CASE REPORT

Early prosthetic valve endocarditis after transcatheter aortic valve implantation using St Jude Medical Portico valve

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SUMMARY

An 87-year-old woman presented to the emergency department with a 2-week history of progressively worsening shortness of breath, fever and generalised myalgia. She underwent a transcatheter Portico aortic valve implantation for severe symptomatic aortic stenosis 3 months prior to this presentation. Examination revealed a temperature of 40°C and a systolic murmur in the aortic area. Inflammatory markers were elevated, and blood cultures were positive for methicillin-sensitive *Staphylococcus aureus*. A possible diagnosis of infective endocarditis was made as one major and one minor criterion in the modified Duke criteria were fulfilled. Subsequent transoesophageal echocardiography (TOE) demonstrated vegetation attached to the prosthetic valve stent frame at the level of the left ventricular outflow tract. She was started on a prolonged course of intravenous antibiotics, and follow-up TOE, 4 weeks later, confirmed resolution of the vegetation. She was discharged home after prolonged hospital stay.

BACKGROUND

Transcatheter aortic valve implantation (TAVI) has recently become the preferred treatment for severe aortic stenosis in patients who are considered high-risk candidates for surgical aortic valve replacement.¹ Portico Transcatheter Aortic Heart Valve (St Jude's Medical, Saint Paul, Minnesota, USA) has been recently developed to surmount the disadvantages of first-generation devices.² Portico valve is unique as it is self-expanding, fully resheathable and repositionable. Studies have shown significantly favourable clinical and haemodynamic results with low immediate and 30-day mortality and neurological events.^{2,3} Prosthetic valve endocarditis (PVE) post-TAVI is rare with a reported incidence of 0.1%–3.03%.^{4,5}

CASE PRESENTATION

An 87-year-old woman presented to the emergency department with a 2-week history of progressively worsening shortness of breath, cough, rigours, lethargy and generalised myalgia. She was haemodynamically stable with temperature of 40°C. On clinical examination, there was no peripheral stigmata of endocarditis. Heart sounds S1 and S2 were audible with a soft systolic murmur loudest in the aortic region. Her respiratory, abdominal, and neurological examinations were unremarkable. After heart team discussion she underwent a transfemoral

TAVI procedure for severe, symptomatic aortic stenosis 3 months prior to this presentation, using a 25 mm Portico Transcatheter Aortic Heart Valve. This was performed under conscious sedation, without complications. The valve was inserted in a good position; postprocedure imaging showed a mean gradient of 10 mm Hg without evidence of aortic incompetence and only trivial paravalvular leak. The patient was not known to have diabetes mellitus or any other known risk factors for PVE and was discharged in a good condition 4 days after the procedure.

INVESTIGATIONS

Her blood tests on admission showed a white cell count of 10.46×10^9 per litre, neutrophils of 9.82×10^9 per litre, haemoglobin of 11.6 g per decilitre and low platelet count of 59×10^9 per litre. Inflammatory markers showed an elevated C reactive protein (CRP) at 339 mg/L (<5 mg/L) and lactate of 1.9. Biochemistry revealed an elevated urea of 10.7 millimole per litre (2.5–7.8) and creatinine of 105 micromole per litre (50–98). Her potassium was low at 2.8 millimole per litre (3.5–5.3) and serum sodium was normal at 137 millimole per litre (133–146). Urine dipstick was negative for nitrates, leucocytes and red blood cells, and chest X-ray showed no evidence of acute infection. Three blood cultures were taken from different sites, from her forearm and antecubital fossae, within 24 hours of presentation, and they were positive for methicillin-sensitive *Staphylococcus aureus* in both aerobic and anaerobic bottles.

Transthoracic echocardiography (TTE) showed normal left ventricular systolic function and mild diastolic dysfunction. Prosthetic aortic valve was noted to be well seated with peak gradient of 27 mm Hg and mean gradient of 13 mm Hg with no obvious vegetation. Due to the high suspicion of PVE, a transoesophageal echocardiography (TOE) was arranged, which clearly visualised the prosthetic aortic valve and confirmed the presence of vegetation attached to the stent frame at the level of the left ventricular outflow tract (videos 1 and 2). Follow-up TOE, 4 weeks after treatment, confirmed resolution of the prosthetic aortic valve vegetation (video 3).

