

Three-valve endocarditis in a patient with bioprosthetic aortic valve replacement and intravenous drug use: a case report

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Background

Here, we outline the case of a US Veteran's Health Administration (VA) patient with a history of recent bioprosthetic aortic valve replacement (AVR) and recent intravenous drug use (IVDU) who was found to have three-valve infective endocarditis (IE) resulting in septic shock. We highlight this case because it represents an uncommon case of three-valve IE in the setting of recent bioprosthetic valve replacement and IVDU, and it raises the need for continued awareness of mental health and drug rehabilitation in the US military veteran population.

Case summary

A 62-year-old gentleman with recent bioprosthetic AVR presented with dyspnoea and lower extremity oedema and was found to have a heart failure exacerbation. He developed sepsis and was found to have three-valve endocarditis, as well as aortic root abscess and pacemaker lead infection. He was treated with broad-spectrum antibiotics and evaluated for surgical intervention. After discussion with the surgical team, the patient decided not to pursue surgery due to prohibitively high perioperative mortality risk. The patient was transferred to hospice and expired within 2 weeks.

Discussion

Three-valve IE is sparingly documented in published literature and can be difficult to treat. Providers must be cognizant of prosthetic valve endocarditis as an uncommon but known complication of valve replacement surgery. Intravenous drug use is a common risk factor for endocarditis and is prevalent in the US military veteran population. Prosthetic valve endocarditis should be treated with broad-spectrum antibiotics, and in general, if it leads to new significant valvular abnormalities, the valve should be replaced.

Keywords

Infective endocarditis • Multivalve endocarditis • Heart failure • Intravenous drug use • Case report

Learning points

- Involvement of three valves in endocarditis is rare and can be difficult to treat.
- Providers must be cognizant of prosthetic valve endocarditis.
- Intravenous drug use is a major risk factor for endocarditis and is a public health concern.

Introduction

Infective endocarditis (IE) remains a disease associated with significant morbidity and mortality. Recent studies estimate an incidence of 10–15 per 100 000 in the USA from the year 2000 to 2015.^{1,2} Approximately 30% of patients die within 1 year of diagnosis. Here, we present a case of three-valve endocarditis refractory to surgical

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management, in the setting of intravenous drug use (IVDU) and recent aortic bioprosthetic valve replacement.

Timeline

Day 1	Patient presented with dyspnoea on exertion, bilateral lower extremity oedema, and rhinorrhoea of 1 week duration Systolic murmur auscultated at aortic area Patient found to be in heart failure exacerbation
Day 3	Patient developed septic shock. Broad-spectrum antibiotics and vasopressors were started
Day 5	Blood cultures resulted in methicillin-resistant <i>Staphylococcus aureus</i> and <i>Lactobacillus</i> . Repeat transthoracic echocardiogram showed 2- to 3-mm vegetation on the aortic valve
Day 8	Patient transferred to private hospital. Transoesophageal echocardiogram reveals three-valve endocarditis, aortic root abscess, and pacemaker lead infection
Day 9	Cardiovascular and thoracic surgery service determines patient is not a candidate for surgery. Patient decides to be transferred to hospice
Day 22	Patient expired

Case presentation

A 62-year-old gentleman presented to a VA hospital in 2018 with dyspnoea on exertion, bilateral lower extremity oedema, fever, and rhinorrhoea of 1 week duration. His past medical history was significant for diastolic heart failure with preserved ejection fraction, coronary artery disease (CAD) status post (s/p) three stents in early 2015, coronary artery bypass graft (CABG) in late 2015, aortic stenosis s/p aortic valve replacement (AVR) in 2015, aortic valve thrombosis in 2018 requiring bioprosthetic valve replacement, sick sinus syndrome s/p dual-chamber pacemaker 2016, atrial fibrillation, and IVDU. Other morbidities included diabetes mellitus, hypertension, post-traumatic stress disorder (PTSD), and chronic back pain. On admission, a systolic murmur was auscultated at the aortic area. Erythematous, non-tender macules were noted on the bilateral palms. The patient was found to have a heart failure exacerbation, likely secondary to an upper respiratory tract infection and recent inability to obtain diuretic medication. On admission, the patient's nares were found to be methicillin-resistant *Staphylococcus aureus* (MRSA) positive, for which he was on contact isolation for the entirety of his hospitalization. The patient also reported amphetamine and opiate IVDU. Transthoracic echocardiogram (TTE) on admission revealed impaired left ventricular relaxation, but the valves were not adequately visualized. The patient symptomatically and objectively improved with diuretics over the next 5 days.

