Case Report

Multimodality imaging in the diagnosis of bioprosthetic aortic valve endocarditis: A case report

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Abstract

Introduction: Prosthetic valve infective endocarditis (PVE) is a diagnostic challenge even in the era of multimodality cardiovascular imaging.

Case presentation: The patient was a 67-year-old male with a three-year history of bioprosthetic aortic valve replacement who presented with persistent fever and negative blood cultures. The initial transthoracic echocardiographic and clinical assessments are possible alternatives when the access to advanced cardiovascular imaging modalities is limited.

Clinical discussion: The diagnosis of PVE and its complications requires the integration of clinical, microbiological, and serial imaging data. Although advanced imaging modalities like PET/CT allow a timely diagnosis and management, their routine use in resource-limited scenarios is difficult.

Conclusion: Multimodality cardiovascular imaging plays an important role in the diagnosis of PVE. Serial echocardiographic and clinical assessments are possible alternatives when the access to advanced cardiovascular imaging modalities is limited.

1. Introduction and importance

Bioprosthetic valve endocarditis (PVE) accounts for approximately one-fifth of infective endocarditis (IE) cases and affects 1–6% of patients with prosthetic heart valves [2]. The in-hospital mortality rate of PVE is 19–40% [2], even with recent advances in surgical techniques and antibiotic treatment. Early diagnosis and treatment of PVE are crucial to prevent complications and improve the prognosis. Nevertheless, this is difficult because PVE has atypical symptoms and higher rates of negative echocardiography and blood culture compared to native valve endocarditis (NVE) [2]. The integration of multiple imaging modalities was introduced in the 2015 European Society of Cardiology (ESC) guidelines [2]. In the era of multimodality imaging, this case report highlights the current diagnostic difficulties in resource-limited settings with a late PVE case complicated by aortic root abscess. The case report was presented in line with the SCARE criteria [3].

2. Case presentation

A 67-year-old male was admitted to the cardiology department with
a one-month history of persistent fever, chills, and fatigue. The patient underwent a bioprosthetic aortic valve replacement (AVR) with a Sorin Freedom SOLO Stentless Tissue Valve aortic valve due to IE three years ago. He reported an unremarkable family history, no illicit drug use, and no recent invasive or dental procedures. Before the admission to our hospital, he was diagnosed with blood culture-negative PVE and was treated with cefoperazone/sulbactam 2g every 12 hours in a secondary hospital for 11 days.

On admission, the patient was febrile (37.7 °C), hemodynamically stable, and had no murmur on cardiac auscultation. The electrocardiogram showed sinus tachycardia at 103 beats per minute. Complete blood count (CBC) showed an increased white blood cell count at 11.12x10^9 per liter and no anemia. His erythrocyte sedimentation rate was elevated (28mm/h), but the level of high sensitivity C-reactive protein (CRP-hs) was normal (0.4 mg/dl). The liver, renal function tests and urine analysis were within the normal range. Three sets of blood cultures using the BacT/AlerT® automated microbial identification system and Vitek-2 compact® identification system were negative. Serologic testing (for Coxiella burnetti, Bartonella spp., Legionella Pneumophila, Brucella spp., Mycoplasma spp., Aspergillus spp.), blood real-time polymerase chain reaction (RT-PCR, for Staphylococcus aureus, Tropheryma whipplei, fungi, Escherichia coli, Streptococci, Enterococci), and antinuclear antibodies were negative.

Initial transthoracic echocardiogram revealed a thickened, non-homogeneous perivalvular area with reduced echo density appearance located at the posterior wall of the aortic root (Fig. 1A-D). The bioprosthetic aortic valve functioned normally without valvular regurgitation and vegetations (mean gradient 6 mmHg, aortic valve area by

![Imaging of the aortic root using TTE (A–D) and MSCT (E–F). Fig. 1A: thickened, non-homogeneous perivalvular area with reduced echo density located at the posterior wall of the aortic root. Fig. 1B: thickened zone of reduced echo density without color Doppler flow signals located at the posterior wall of the aortic root. Fig. 1C-D: axial and sagittal sections of the aortic root did not show clear abscess formation. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)](image-url)
continuity equation 2.64 cm²). Systolic pulmonary artery pressure was mildly elevated (40 mmHg). A non-gated multislice computed tomography (MSCT) angiography of the aorta was inconclusive for PVE (Fig. 1E–F).