DIFFERENTIAL DIAGNOSIS

- Sepsis secondary to respiratory tract infection.
- Sepsis secondary to urinary tract infection.

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Video 1 TOE showing the prosthetic aortic valve and vegetation attached to the stent frame at the level of the left ventricular outflow tract. TOE, transoesophageal echocardiography.

TREATMENT

Empiric therapy with rifampicin, vancomycin and gentamycin was initiated due to documented penicillin allergy. After 3 weeks, she developed acute kidney injury (AKI) possibly secondary to this regime of antibiotics. Subsequently, it was changed to meropenem and daptomycin for 6 weeks as advised by our local microbiology and infectious disease (ID) departments, as she spiked a temperature up to 38.9°C on the first regime of antibiotics (total duration of 9 weeks of antibiotics).

OUTCOME AND FOLLOW-UP

After completion of antibiotic treatment, her symptoms and temperature had resolved, CRP normalised (14 mg/L) and her AKI resolved with conservative treatment. She was discharged in a good condition. She remained well at 3-month follow-up and returned to baseline functional capacity post-TAVI.

DISCUSSION

TAVI has become the treatment of choice in patients with symptomatic severe aortic stenosis who are either inoperable or at

Video 2 TOE showing the prosthetic aortic valve and vegetation attached to the stent frame at the level of the left ventricular outflow tract. TOE, transoesophageal echocardiography.

Video 3 Follow-up TOE, 4 weeks after treatment, showing resolution of the prosthetic aortic valve vegetation. TOE, transoesophageal echocardiography.

high risk for conventional surgical aortic valve replacement.⁶ PVE post-TAVI is a rare but serious condition that has potential life-threatening complications.⁷ Many cases of PVE post-TAVI have been reported in the literature in the last few years, involving the Medtronic CoreValve, Edwards Sapien and Lotus valves.^{8–10} To our knowledge, this is the first case of infective endocarditis (IE) post-Portico prosthetic aortic valve implantation that was successfully treated medically with complete resolution of symptoms, inflammatory markers and vegetation on follow-up imaging.

The diagnosis of PVE post-TAVI is particularly difficult to establish for various reasons. Patients are elderly, frail, with multiple medical comorbidities, are more likely to present with atypical symptoms, may not have fever and with lesser degree of inflammatory response.¹¹ Duke criteria have 70%–80% sensitivity in native valve endocarditis (NVE), but they have been shown to be less sensitive in PVE with a previously reported sensitivity of 50%–65%.^{12,13} In contrast to NVE, blood cultures are more likely to be negative in PVE, and another major criterion (new valvular regurgitation) is unreliable as patients with prosthetic valves commonly have an audible murmur.¹⁴ Moreover, echocardiography is less sensitive in visualising the vegetation due to native valve extensive calcifications, reflections and shadows of the prosthetic valve. Furthermore, it is difficult to visualise small vegetations in the space between the prosthetic and native valve as a degree of paravalvular regurgitation is relatively common after TAVI.^{9,15} Duke criteria should be used to guide diagnosis of IE and not to replace our clinical judgement.¹⁶ TOE is indicated in all patients with suspected PVE, but a negative or inconclusive study is often observed.¹⁷ Recent study demonstrated significant benefit of ¹⁸F-fluorodeoxyglucose positron emission tomography/CT (¹⁸F-FDG PET/CT) in diagnosing PVE. It showed that 50% of the patients with suspected PVE had abnormal FDG uptake around the prosthetic valve (sensitivity 95%, specificity 73%). The study also demonstrated significantly increased sensitivity of modified Duke criteria (97% vs 70%) when abnormal FDG uptake added as a new major criterion.¹⁸ If there is a suspicion of PVE, repeated blood cultures and repeated TTE and TOE should be performed along with consideration of PET/CT to aid confirmation of the diagnosis.¹⁹

