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Case report

A fatal case of early prosthetic valve endocarditis caused by multidrug-resistant (MDR) – *Sphingomonas paucimobilis*

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ABSTRACT

Sphyngomonas paucimobilis (*S. paucimobilis*) is a low-pathogenicity, gram-negative bacilli (GNB) that are previously known as an opportunist microorganism. Recent studies have shown that *S. paucimobilis* is an emerging pathogen causing various infections. Multidrug-resistant GNB has emerged as a major clinical and therapeutic dilemma in various hospital-associated infections.

Although rare, *S. paucimobilis* could be associated with infective endocarditis (IE). Prosthetic valve endocarditis (PVE) is the most severe type of IE, which has high mortality rates despite diagnostic and treatment advances. We report a fatal case of early PVE associated with multidrug-resistant (MDR) - *S. paucimobilis* complicated with perivalvular abscess, complete heart block, valve detachment, and septic arthritis.

Introduction

Early prosthetic valve endocarditis (PVE) is a life-threatening condition. Rapid treatment with antibiotic therapy and early surgery are the treatment of choice in managing this disease. However, the mortality rate remained high [1].

Sphingomonas paucimobilis is a Gram-negative bacillus (GNB) with low pathogenicity that could present in the community or hospital settings. Severe infection and septic shock caused by *S. paucimobilis* have been described in immunodeficient patients [2]. Only a few recorded cases of *S. paucimobilis* associated with infective endocarditis (IE) exist, and to our knowledge, this is the first case report describing early PVE due to multidrug-resistant (MDR) - *S. paucimobilis*.

Case presentation

A 53 years old man presented to the emergency department with dyspnea and fever one week ago. He also complained of pain and swelling in his right knee. He had a history of coronary artery bypass graft (CABG), mitral valve (MV) replacement with a prosthetic valve, and tricuspid valve (TV) repair four weeks before admission. The post-operative period was complicated with hemolytic anemia, hospital-acquired pneumonia, and gout arthritis. He was treated with intravenous ceftazidime and levofloxacin for pneumonia and intraarticular triamcinolone for arthritis. His condition was improved and discharged with colchicine, methylprednisolone, acetylsalicylic acid, warfarin, and atorvastatin. Echocardiography before discharged showed good prosthetic MV position and functions (Fig. 1).

On examination, his vital signs were stable. Remarkable physical examinations were pale conjunctiva, rales, and systolic murmur grade 3 at the cardiac apex with the absence of mechanical clicking sound. Initial laboratory findings reported hemoglobin 7.8 g/dL, leukocyte 27.990/mm^3, INR 1.12, thrombocyte 369.000/mm^3 and high C-reactive protein (13.80 mg/dL) and procalcitonin (1.23 ng/mL) levels. Electrocardiography (ECG) revealed a junctional rhythm with ventricular extrasystole