Further examination by transesophageal echocardiography (TEE) unveiled an 8 mm focal thickening of the posterior sinus of Valsalva which extended beyond the sinotubular junction (see Fig. 2). The patient was referred for 18F-fluorodeoxyglucose (18F-FDG) PET/CT. Patient preparation and image acquisition were in accordance with the European Association of Nuclear Medicine guidelines [4]. A nuclear radiologist with expertise in PET/CT interpreted the results. High focal radiotracer uptake was detected at the thickened zone of the aortic root with a maximal standardized uptake value (SUV max) of 6.7 g/mL. Whole-body imaging did not reveal any extracardiac complications (Fig. 2D–G).

The patient had one major imaging criterion and a minor criterion (fever); therefore, he was classified as possible IE according to the modified Duke criteria [2]. Treatment was initiated with a six-week antibiotic regimen consisting of vancomycin administered intravenously with doses adjusted every 2–4 days to maintain a serum vancomycin concentration of 15–25 mg/L and of gentamycin 1 mg/kg every 8 hours.

After an initial three weeks of good clinical response, the patient had recurrent 40–41 °C fever. His physical examination did not reveal any skin rash. His CBC showed leukocytosis with normal eosinophil count. Repeated chest radiographs, urine and blood cultures were negative. A second three-dimensional TEE (3D-TEE) was performed by a consultant echocardiographer, which revealed a 10 × 30 mm abscess within the area of focal thickening of the posterior aortic root wall, several small vegetations at the aortic side of the prosthetic aortic valve, and trivial aortic regurgitation.

After consulting the Endocarditis Team, the patient was referred for an urgent redo Bentall procedure with a cryopreserved aortic valve and conduit homograft via median sternotomy with cardiopulmonary bypass. Two consultant cardiothoracic surgeons performed the procedure in a cardiac operating room setting. During intraoperative examination, vegetations on the aortic side of the bioprosthetic valve leaflets and the thickened, necrotic aortic root were visualized. Radical debridement of infected tissues followed by a homograft AVR with aortic root reconstruction was performed. Histopathologic examination of the excised heart valve specimens with hematoxylin and eosin (HE) staining showed signs of an acute inflammatory response (Fig. 3A–C). Broad-range 16S rDNA PCR of the specimens is positive for Streptococcus.

The postoperative period was uneventful with no signs and symptoms of recurrent infections and his CRP-hs level lowered to 0.96 mg/dL. The patient was discharged after a six-week antibiotic therapy with linezolid 600 mg every 12 hours and prolonged aspirin. On follow-ups after 1 and 3 months, the patient referred total remission of fever and good weight gain. Subsequent TTEs showed that the aortic homograft functioned normally (mean gradient 4 mmHg) without residual vegetations or abscesses.

3. Clinical discussion

PVE diagnosis is challenging because of its variability in clinical manifestations and the limitation of diagnostic techniques. Besides, in low-and-middle-income countries (LMICs), patients are often under antibiotic treatment before admission [5], which might cause negative blood cultures. Multimodality imaging should be considered to improve

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**Fig. 2.** 3D TEE (A–C) and PET/CT (D–E) imaging of the aortic root. **Fig. 2A–B:** Static images of the aortic valve and sinus of Valsalva on TEE midesophageal longitudinal view (120°) and short axis view (70°). Thickened zone without color Doppler flow signals (arrowhead). **Fig. 2C:** Vegetations were seen on the endocardium of the aortic root (arrow). **Fig. 2D–G:** 18F-FDG-avid lesion with SUV max of 6.7 g/mL around the bioprosthetic aortic valve on CT (**Fig. 2D**), PET (**Fig. 2E**), fused PET/CT (**Fig. 2F**) and multiple projection image (**Fig. 2G**). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)
diagnostic capabilities [2, 6].

Echocardiography is the cornerstone of PVE diagnosis but can be inconclusive in up to 30% [2]. 3D-TEE provide additional information to guide diagnosis and therapeutic decisions by allowing a more realistic view of vegetations and abscesses, their location with regard to valve anatomy, and their relationship with surrounding tissues [7].