A few days later, the patient began feeling confused and less oriented. His temperature rose to 101°F (39.3°C) and his systolic blood pressure dropped to 70 mmHg. The patient was upgraded to the

intensive care unit and started on vasopressors. Computed tomography of the head without contrast showed no acute abnormalities. Blood cultures showed methicillin-susceptible *Staphylococcus aureus* (MSSA). The patient's C-reactive protein was 168 mg/L and the white blood cell count was $21 \times 10^9/L$. He was started on broad-spectrum intravenous (IV) antibiotics and the infectious disease service was consulted. Repeat blood cultures showed MRSA and *Lactobacillus*. Repeat TTE showed a 3-mm vegetation on the aortic valve. After consultation with the infectious disease team, IV antibiotics were initiated, including vancomycin, rifampin, and gentamicin, as well as piperacillin-tazobactam for *Lactobacillus*. The cardiology service attempted a transoesophageal echocardiogram (TEE), but it was aborted because the patient's oxygen saturation dropped to 70% on 2L nasal cannula with anaesthesia administration. After 5 days of broad-spectrum IV antibiotics, the patient's temperature and inflammatory lab markers remained elevated. His orientation had improved but was still not at baseline. The decision was made to transfer him to a private hospital, as the admitting hospital did not have a cardiovascular and thoracic (CVT) surgery service.

After transfer, the patient was continued on broad-spectrum IV antibiotics. TEE showed extensive vegetations of the aortic, mitral, and tricuspid valve with new-onset severe mitral regurgitation and severe tricuspid regurgitation (Figure 1, Supplementary material online, Video S1). The aortic valve showed fusion of all cusps and critical valvular stenosis. The tricuspid valve showed valvular destruction.

Aortic root abscess and pacemaker lead infection was also noted. The CVT service evaluated and determined that full intervention would include aortic root repair, AVR, mitral valve replacement, tricuspid valve replacement, and pacemaker removal. Using an updated version of The Society of Thoracic Surgeons risk calculator mentioned in the European Heart Journal (EHJ), they approximated the risk of mortality for intervention as greater than 90%.³⁻⁵ Several factors contributed to this elevated risk. This would have been the third reoperation of the aortic valve. Also, multiple severe valvular abnormalities were present, which would each require replacement and could not be salvaged by debridement only. Other significant causes of increased mortality risk were the patient's acute kidney injury with creatinine of 5.1 mg/dL, history of CAD with CABG, heart failure, atrial fibrillation, and age. This mortality risk was for isolated AVR only, which led surgeons to believe that the replacement of three valves would be even more complicated. When presented with this information, the patient decided that surgical intervention would not be beneficial and chose hospice care so that he could have an opportunity to pass away in a more peaceful manner. He was continued on IV antibiotics and expired under hospice care in the hospital 2 weeks after his transfer, due to septic shock and disseminated intravascular coagulation.