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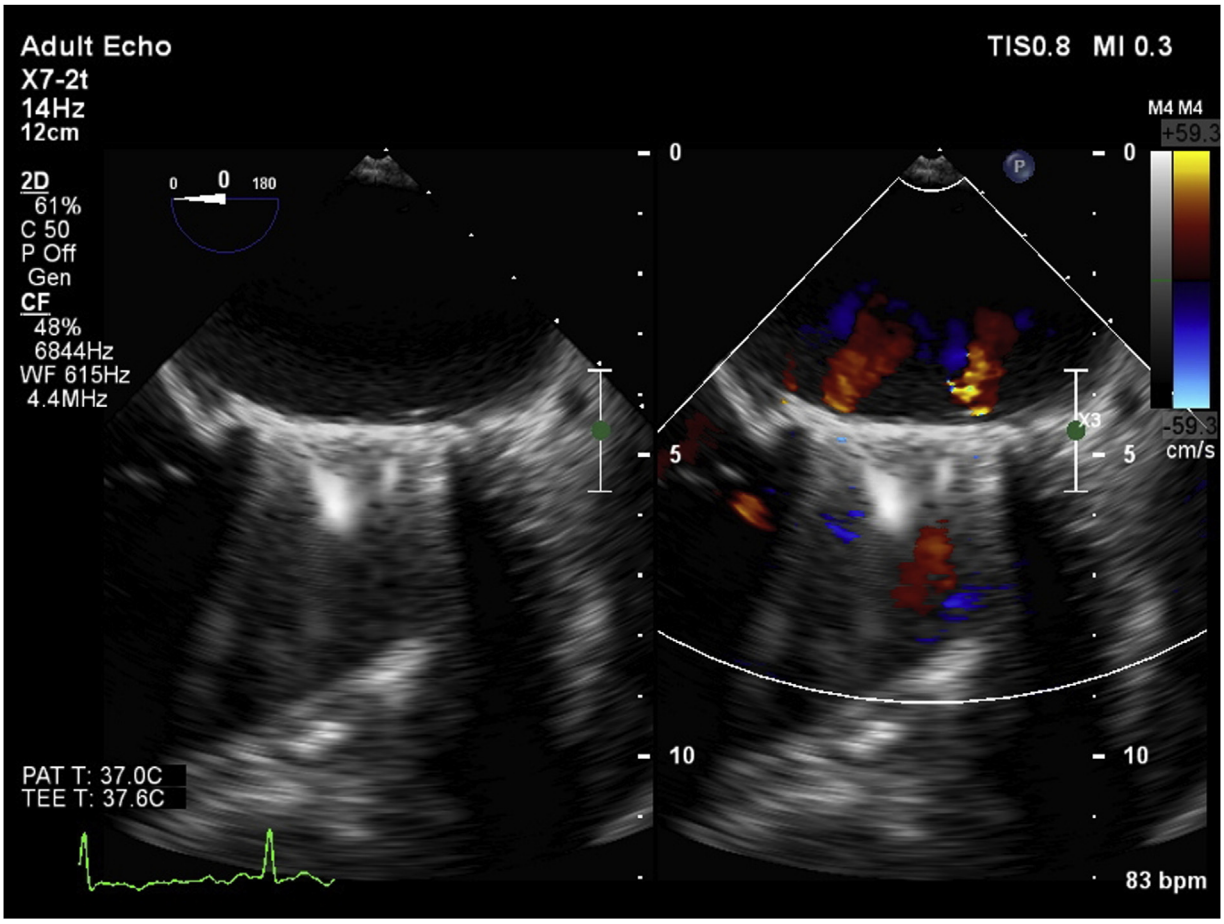

Fig. 1. Transesophageal echocardiogram (TEE) before discharged showed good prosthetic mechanical MV position and functions.

Transthoracic and transesophageal echocardiography showed prosthetic mechanical MV with mild perivalvular leakage and periannular abscess (Fig. 2 a,b,c). Vegetations were visualized at the edges of prosthetic MV, cusps of aortic valves (AoV), and leaflets of TV. The synovial fluid examination results are yellowish opaque in color, a leukocyte count of 23,372 cells/μL, polymorphonuclear cells of 83 %, and negative gram staining and culture.

The patient was diagnosed with early prosthetic endocarditis (PVE) with multivalvular involvement, perivalvular extension (abscess) and septic arthritis. We planned for urgent surgery, but the patient was refused. He was treated with IV furosemide and empiric antibiotic therapy with IV vancomycin and IV gentamycin.

On Day-6 hospitalization, the patient complained of worsening dyspnea. His blood pressure was 90/60 mmHg, heart rate 38 bpm, SpO2 88 %, and bilateral rales on physical examination. ECG revealed atrial fibrillation with complete heart block. Serial echocardiography revealed detachment of prosthetic MV with left ventricular inflow obstruction (Fig. 2D). The patient was managed with mechanical ventilation, temporary pacemaker, IV vasopressor, and IV inotropic.

On Day-7 hospitalization, multidrug-resistant (MDR) *S. paucimobilis* was grown in three consecutive blood cultures, only susceptible to tigecycline (Table 1). Tigecycline was started immediately; however, the patient's condition worsened, and he passed away. (Timeline of the patient's medical history, present illness, treatment, and the outcome is in Fig. 3)

Discussion

PVE is one of the most complicated forms of Infective Endocarditis (IE) due to difficulties in its management. Although rare, it is a life-threatening condition, which occurs in 1–6% of patients with prosthetic valves with a mortality rate ranging from 20 % to 80 %. PVE can be classified into two categories based on time of onset after valve surgery, whereas early PVE is within 12 months and late is after 12 months [1].

