CASE REPORT

Healthcare-associated Infective Endocarditis by Incredibly Aggressive *Staphylococcus lugdunensis*

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ABSTRACT

A man in his 50s with underlying end stage renal failure presented with fever for one day and unconsciousness. Transthoracic echocardiogram showed large regurgitation over anterior mitral valve suggestive of infective endocarditis. Three sets of blood culture grew *S. lugdunensis*. He was started on intravenous cloxacillin 2g six hourly. Patient's condition did not improve despite optimum therapy given. He died after twenty days of treatment due to septic shock secondary to mitral valve IE with septic encephalopathy. *S. lugdunensis* is an aggressive pathogen causing destructive IE in immunocompromised patients. Infection begins with colonization of the internal jugular vein catheter resulting in bacteremia. Matrix-assisted laser desorption/ionization–time-of-flight mass spectrometer (MALDI-TOF) reduces the timing of pathogen identification thus allowing early initiation of antimicrobial therapy. Appropriate antibiotic therapy reduces mortality however he died due to severe complications of sepsis and encephalopathy.
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Keywords: Healthcare-associated infective endocarditis, *Staphylococcus lugdunensis*, Matrix-assisted laser desorption/ionization–time-of-flight mass spectrometer (MALDI-TOF) , End stage renal failure, Septic shock

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INTRODUCTION

Health-care-associated infective endocarditis (HCA-IE) has been a critical concern in the healthcare sector. The prevalence of HCA-IE reached approximately 50% of all cases of infective endocarditis (IE) (1). This increasing number has been credited to advances in invasive medical procedures, especially the use of intravenous catheters. Haemodialysis is one of the independent risk factors for HCA-IE (2).

The most common causative agents for HCA-IE are *Staphylococcus aureus* followed by coagulase-negative *Staphylococcus* (CoNS). *Staphylococcus lugdunensis*, which is part of the CoNS group, was first identified as causative agent of infective endocarditis in 1988 (3). *S. lugdunensis* IE has been reported causing severe clinical manifestation with high mortality rate. We report a fatal case of mitral valve endocarditis in end stage renal failure (ESRF) patient caused by *S. lugdunensis*.

CASE REPORT

A 50-year-old man with underlying diabetes mellitus, hypertension, left sided cerebrovascular accident (CVA), and end stage renal failure (ESRF) was admitted to the hospital after been found unconscious at home. History was taken from his daughter which revealed he had been coughing for one week and then had fever for one day. He was on regular haemodialysis via right internal jugular vein catheter (IJC) for the past five months.

On clinical examination, the Glasgow coma scale (GCS) was E4V2M5. The patient was afebrile, with pulse rate 124 beats/min, blood pressure 130/82mmHg, respiratory rate 32/minute, oxygen saturation 100% on 15-liter oxygen high flow mask, and blood glucose 4.7g/dL.

Routine blood investigation showed mild anaemia, leucocytosis predominantly neutrophil, and high C-reactive protein level. Other blood parameters were within normal range. Chest X-ray was suggestive of infection with perihilar haziness. Two-dimensional echocardiography for initial evaluation of infective endocarditis was done, which showed hyperdynamic left ventricle with no pericardial effusion and no

regurgitation seen. CT scan of the brain showed multifocal old infarct with underlying cerebral atrophy. He was treated for aspiration pneumonia secondary to CVA.

On Day 2 of admission, he was noted to be suddenly hypotensive and tachycardic. He was intubated and started on vasoconstriction drug (noradrenaline) infusion. Cardiovascular examination found loud pansystolic murmur best heard over the mitral area, and transthoracic echocardiogram (TTE) showed an ejection fraction of 60%, with homogenous mass seen measuring 10 x 20mm, attached to the middle of anterior mitral valve leaflets, suggestive of infective endocarditis (Figure 1). Three sets of blood culture were positive for Gram positive cocci in clusters. Small beta lysis colonies grew on blood agar (Figure 2), positive for catalase and negative for coagulase test.

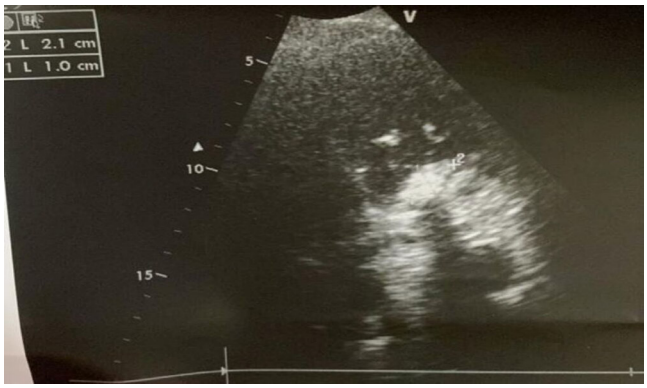

Figure 1: A homogenous mass measuring 10 x 20mm, attached to middle of anterior mitral valve leaflets on transthoracic echocardiogram (TTE).

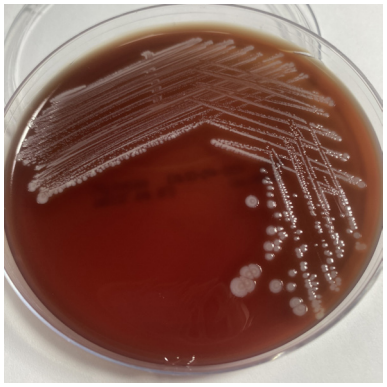

Figure 2: Colony morphology of *Staphylococcus lugdunensis* on blood agar shows small grey beta lysis.