Discussion

The patient had multiple risk factors for endocarditis, many of which merit separate discussion. In a large study in Spain, focusing on multi-valve endocarditis, 680 patients diagnosed with endocarditis were studied over a 13-year period, and 17% had multiple valves affected.⁶ Predictors of hospital mortality were heart failure and persistent infection despite antibiotics, both of which were present in our

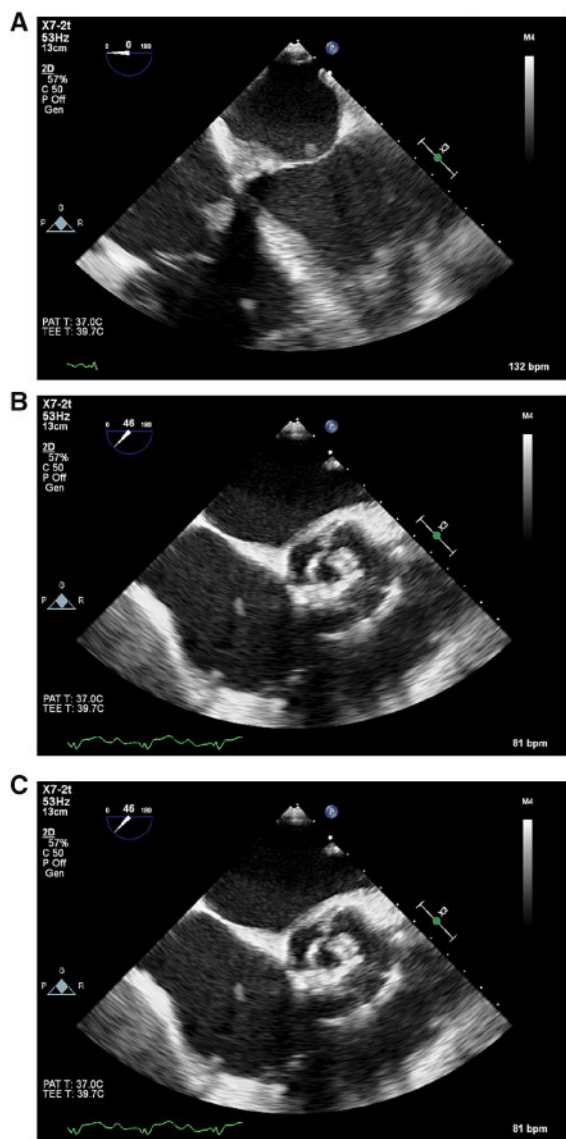


Figure 1 Transoesophageal echocardiogram. (A) Mitral valve vegetation. (B) Tricuspid valve vegetation with localized destruction of valve. (C) Bioprosthetic aortic valve vegetation.

patient's case. Similar findings were present in a study of 77 patients with endocarditis at Winthrop Hospital in New York from 1990 to 1994. The study found that 18% of patients had multivalve endocarditis, with no patients having involvement of three valves.⁷ Only congestive heart failure was found to be statistically more common in multivalve than single valve endocarditis. In general, endocarditis with involvement of three or more valves is rare and literature consists of isolated case reports.

Prosthetic valve endocarditis (PVE) is defined as early if it occurs in 12 months or less post-operatively and late if it occurs greater than 12 months post-operatively.^{3,8} Our patient had early PVE, as he had a bioprosthetic AVR 8 months before his hospitalization. A study

published in 2018 in the EHJ analysed 18 041 patients who underwent left-sided valve replacement from 1996 to 2015 in Denmark.⁹ The incidence of IE was 44.3 per 10 000 person-years in patients with mechanical valve and 88.4 per 10 000 person-years in patients with bioprosthetic AVR. The prevalence of endocarditis in AVR was 64.9 per 10 000 person-years. For patients with AVR, cardiovascular implantable electronic device, male sex, bioprosthetic valve, atrial fibrillation, cancer, and diabetes were associated with an increased risk of IE. Our patient had all of these risk factors except for cancer. Three-valve endocarditis as a complication of recent bioprosthetic valve replacement is exceedingly rare and we were unable to find any specific instances in published literature.