Previous studies have described risk factors for early PVE, including pre-operative active endocarditis, higher NYHA heart failure class, poor oral hygiene, prolonged CPB time, multi-valvular surgery, and post-operative fever or infection [3,4]. Tanioka et al. also reported a case of early PVE associated with immunosuppressive therapy [5]. Immunocompromised condition is also associated with *S. paucimobilis* infection [2,6]. In our case, the patient was diagnosed with early PVE four weeks after cardiac surgery. He had several risk factors, such as multi-valvular surgery, congestive heart failure, and steroid usage. Also, he had a fever during post-operative periods, which could be related to bacteremia. Ivanovic et al. described PVE within two months after cardiac surgery could be caused by hematogenic dissemination in post-operative periods or direct invasion of microorganisms during valve surgery [7].

The mechanism of PVE is intricate, particularly regarding biofilm formation. Biofilm formation creates a complex and unique environment, which organisms can thrive and attach to the

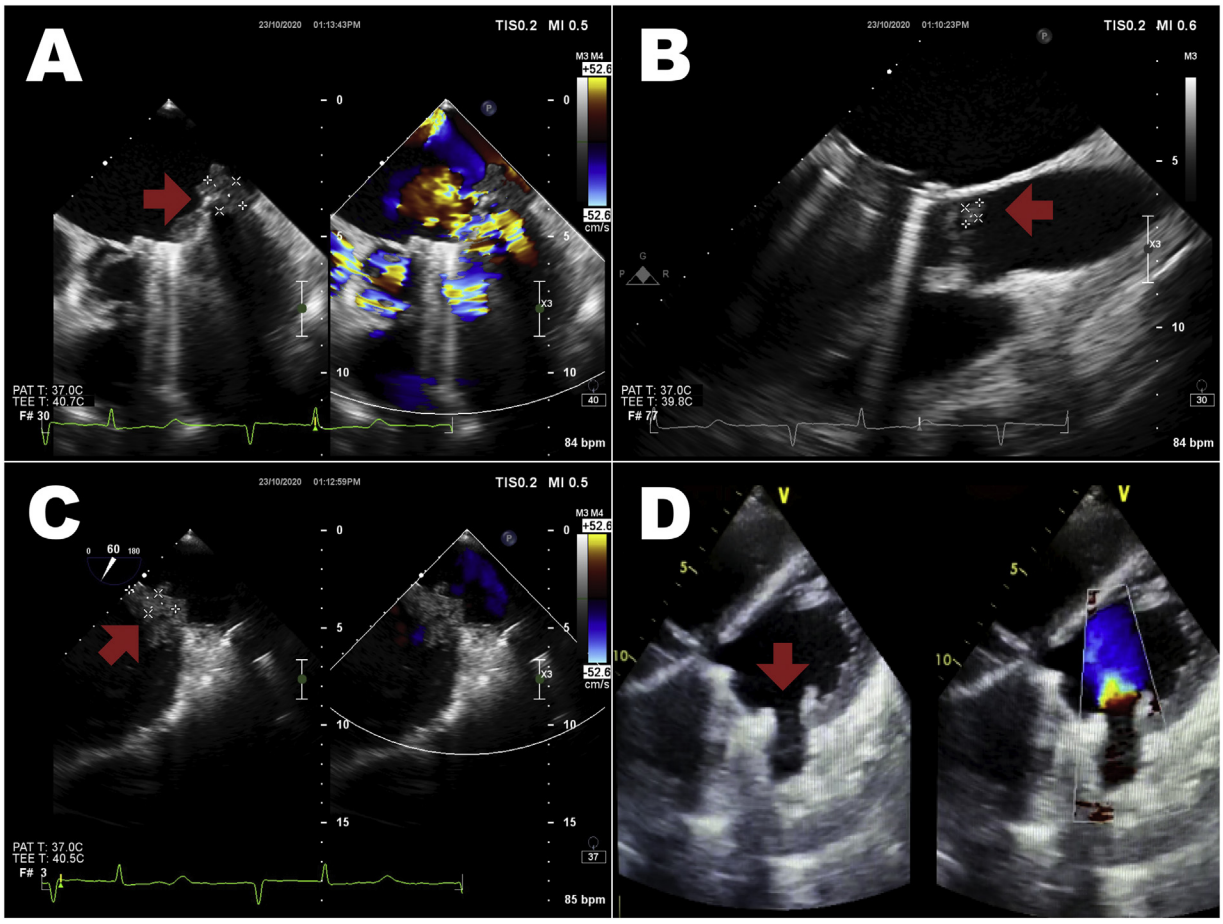

Fig. 2. (A) Echocardiography reveals multiple large vegetation at the edges of prosthetic MV (arrow); (B) Small vegetation at aorta (arrow); (C) multiple small undulating mass attached to septal tricuspid leaflet (arrow); and (D) MV detachment with left ventricular inflow obstruction (arrow).

