with a white blood cell count of $15.33x10^3$/uL and a neutrophil count of $13.79x10^3$/uL, and high C-reactive protein (206 mg/L) (Table 1). The rest of the basic investigations revealed mild anaemia with haemoglobin of 9.3 g/dL and an erythrocyte sedimentation rate of 132 mm in the 1st hour. Liver function tests revealed normal transaminase levels (alanine transaminase – 63 U/L, aspartate transaminase – 42 U/L) with elevated alkaline phosphatase (459 U/L) and gamma-glutamyl transferase (172 U/L) levels. The renal function test was unremarkable. Gram-negative bacilli which were identified as *Burkholderia spp.* was isolated from his blood and urine cultures. Transthoracic echocardiography revealed a hypoechoic lesion attached to the anterior mitral valve leaflet suggestive of a healed vegetation with normal biventricular function. No pericardial effusion or abscess was identified in the echocardiogram. Contrast-enhanced computed tomography of the chest, abdomen, and pelvis revealed multiple abscesses involving the liver, lungs, and kidneys with multiple infarcts involving the spleen. Ultrasound of the left knee joint suggested septic arthritis of the left knee joint.

Table 01: Investigation findings of the patient

Investigation		Results		Normal range
		On admission	Upon Discharge (One month later)	
Full blood count	Hemoglobin (g/dL)	9.3	10.2	11-13
	White cells ($\times 10^9$ /L)	15.33	13.47	4.5 – 11
	Platelets (x 10^9/L)	352	360	150 – 400
	Neutrophils %	90	75	50-70
	Lymphocytes %	69	45	20-40
Serum Electrolytes	Serum potassium (mmol/L)	4.2	4.3	3.5 – 5.5
	Serum sodium (mmol/L)	119	129	135 – 145
	Serum-corrected calcium (mg//dL)	2.5	2.7	8.5-10.2
	Serum magnesium (mmol/L)	0.8	1.1	0.85-1.10
Liver Biochemistry	Aspartate transaminase (U/L)	72	42	< 40
	Alanine transaminase (U/L)	101	63	< 40
	Alkaline phosphatase (U/L)	459	-	< 120
	Total Bilirubin (µmol/ L)	9.5	-	5 – 17
	Direct Bilirubin (µmol/ L)	7.5	-	<5
	Serum albumin (g/L)	16	27	34-54
	Serum globulin (g/L)	47	-	20-35
	Gamma glutamyl transferase (GGT) (U/L)	172	-	5-40
Inflammatory Markers	C-reactive protein (mg/L)	206	6.6	< 5
	Erythrocyte sedimentation rate (mm in 1st hr)	132	124	< 20
Clotting Profile	PT/INR (International Normalizing Ratio)	17/1.25	-	<1
	Activated partial Thromboplastin Time (sec)	33	-	
Tumor Markers	Carcinoembryonic antigen (CEA)	-	7.68	<3
	CA 19.9	-	50	0-37
	Alpha feto protein levels (AFP) (ng/ml)	-	1.05	0-40
Hormonal Profile	Random Cortisol levels (µ/dl)	-	129	10-20
	Thyroid stimulating hormone levels (µIU/ml)	-	1.71	0.5-5
Infection Screening	Blood Culture & ABST	Burkholderia spp + Sensitive for TMP/SMX		
	Urine for Culture and ABST	Burkholderia spp + Sensitive for TMP/SMX		
	Melioidosis Antibody titer (IgM)	1:640 (measured by enzyme linked immunosorbent assay) (ELISA) rising upto 1:10240 in 2 weeks		
	Mantoux test	Negative		
	Microscopy for malaria parasites	Negative		
Serum creatinine (µmol/L)		174	157	< 100
Fasting blood sugar (mmol/L)		13.9	4.3	< 200
USS of abdomen		Splenic Vein thrombosis with features of early chronic liver cell disease		
2D echocardiogram		Ejection fraction > 60% No regional wall motion abnormality Anterior mitral valve hyperechoic lesion noted Trivial Mitral regurgitation Right heart normal		
Trans esophageal echocardiography		Could not be performed		
Urine full report		Red Cells – 2-5 Pus Cells – Moderately field full Albumin - +		
Blood Picture		Normochromic Normocytic Red cells Neutrophil Leukocytosis with toxic granules Morphology favours moderate anaemia. This could be due to acute on chronic bleeding		

