Dehiscence of a Mechanical Aortic Valve Secondary to Culture-Negative Endocarditis Complicated by Acute Heart Failure

Harry Klimis, MBBS, FRACP, Mikhail Altman, MD, PhD, FRACP, Richard Chard, MBBS, FRACS, Michael Skinner, MBBS, PhD, FRACP, and Liza Thomas, MBBS, PhD, FRACP, Camperdown, Westmead, and Sydney, Australia

INTRODUCTION

Culture-negative endocarditis constitutes up to 16% to 18% of prosthetic valve endocarditis (PVE)\(^1,2\) and can rarely be complicated by prosthetic aortic valve (AV) dehiscence. We report the case of a patient with culture-negative endocarditis affecting a mechanical bileaflet AV resulting in valve dehiscence, severe paravalvular aortic regurgitation (AR) and acute left ventricular (LV) failure, complicated by aortic root homograft pseudoaneurysm. A detailed case report and brief overview of dehiscence of prosthetic valves are presented, and the utility of three-dimensional echocardiography and multimodality imaging highlighted.

CASE PRESENTATION

A 66-year-old man presented to the emergency department with sudden-onset dyspnea and was found to be in heart failure. The patient had undergone mechanical AV replacement (25-mm On-X bileaflet; CryoLife, Kennesaw, GA) 1 year prior for severe aortic stenosis with preserved LV ejection fraction. There was only minor coronary artery disease on computed tomographic coronary angiography before valve replacement. Other background medical history included permanent pacemaker with single right ventricular lead for complete heart block in the context of permanent atrial fibrillation and sick sinus syndrome and chronic obstructive pulmonary disease. His predominant symptom was exertional dyspnea, elicited on mobilizing very short distances. This was associated with atypical nonpleuritic right-sided chest pain. However, the patient reported no fevers or cough. The patient was independent in activities of daily living before onset dyspnea and was found to be in heart failure. The patient had a cardiac arrest with pulseless electrical activity and downtime of 30 min before return of spontaneous circulation. There was no pulmonary embolus on computed tomographic pulmonary angiography. The patient developed cardiorespiratory failure necessitating intubation and inotropes (dobutamine and noradrenaline), complicated by ischemic hepatitis with coagulopathy (international normalized ratio 8.9), and acute renal failure (creatinine 150 \(\mu\)mol/L, 90 mmol/L at baseline) with lactic acidosis (lactate 16 mmol/L, pH 7.19). The cause for acute deterioration was unclear. Inflammatory markers were raised (white cell count 22.0 \(\times\) 10\(^9\)/L, C-reactive protein 150 mg/L), but the patient was never febrile, and detailed septic screen was negative. The patient was treated for presumed sepsis with meropenem after consultation with the infectious diseases team.

The patient’s condition deteriorated gradually over 4 days, and he had a cardiac arrest with pulseless electrical activity and downtime of 30 min before return of spontaneous circulation. There was no pulmonary embolus on computed tomographic pulmonary angiography. The patient developed cardiopulmonary arrest necessitating intubation and inotropes (dobutamine and noradrenaline), complicated by ischemic hepatitis with coagulopathy (international normalized ratio 8.9), and acute renal failure (creatinine 150 \(\mu\)mol/L, 90 mmol/L at baseline) with lactic acidosis (lactate 16 mmol/L, pH 7.19). The cause for acute deterioration was unclear. Inflammatory markers were raised (white cell count 22.0 \(\times\) 10\(^9\)/L, C-reactive protein 150 mg/L), but the patient was never febrile, and detailed septic screen was negative. The patient was treated for presumed sepsis with meropenem after consultation with the infectious diseases team.