Deterioration of image quality due to motion artifacts is a major limitation of CT imaging of the aortic root and ascending aorta. Electrocardiogram-synchronized protocols may improve the temporal resolution but only when the heart rate is low [8]. However, high resting heart rate is common among IE patients due to fever or heart failure. Even when our patient was afebrile and received rate-control medications (metoprolol 25mg and ivabradine 5mg), the target heart rate could not be achieved. Therefore, non-gated CT was our only option.

The 2015 ESC Guidelines endorsed the use of nuclear imaging in difficult suspected PVE cases because of their excellent sensitivity and specificity in this subset of patients [2]. PET/CT was chosen because it was the only nuclear imaging modality available in our center. It revealed abnormal 18F-FDG uptake of perivalvular tissues beyond 3 months of valve replacement. This constituted a major imaging criterion in the 2015 ESC guidelines; thus, in this patient, a diagnosis of possible IE was established. Definite PVE lesions on TEE may only appear several weeks after disease onset as in this patient.

Aortic wall thickening may be the earliest manifestation of perivalvular abscess formation which mandates serial followed-up imaging [9]. A cut-off value of 5mm on TEE or CT has a sensitivity of 67% and specificity of 95% in detecting PVE beyond three months after AVR [8]. Nevertheless, there is a paucity of literature regarding the optimal imaging follow-up timing. Our patient had a fever relapse during the treatment of IE. The most common causes of fever relapse in IE are abscess formation, extensive infection, drug hypersensitivity, and nosocomial infections [10]. Yeter et al. reported an NVE case with aortic root thickening subsequently became a root abscess after one month despite excellent clinical response to antibiotic therapy [9]. Repeated TTE and TEE are necessary to detect the formation of abscess and the extension of infection.

When the clinical and echocardiographic features are atypical, nuclear cardiac imaging is an invaluable asset to ensure timely diagnosis and appropriate management of PVE because of its ability to pinpoint the exact infection foci. However, the use of this advanced cardiovascular imaging modality in LMICs is not widely applicable. Firstly, the costs of purchasing, long-term maintenance and operating of PET/CT are high. Secondly, a properly trained workforce is needed to operate PET/CT scanners [11]. Finally and most importantly, policies, standards, and guidelines regarding the use of nuclear cardiac imaging are lacking in LMICs [11]. Paradoxically, a high proportion of insurance in LMICs is ineffective, particularly among those who need it most (i.e., poorest) [12]. In our country, because PET/CT scans for the diagnosis of IE is not yet fully covered by the public health insurance, our patient had to go through a lot of paperwork to get insurance coverage. Otherwise, the diagnosis would have been made sooner. Initiatives to improve access to necessary diagnostic imaging tests should be encouraged to implement in a short period of time. In the absence of advanced imaging modalities, serial TTEs and TEEs are possible alternatives.

4. Conclusion

Multimodality imaging is shown to be useful in the diagnosis and management of PVE. Serial echocardiographic and clinical assessments are possible alternatives when the access to advanced cardiovascular imaging modalities is limited.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval

The study received the permission of ethical and scientific committee of Bach Mai hospital to publish patient as paper.
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Author contribution

Hoai Thi Thu Nguyen, Son Tran Thanh Bui, Thom Thi Vu devised the manuscript concept. Son Tran Thanh Bui, Hoai Thi Thu Nguyen, Anh Van Nguyen, Thom Thi Vu belonged to patient’s management team. Hoai Thi Thu Nguyen, Son Tran Thanh Bui performed two-dimensional and three-dimensional echocardiography. Hung Duc Duong, Nam Thanh Phan were the main surgeons. Son Hong Mai interpreted the PET/CT data. Son Tran Thanh Bui wrote the manuscript in collaboration with Hoai Thi Thu Nguyen, Thom Thi Vu, Hung Duc Duong, Nam Thanh Phan, Anh Van Nguyen, Son Hong Mai. Hoai Thi Thu Nguyen took care of revising and submitting the manuscript. All authors read and approved the final manuscript.

Consent

Written informed consent was obtain from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Registration of research studies

As this is a case report and not a human studies, it is exempt from registering.

Guarantor

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Declaration of competing interest

No conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jamsu.2022.104238.

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