The patient was initially treated with intravenous ceftriaxone and later with the blood culture results, after obtaining the microbiologist's opinion, intravenous meropenem and oral TMP-SMX were commenced. The intravenous antibiotic therapy was continued for 21 days. The patient was carefully monitored for refeeding syndrome, and glycemic control was achieved with subcutaneous short-acting insulin during the hospital stay. A nutritional referral was done to ensure adequate and gradual escalation of calorie intake. The input of the orthopaedic team was sought out for the left knee joint arthritis and the diagnosis of septic arthritis was clinically excluded. Physiotherapy was arranged to encourage mobilization and strengthen the muscles. The patient was afebrile and symptom-free at the end of three weeks into the antibiotic course and was successfully discharged with the continuation of oral TMP-SMX for three months.

Discussion

Melioidosis is endemic to Sri Lanka and has a wide range of presentations [5]. It is one of the diseases which are greatly underdiagnosed worldwide [4]. This present case depicts a rare presentation of disseminated melioidosis which could have been missed if not for the higher index of suspicion placed at the initial setting. He presented with a clinical picture accounting to infective endocarditis with a background history of poorly controlled diabetes mellitus and had intermittent low-grade fever along with loss of appetite, and malaise for 5 months duration. This presentation is a great imitator of tuberculosis which is also a very common disease in Sri Lanka [1]. Melioidosis has a high case fatality rate despite treatment and timely intervention and can potentially change the disease course, as the disease can be successfully treated with intravenous antibiotics [4,9]. Hence the knowledge of varying presntations of Melioidosis is of paramount importance for a better outcome.

The majority of patients diagnosed with Melioidosis are middle-aged men in rural settings. It was keeping in line with our patient as well. The clinical presentation of melioidosis is affected by the presence of the host risk factors and immune response, bacterial load and strain, the presence of virulent genes and the route of infection [1,2]. Our patient had a significant exposure to soil for longer periods in combination with diabetes which easily predisposed him to the infection. The commonest presentation is pneumonia which is present in about half of the patients [1]. Even though our patient did not present with pneumonia, lung abscesses were evident in the CT. Involvement of the heart, especially in a native heart valve is a rare occurrence and has been only reported in a few cases globally [6,7,10]. Pericarditis and pericardial effusion are the most common cardiac manifestations, followed by myocardial abscess and endocarditis occurring in a small number of patients [10]. This patient was evaluated for fever with constitutional symptoms and the diagnosis of infective endocarditis was suspected as a cause of prolonged fever. The absence of an audible murmur throughout the stay was a challenge in the diagnosis. The splenic infarcts were most likely the result of the septic emboli from vegetation occluding the splenic vessels. Fortunately, no evidence of brain involvement such as abscess or infarct was noted.

Treatment for infective endocarditis depends on the causative organism and its sensitivity patterns. There are currently no accepted treatment guidelines for IE associated with melioidosis, and *B. pseudomallei* is intrinsically resistant to penicillin, first and second-generation cephalosporin, aminoglycosides, and macrolides [6]. Treatment of melioidosis involves an intensive phase with ceftazidime or a carbapenem followed by eradication therapy with TMP-SMX or doxycycline [1]. In our patient, the intensive therapy was commenced with intravenous meropenem due to septicemia with multiple foci and the severe nature of the disease, with the addition of oral TMP-SMX as an adjunct due to its penetration abilities in non-pulmonary foci of infection which was continued for three weeks, followed by TMP-SMX monotherapy for eradication for three months. Although the treatment of endocarditis generally involves six weeks of antibiotic therapy, due to excellent response and the presence of the 'healed' vegetation at the time of initial diagnosis, the decision was made to stop the intravenous course at 21 days.

Conclusion

Infective endocarditis caused by melioidosis is rare and needs to be excluded in the presence of disseminated infection. Underdiagnosis had been a huge challenge in many instances due to a lack of knowledge about the organism and overlap features associated with other Gram-negative bacteria, especially of the *Pseudomonas* group. Hence high index of suspicion is needed for early diagnosis.

Cultures are crucial to guide the choice of antibiotics. Treatment includes initial intravenous intensive therapy followed by prolonged eradication therapy, and the duration is best decided according to individual cases.

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Consent

Written informed consent was obtained from the patient for publishing this case report.

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