The coagulopathy was corrected, and the patient stabilized with a new AR murmur heard. Thus, transthoracic echocardiography (TTE) was performed, which demonstrated rocking of the prosthetic AV (Figure 3C, Video 3C) with severe eccentric paravalvular AR (diasstolic flow reversal in the descending aorta). Three-dimensional acquisition demonstrated dehiscence of the prosthetic valve annulus (or sewing ring) in the region of the native left coronary cusp (\(\sim\)3 o’clock to 6 o’clock using the interatrial septum as 12 o’clock) involving 25% of the circumference (Figures 3A and 3B). There were no obvious vegetations or root abscess. The aortic root was dilated (42 × 44 mm at the sinuses of Valsalva), the left ventricle was dilated, and there was moderate to severe biventricular dysfunction despite inotropes. Antimicrobial treatment was changed to ceftriaxone and vancomycin for broad-spectrum coverage and moxifloxacin, azithromycin, and rifampicin for Mycobacterium spp. The

From the University of Sydney, Camperdown, Australia (H.K., M.A., L.T.); the Department of Cardiology, Westmead Hospital, Westmead (H.K., M.A., M.S., L.T.); the Westmead Applied Research Centre, Westmead Clinical School, University of Sydney (H.K.); South West Clinical School, University of New South Wales (L.T.); and the Department of Cardiothoracics, Westmead Hospital (R.C.), Sydney, Australia.

Keywords: Infective endocarditis, Culture-negative endocarditis, Prosthetic valve endocarditis, Aortic valve, Dehiscence

Conflicts of interest: The authors reported no actual or potential conflicts of interest relative to this document.

Crown Copyright 2019. Published by Elsevier Inc. on behalf of the American Society of Echocardiography. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

2468-6441
https://doi.org/10.1016/j.case.2019.04.008
patient proceeded to undergo an urgent redo sternotomy with AV, root, and ascending aorta replacement with a 24-mm cadaveric homograft. The surgeon noted that the mechanical prosthesis was held only by two sutures, and the annulus was largely “liquified” along the suture line. There was no overt abscess formation. The cause of dehiscence appeared infectious. Blood and tissue fungal cultures were negative. Blood and tissue mycobacterial cultures, polymerase chain reaction, and acid-fast bacilli cultures were negative. Blood and tissue Legionella nucleic acid test results were similarly negative. Blood polymerase chain reaction for Bartonella henselae and Tropheryma whippelii were negative. We performed 16S recombinant ribonucleic acid gene sequencing using polymerase chain reaction on AV tissue samples, and similarly this did not identify any pathogen, including Coxiella burnetii.

Repeat TTE 3 days postoperatively demonstrated marked improvement in LV systolic function, and the homograft appeared to function normally with trivial central AR (Figure 4, Video 4). The patient was discharged 1 month later on a 6-week course of ceftriaxone 2 g daily intravenously.

The patient underwent cardiac computed tomography 1 month after discharge. This showed a false aneurysm anterior to the noncoronary cusp of the homograft extending from the LV outflow tract (Figure 5). TEE confirmed this and demonstrated flow during systole into the false aneurysm with systolic collapse of the noncoronary cusp of the AV. The aortic root was dilated, measuring 42 x 44 mm at the sinuses of Valsalva.

**DISCUSSION**

This case highlights the occurrence of early-onset (within 12 months) culture-negative endocarditis in the setting of a mechanical AV and the importance of three-dimensional TEE in both diagnosis and guidance of surgical treatment. In our case, absence of fevers, negative blood cultures, and early TTE, which did not demonstrate vegetations with what was considered mild paravalvular leak (severely underestimated because of the extremely eccentric AR jet, with shadowing and artifact from the mechanical prosthesis), delayed the diagnosis and urgent surgical treatment. TEE using three-dimensional echocardiography identified severe paravalvular leak and dehiscence of the mechanical prosthesis, including the point of disjunction along the annulus, which was able to direct surgical treatment. Microbiologic test results of blood and tissue samples were negative for the usual bacterial pathogens, Mycobacterium spp, HACEK organisms, C burnetii, Bartonella...
spp, and *T. whipplei*. The reason for culture-negative endocarditis may be because of antibiotic treatment before adequate microbiologic investigation or, much less likely, noninfective endocarditis. This case also documents the rare occurrence of a noninfective pseudoaneurysm complicating homograft treatment of early PVE.