PVE can occur early or late depending on the onset of symptoms after implantation of the prosthetic valve. Early PVE occurs

within the first 12 months after implantation, whereas late PVE occurs after 12 months.²⁰ Previous studies showed that approximately 70% of PVE cases occur within the first 12 months after valve replacement. This was thought to be due the potential attachment of bacteria to the exposed prosthetic valve material as endothelialisation takes around 12 months to complete.²¹ Early PVE carries a higher risk of mortality and tends to have a more serious clinical course compared with late PVE.²⁰ A retrospective multicentre cohort study of 104 patients with early PVE revealed that 22 (21%) died in hospital without significant difference in mortality between patients who had surgical intervention and those who were treated medically.²² The causative micro-organism commonly isolated in PVE differs according to the time elapsed from the procedure. Coagulase-negative Staphylococci are seen more frequently in early PVE when the majority of cases of PVE occur, whereas Streptococci are more commonly isolated in late PVE.²³ Other micro-organisms such as *Enterococcus faecalis* and *Escherichia coli* have also been isolated in some cases.²⁴

Retrospective studies have identified possible predictors of PVE post-TAVI. These include intubation, implantation of self-expandable CoreValve system, vascular complications and suboptimal valve position during implantation.^{25 26} Regueiro *et al* recently identified other factors that are significantly associated with an increased risk of PVE post-TAVI. These include younger age (78.9 vs 81.8), history of diabetes mellitus and moderate to severe residual aortic incompetence.²⁷ While there are no randomised trials to support this, observational studies have suggested reasons that might contribute to the increased risk of PVE with self-expandable valves compared with balloon expandable valves. The large size of the stent frame and the large attachment area between stent frame and the native tissue can be a potential mooring and dissemination point for bacteria and vegetation.²⁵ General measures can be implemented to reduce the risk of IE in patients undergoing TAVI, including perioperative prophylactic antibiotics, strict dental, cutaneous and infection control measures. Performing TAVI under conscious sedation may reduce the risk of PVE by reducing the need for orotracheal intubation and urinary catheterisation.¹⁹

Patients with suspected IE should be managed under the supervision of an endocarditis team (ET). The ET should include a structural and imaging cardiologist, ID specialist, microbiologist and possibly a neurologist. A cardiothoracic surgeon should also be notified and involved early in the patient's care in case surgical intervention is required.¹⁹ Kaura *et al* demonstrated that the involvement of an ET is associated with significant reduction in 1-year mortality of patients with NVE. The study showed a 66.7% survival at 1 year in the group treated under the ET supervision compared with 42.9% without ET supervision ($p=0.03$). Moreover, early involvement of ET showed significant reduction in the time to starting treatment for IE and the time to surgical intervention when indicated ($p=0.004$).²⁸ Therefore, early involvement of the ET is recommended in patients with suspected PVE after TAVI to help reduce mortality and facilitate early diagnosis and treatment. Antibiotic treatment of PVE is similar to NVE; however, a more prolonged course of antibiotics may be needed in *S. aureus* PVE.¹⁹ Prognostic assessment and identification of high-risk patients with PVE is very important as aggressive treatment strategy might be necessary. Poor prognostic features include old age, early staphylococcal PVE and the presence of other chronic comorbidities such as diabetes and heart failure.^{29 30} Surgical intervention can be considered as a treatment option in patients with severe uncontrolled infection

or heart failure, large vegetation or abscess, aneurysm and thromboembolic complications.¹⁵

Learning points

- ▶ Prosthetic valve endocarditis (PVE) post-transcatheter aortic valve implantation (TAVI) is a rare but serious condition that has potential life-threatening complications.
- ▶ Recognising the importance of PVE post-TAVI is crucial in view of the increasing use of TAVI procedures and the anticipated expansion of its indication to low-risk patients.
- ▶ High index of suspicion should be maintained to ensure the diagnosis is not missed or delayed.
- ▶ Modified Duke criteria and echocardiography are less sensitive in the diagnosis of PVE post-TAVI.
- ▶ Transoesophageal echocardiography is more helpful than transthoracic echocardiography, but repeated studies and other imaging modalities such as positron emission tomography/CT should be considered if high index of suspicion of PVE post-TAVI.

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