The risk of PVE is highest during the first 60 days and gradually decreases. The overall risk is approximately 0.1–2.3% per person years.^{8–12} Early-onset PVE can occur because the sewing ring, annulus, and sutures are not endothelialized, which provides a nidus for abscesses and can lead to dehiscence.¹³ The pathogenesis of late infection is thought to be similar to native valve endocarditis.¹⁴ *Staphylococcus aureus* is the most common organism in PVE and accounted for 23% of total cases in the International Collaboration on Endocarditis Prospective Cohort Study, which studied 2670 patients with endocarditis from June 2000 to August 2005. About 14.7% of patients had MSSA infection, while 6.5% had MRSA infection, as the patient in our case did.¹⁵

The American Heart Association guidelines recommend combination therapy for PVE due to the high mortality rate.⁸ For endocarditis involving prosthetic heart valve caused by MRSA, a regimen of IV vancomycin and IV rifampin is recommended for at least 6 weeks, in combination with gentamicin for the initial 2 weeks of therapy. Specifically mentioned in the guidelines is rifampin's role in sterilization of foreign bodies infected by MRSA.⁸ Valvular abnormalities with indications for surgery include acute aortic or mitral insufficiency with signs of ventricular failure, perforation, dehiscence, rupture, fistula, or perivalvular extension.⁸ Other indications include new heart block, heart failure unresponsive to medical therapy, large abscess, or extension of abscess despite appropriate antimicrobial therapy, persistent vegetation after systemic embolization, anterior mitral leaflet vegetation particularly with size >10 mm, embolic events during first 2 weeks of antimicrobial therapy, increase in vegetation size or persistent bacteraemia despite appropriate antimicrobial therapy, and PVE caused by fungi or other highly resistant organisms.⁸

Our patient's other significant factor for endocarditis was IV amphetamine and opiate use after his AVR. IV drug users are at increased risk for endocarditis due to the use of contaminated injection equipment, increased rates of *S. aureus* nasal colonization, and damage to the endothelium of valves by injected particles.^{16–19} Patients with IVU are especially prone to developing right-sided endocarditis (RSE). As our patient also had a pacemaker, he was at marked risk for RSE. Indications for surgery for RSE include microorganisms difficult to eradicate, bacteraemia for 7 or more days despite antimicrobial therapy, persistent vegetation greater than 20 mm after recurrent pulmonary emboli with or without concomitant right heart failure or, right heart failure due to severe tricuspid regurgitation that does not respond to diuretic therapy.³ Right-sided endocarditis is generally associated with better outcomes than left-sided endocarditis (LSE), while surgical outcomes are similar for RSE and LSE.²⁰ Right-sided

endocarditis is associated with less mortality compared with patients such as ours with endocarditis involving both the right and left side.²¹

Although IV drug users are generally in the age range of 20–30,¹⁹ this case brings to attention the risk of opiate use and IVDU in the US veteran population. This patient had chronic back pain due to injuries suffered during military service and had been diagnosed with PTSD and major depressive disorder. He was following at the mental health clinic at the VA but was lost to follow-up for more than 1 year before this hospitalization and began using IV drugs as a coping mechanism. Per the VA, more than 2 out of 10 veterans with PTSD have substance use disorder (SUD) and almost one of three veterans seeking treatment for SUD also has PTSD.²² Veterans with co-occurring depression and substance use require close follow-up and special interventions with a multidisciplinary approach to prevent IVDU and opiate addiction. The VA has recently put forth a large-scale effort towards treating veterans' chronic pain and depression, but much effort remains to be undertaken, as witnessed by this case.²³

Conclusion

We describe this patient's case, because it represents a unique presentation of early bioprosthetic valve replacement endocarditis with three-valve involvement in the setting of IVDU in a military veteran with history of PTSD and depression. The intersection of multiple disciplines in this case provides medical, social, and behavioural learning points and underscores the role of primary prevention for such patients, as every patient cannot be cured with surgery. The unfortunate outcome in this case stresses the importance of early intervention and close follow-up in patients with multiple comorbidities and risk factors for endocarditis.

Lead author biography



Dr Awad Javaid is currently completing his internal medicine residency at the University of Nevada Las Vegas School of Medicine. He plans to pursue a fellowship in cardiology. He was born and raised in Houston, TX, USA.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

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's next of kin in line with COPE guidance.

Conflict of interest: none declared.

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