PVE has an incidence of 0.3% to 1.2% per patient-year, and is a serious complication of surgical valve replacement, with combined risk for mortality and morbidity ranging from 20% up to 80% for AV endocarditis. Most patients die of heart failure and cardiogenic shock. The most common organism in PVE is *Staphylococcus aureus* (23%), followed by coagulase-negative *Staphylococcus* (17%), and health-care–associated PVE has been seen to occur in 37% of patients. The clinical presentation of PVE can be atypical and more difficult to diagnose than native valve endocarditis. Positive blood cultures and vegetations are less frequently seen in PVE compared with native valve endocarditis, whereas abscess formation is more frequent. Negative echocardiographic findings may occur because of small or absent (as in our case) vegetations or because of difficulty with detecting them in the context of a prosthesis with associated shadowing and artifact. Unlike native valve endocarditis, the Duke criteria cannot be applied to PVE, because of lower sensitivity. The infection in PVE is usually localized to the prosthesis-tissue junction at the sewing ring, accompanied by tissue destruction leading to dehiscence and paravalvular leak. TEE is crucial in the diagnosis of infective endocarditis, especially PVE. However, both TTE and TEE have lower sensitivity and specificity for PVE compared with native valve endocarditis.

Complications of PVE include paravalvular abscess formation, prosthetic regurgitation, heart failure, dehiscence or prosthesis malfunction, systemic embolization of vegetations, complete heart block, and multiorgan failure. In a prospective, observational multicenter cohort study involving 556 patients with definite PVE, 71% of health care–associated PVE occurred between 60 days and 1 years of implantation. Surgery was performed in 49% during the index hospitalization,
In-hospital death occurred in 23%. In-hospital death was predicted by older age, healthcare–associated infection, *S. aureus* infection, and complications of PVE, including heart failure (33%), stroke (34%), intracardiac abscess (33%), and persistent bacteremia (55%).

Severe heart failure, prosthetic valve dehiscence, and *Staphylococcus* infection are independent predictors of long-term mortality.

Blood culture–negative endocarditis may be due to highly fastidious microorganisms (e.g., HACEK bacteria) or intracellular bacteria that cannot be routinely cultured in blood (e.g., *C. burnetii*, *Bartonella* spp, *T. whipplei*), and inadequate microbiological techniques. Culture-negative endocarditis has a slow clinical progression and history of treatment with antimicrobials before blood cultures. Noninfectious endocarditis is rare and usually due to marantic endocarditis and endocarditis secondary to autoimmune diseases. The predominant etiologies of culture-negative endocarditis after PVE have been shown in a study to be predominately fungal infections (16%), compared with community-acquired culture-negative endocarditis, which is due predominately to *C. burnetii* (36.5%) and *Bartonella* spp (14%).

Surgery is the recommended treatment strategy in PVE complicated by prosthetic dysfunction or heart failure (as in our case) and is associated with a better prognosis compared with medical therapy. However, there is no difference in mortality in
uncomplicated PVE treated with a medical versus surgical approach. Our case was additionally complicated by pseudoaneurysm formation involving the homograft requiring early reoperation. Reinfection following homograft replacement for PVE has been reported to occur in 4.9%, and most occurred early (i.e., <60 days after surgery). However, in our case, the cause of the pseudoaneurysm did not appear to be reinfection from macroscopic appearance of tissue during the surgery. A review of the literature regarding aortic root pseudoaneurysms (outside the context of reinfection) following homograft for PVE yielded no similar reports. However, there was a similar case involving a pseudoaneurysm following porcine AV replacement treated with a homograft.