Further identification by matrix-assisted laser desorption/ ionization – time-of-flight mass spectrometer (MALDI-TOF) revealed *Staphylococcus lugdunensis*. Further susceptibility testing was done, and the result showed pan sensitivity to all antibiotics. Initial antibiotic treatment which consisted of intravenous (IV) penicillin, gentamicin, and vancomycin were given prior to blood culture results, and then switched to IV cloxacillin with an adjusted dose for haemodialysis patients (2g six times a day).

After three days on IV cloxacillin, he did not show any signs of clinical intravenous mprovement. His GCS was not improving, and his blood pressure was persistently hypotensive. Another set of blood culture was repeated and showed no growth after five days incubation. CT scan of the brain was performed, and the report showed no cerebral haemorrhage or embolism seen. TTE examination was done and showed increased size of vegetation (13 x 25mm) attached to mid anterior mitral valve leaflets, no pericardial effusion and no other lesion seen. An electroencephalogram (EEG) was performed and revealed abnormal EEG consistent with severe diffuse cortical dysfunction.

The patient passed away after twenty days of admission, the diagnosis being septic shock secondary to mitral valve IE with septic encephalopathy.

DISCUSSION

S. lugdunensis was discovered to be a novel species of coagulase-negative *Staphylococcus* (CoNS) in the late 1980 (1). It is typically considered as part of the cutaneous microbiota which preferentially colonizes the perineal region. *S. lugdunensis* has been reported to cause wide range of diseases including skin and soft tissue infections, bacteraemia, infective endocarditis (IE), urinary tract infection, peritonitis, prosthetic joint infection, osteomyelitis, arthritis, and catheter-related infection.

Cases of IE in Malaysia continue to be under-reported, despite the significant number of morbidity and mortality rates. A retrospective study conducted at a local tertiary hospital over 12 years identified a total of 182 cases of infective endocarditis (IE). Among these cases, only 10 cases were caused by CoNS (2). As of now, only a single case of *S. lugdunensis* infective endocarditis reported in Malaysia (3).

Generally, coagulase-negative staphylococci (CoNS) are not always identified to the species level in clinical laboratories due to their high prevalence as contaminants. This lack of detailed identification can lead to underestimations of the true burden of infections caused by *S. lugdunensis*.

S. lugdunensis is notorious for its aggressive courses similar to *S. aureus*. Patients with *S. lugdunensis* endocarditis are more likely to present with severe and rapid onset symptoms of heart failure and decreased organ perfusion leading to shock, as seen in our patient. Unlike other CoNS, these infections are associated with a higher mortality rate.

Patients on chronic haemodialysis (CHD) are susceptible to IE. Over half of IE cases in CHD are preceded by a bacteraemia episode and the majority of the cases originate from bacteria colonization in central

venous catheter. *S. lugdunensis* produces extracellular slime or glycocalyx, which is important in bacterial adherence and colonization of the venous catheter. This extracellular slime is able to inhibit phagocytosis and act as barrier against systemic antibiotic. *S lugdunensis* secretes von Willebrand factor binding protein (vWbp) which is important in enhancing platelet aggregation and promote growing of vegetation.

This case study demonstrates the virulency of *S. lugdunensis* characterized by rapidly growing large vegetation and valve destruction, leading to fulminant sepsis and fatal outcomes. During the first day of admission, there was no heart murmur on auscultation and echocardiography revealed negative findings for endocarditis. However, on the next day, the patient's condition suddenly deteriorated. Echocardiography detected a large vegetation on the mitral valve measuring 10 x 20mm. The acute and rapid growth of vegetation by *S. lugdunensis* has also been highlighted in a previous case report (1).

Nowadays, matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF) has been routinely used to profile bacterial proteins and obtain a bacterial fingerprint able to differentiate microorganisms from different genera and species. By this technology, bacterial identification can be achieved within minutes, rather than traditional biochemical testing which require at least 24-48 hours. MALDI-TOF has significantly reduced the turnaround time (TAT) for identifying bacteria and determining their susceptibility testing. Therefore, it facilitates the early initiation of appropriate antimicrobial therapy. MALDI-TOF contributes to a reduced mortality rate and shorter hospitalization times, leading to cost savings and benefiting public health overall. Yo et al. conducted a systematic review that demonstrated MALDI-TOF mass spectrometry was linked to a 23% reduction in in-hospital mortality among patients with bloodstream infections (4).

According to a 2016 American Association for Thoracic Surgery (AATS) guideline, patients who have native valve endocarditis on the left side and have mobile vegetation longer than 10mm ought to have surgery (5). This guideline also emphasized that patient who are unconscious, and have experienced a stroke, or significant neurologic injury, should not undergo surgery until their chance of recovery has been confirmed. After taking into account several factors including complications, primarily neurologic status, and multiple comorbidities in this patient, surgical intervention was not opted for our patient.

CONCLUSION

Staphylococcus lugdunensis is a coagulase-negative *Staphylococcus* (CoNS) that is often reported as of doubtful clinical significance. However, in certain cases it may cause servere infection that leads to significant morbidity and mortality if not properly detected and treated. Hence an involvement of a clinical microbiologist (CM) is needed for comprehensive investigation to support the diagnosis of infective endocarditis. As for this case, the aggressiveness of *S. lugdunensis* infection resulted in severe complications and subsequently fatal outcome.

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