Table 1
The blood culture and susceptibility tests. MDR- *S. paucimobilis* was yielded in blood cultures and susceptible only to tigecycline.

Blood Culture 1,2, and 3	
Isolate: *Sphingomonas paucimobilis*	
Antibiotics susceptibility and resistance test	
Ceftriaxone	Resistant
Gentamycin	Resistant
Amikacin	Resistant
Piperacillin/Tazobactam	ResistantResistant
Cefazolin	Resistant
Ceftazidime	Resistant
Cefepime	Resistant
Ciprofloxacin	Resistant
Cotrimoxazole	Resistant
Tigecycline	**Sensitive**
Aztreonam	Resistant
Meropenem	Resistant

prosthetic material's surface while protected under the biofilm. Hence, making it more difficult for the immune cells and antimicrobial agents to saturate the biofilm [8]. Moreover, the prosthetic valve's endothelization process is still incomplete during early post-operative conditions; thus, microorganisms could directly access the suture pathways to the prosthesis-annulus and paravalvular tissue interface, causing abscess and valvular dehiscence [7]. Erosive anatomical destruction by abscess or extension of inflammation and edema could affect the cardiac conduction system, leading to heart block, as in our case [9].

Osteoarticular manifestations in IE are relatively rare. Anis et al. described osteoarticular involvement occurs in 6.8 % of IE cases, in which spondylodiscitis and septic arthritis are the most common presentations, and *Staphylococcus aureus* is the most common pathogen [10]. Septic arthritis usually affecting large joints, such as the knee, as in our case [10,11]. Several studies have described septic arthritis associated with *S. paucimobilis*; whichthe mechanisms is presumably due to hematogenous spreading in systemic infection or contiguous spreading from the surrounding structure [6,12].

S. paucimobilis is a single-flagellum, yellow-pigmented, GNB. Although considered as low pathogenicity bacteria, several infections and fatal cases associated with *S. paucimobilis* had been increasingly reported. In community settings, *S. paucimobilis* is frequently found in water reservoirs and soil. While in hospital settings, *S. paucimobilis* could cause hospital-associated infection by transmission from intravenous fluid, implanted indwelling catheters, ventilators, nebulizers, and other various hospital devices [6,13]. In our case, *S. paucimobilis* was yielded from three consecutive blood cultures. Previous studies have reported IE associated with *S. paucimobilis*; however, early PVE associated with *S. paucimobilis* has never been described [14–17].

Typically, *S. paucimobilis* is resistant to penicillin and first-generation cephalosporins. This is caused by the synthesis of chromosomally encoded beta-lactamase by the bacteria. Further, *S. paucimobilis* is usually sensitive to carbapenems, aminoglycosides, trimethoprim-sulfamethoxazole, and piperacillin/tazobactam with variable susceptibility to fluoroquinolones and third-generation cephalosporins [18]. Nonetheless, MDR-*S. paucimobilis* was