CONCLUSION

We report a case of severe paravalvular AR causing acute LV failure secondary to culture-negative endocarditis with mechanical AV dehiscence. Absence of fever, negative blood cultures, and lack of vegetations on TTE may delay correct diagnosis and appropriate treatment, hence causing progressive tissue damage. Early diagnosis and prompt surgical treatment of complicated PVE is required. Three-dimensional TEE is useful in identifying the etiology of the severity of AR in this instance. In the absence of typical features of infective endocarditis (fever, positive blood cultures, and vegetations), acute valvular insufficiency (especially an eccentric jet) and LV failure should still raise the suspicion of culture negative endocarditis. Pseudoaneurysm involving aortic homograft is rare and can occur without reinfection.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2019.04.008.

REFERENCES

1. Lopez J, Revilla A, Vilacosta I, Villacorta E, Gonzalez-Juanatey C, Gomez I, et al. Definition, clinical profile, microbiological spectrum, and prognostic factors of early-onset prosthetic valve endocarditis. Eur Heart J 2007;28:760-5.
2. Alonso-Valle H, Farinas-Alvarez C, Garcia-Palomino JD, Bernal JM, Martin-Duran R, Gutierrez Diez IF, et al. Clinical course and predictors of death in prosthetic valve endocarditis over a 20 year period. J Thorac Cardiovasc Surg 2010;139:887-93.
3. Habib G, Thuny F, Avierinos JF. Prosthetic valve endocarditis: current approach and therapeutic options. Prog Cardiovasc Dis 2008;50:274-81.
4. Foster E. Clinical practice. Mitral regurgitation due to degenerative mitral-valve disease. N Engl J Med 2010;363:156-65.
5. Wang A, Athan E, Pappas PA, Fowler VG Jr, Olaison L, Pare C, et al. Contemporary clinical profile and outcome of prosthetic valve endocarditis. JAMA 2007;297:1354-61.
6. Matsukuma S, Eishi K, Tanigawa K, Miura T, Matsumaru I, Hisatomy K, et al. Afebrile pannus-induced blood culture-negative mechanical valve endocarditis. Ann Thorac Surg 2016;102:e511-3.
7. Habib G, Derumeaux G, Avierinos JF, Casalta JP, Jamal F, Volot F, et al. Value and limitations of the Duke criteria for the diagnosis of infective endocarditis. J Am Coll Cardiol 1999;33:2023-9.
8. Habib G. Management of infective endocarditis. Heart 2006;92:124-30.
9. Lamas CC, Eykyn SJ. Suggested modifications to the Duke criteria for the clinical diagnosis of native valve and prosthetic valve endocarditis: analysis of 118 pathologically proven cases. Clin Infect Dis 1997;25:713-9.
10. Mahesh B, Angelini G, Caputo M, Jin XY, Bryan A. Prosthetic valve endocarditis. Ann Thorac Surg 2005;80:1151-8.
11. Habib G, Tribouilloy C, Thuny F, Giorgi R, Brahimi A, Amazouz M, et al. Prosthetic valve endocarditis: who needs surgery? A multicentre study of 104 cases. Heart 2005;91:954-9.
12. Thuny F, Fournier PE, Casalta JP, Gouret F, Lepidi H, Riberi A, et al. Investigation of blood culture-negative early prosthetic valve endocarditis reveals high prevalence of fungi. Heart 2010;96:743-7.
13. Tattevin P, Watt G, Revest M, Arvieux C, Fournier PE. Update on blood culture-negative endocarditis. Med Mal Infect 2015;45:1-8.
14. Musci M, Weng Y, Hubler M, Amiri A, Pasic M, Kosky S, et al. Homograft aortic root replacement in native or prosthetic active infective endocarditis: twenty-year single-center experience. J Thorac Cardiovasc Surg 2010;139:665-73.
15. Tsai KT, Cheng NJ, Chu JJ, Lin PJ. Aortic root pseudoaneurysm following surgery for aortic valve endocarditis. Chang Gung Med J 2002;25:133-8.