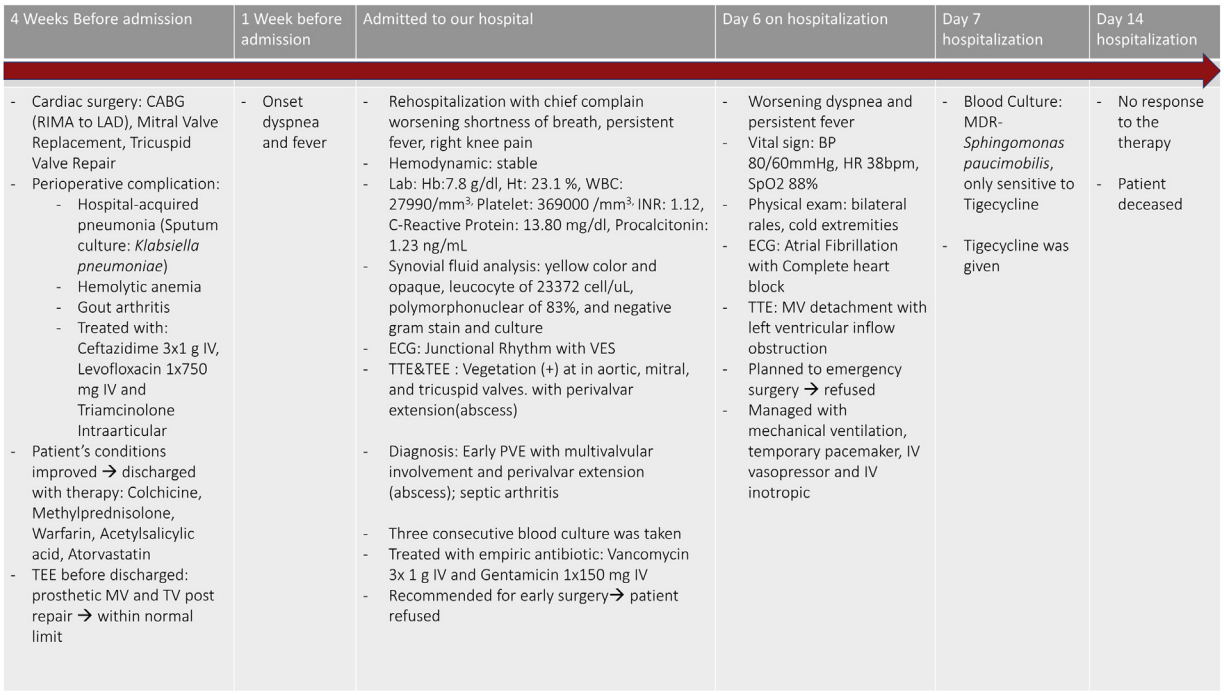

Fig. 3. Timeline of the patient's medical history, present illness, treatment, and outcome.

yielded on antibiotic susceptibility testing in our case (Table 1). Mechanisms of antimicrobial resistance in GNB could be caused by the enzymatic and non-enzymatic processes. Additionally, mutations in chromosomal genes, loss of outer membrane porins resulting in increased permeability alterations, and various intrinsic mechanisms could also contribute to antimicrobial resistance [19]. To date, there is no uniformity on antibiotic therapy in *S. paucimobilis* infection, which imposes the need for individualized, case-by-case management, as in our case, which only sensitive to tigecycline.

We recommended early valve surgery, which is based on recommendations of current IE guidelines, including mobile vegetation > 10 mm, sign and symptoms of heart failure resulting from valve dehiscence, severe prosthetic valve dysfunction, and IE complicated by heart block with annular abscess, as in our patient [20]. Unfortunately, our patient refused. A paravalvular abscess is an independent predictor of in-hospital mortality, with a 27 % mortality rate. If left untreated without surgical intervention, the mortality rate of paravalvular infection is expected to be 100 % [2,21]. Nevertheless, the risk of surgery in PVE with perivalvular extension is also high; prior studies have shown the operative mortality rates of 10–30 % with experienced cardiac surgeons [21].

Finally, in this case, we conclude that MDR - *S. paucimobilis* could cause early PVE, particularly in the immunocompromised patient. Even though early surgery is associated with a high mortality rate, it should be proposed to prevent death.

Limitation

We did not perform any cultures of solutions or devices from the OR environment.

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Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent

Informed consent was obtained from all individual participants included in the study.

CRediT authorship contribution statement

Aninka Saboe: Conceptualization, Data curation, Writing - original draft, Writing - review & editing, Supervision. **Yudri Adrian:** Conceptualization, Writing - original draft, Data curation. **Leonardus Widyatmoko:** Conceptualization, Writing - original draft, Data curation. **Melawati Hasan:** Writing - review & editing, Data curation. **Charlotte Johanna Cool:** Writing - review & editing. **Yovita Hartantri:** Writing - review & editing. **Andri Reza Rahmadi:** Writing - review & editing. **Rama Nusjirwan:** Writing - review & editing. **Mohammad Rizki Akbar:** Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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