CASE REPORT

Diagnosing pulmonic valve infective endocarditis with positron emission tomography-CT

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SUMMARY

Infective endocarditis (IE) affects the pulmonic valve in less than 2% of cases. Not only is pulmonary valve IE rare, it is also challenging to visualise with commonly used imaging modalities. In this vignette, we present a 50-year-old patient with a history of repaired Tetralogy of Fallot who underwent a prolonged hospitalisation and extensive work up for fever of unknown origin. Although we suspected IE as the source of his fevers, he had persistently negative transthoracic and transoesophageal echocardiograms. We were ultimately able to establish the diagnosis with the use of positron emission tomography-CT (PET-CT). Although PET-CT is not part of the traditional work up for IE, it can be a useful imaging modality when there is a high index of suspicion for IE with negative echocardiography findings.

BACKGROUND

Pulmonic valve infective endocarditis (IE) is a rare clinical entity. Only 5–10% of all cases of IE involve the right side of the heart, and the vast majority of these involve the tricuspid valve.¹ Given its rarity, epidemiological data on pulmonic valve IE are lacking, but it is estimated to account for less than 2% of all cases of IE.² Known risk factors for pulmonic valve IE include intravenous drug use, alcohol use disorders, prior cardiac surgery, congenital heart disease, central venous lines and pacemaker insertion.^{2–4}

Prompt diagnosis of pulmonary valve IE can be challenging. Transthoracic echocardiography (TTE) has an estimated 70% sensitivity for detecting pulmonic valve vegetations, and because of its anterior position, visualisation of the pulmonic valve with transoesophageal echocardiography (TOE) is often inadequate.³ In this report, we discuss a patient with pulmonic valve IE who was hospitalised for over a month for work up of fever of unknown origin (FUO). We ultimately were able to establish the diagnosis using positron emission tomography-CT (PET-CT), an emerging technique for the diagnosis of pulmonary valve IE.

CASE PRESENTATION

We present a case of a 50-year-old man with Tetralogy of Fallot who had undergone repair at 20 years of age, with pulmonary valvuloplasty and ventricular septal defect patch, followed by surgical bioprosthetic pulmonic valve replacement at 39 years of age. He had also undergone multiple ablations for subsequent atypical atrial flutter and supraventricular tachycardia. His medical history was

otherwise unremarkable. He was born in Honduras but immigrated to the USA as a child.

Three days prior to presentation, the patient developed sudden onset of fevers, chills and malaise, and presented to the emergency department. Physical examination revealed no audible murmur, no peripheral oedema and no sequelae of thromboembolic phenomena. Two blood cultures grew methicillin-susceptible *Staphylococcus aureus* (MSSA) within 24 h. A chest CT demonstrated multiple subpleural nodules, concerning for septic pulmonary emboli. Neither TTE nor TOE demonstrated valvular regurgitation or vegetations. Despite the negative echocardiography findings, the patient met the modified Duke's Criteria for definite IE (1 major criterion: positive *S. aureus* blood cultures, and 3 minor criteria: fevers, a predisposing heart condition and septic emboli).⁵

He was started on empiric antibiotic therapy with nafcillin and rifampin. However, after 4 days on this regimen, he developed progressive renal dysfunction and eosinophiluria, concerning for acute interstitial nephritis. Nafcillin and rifampin were discontinued, and the patient was started on ceftriaxone. Over the next several days, the patient experienced migratory arthralgias. Examination was unremarkable for localising features and plain film of affected joints radiography was normal. One week into this course, the patient developed a palpable, purpuric rash in dependent locations on his back, buttocks and thighs. Biopsy revealed a leukocytoclastic vasculitis with IgA-deposition, consistent with Henoch-Schönlein Purpura (HSP). Ceftriaxone was switched to vancomycin, which led to resolution of the patient's rash and arthralgias and normalisation of his renal function.

Despite appropriate antibiotic coverage of MSSA and resolution of the vasculitic rash, the patient continued to experience daily fevers with temperatures as high as 39.4°C. While febrile, he felt malaise and developed rigours. In between fevers, the patient felt well. Throughout his hospital course, he had a persistent leukocytosis with a white cell count between 20 and 30 000 and a predominance of neutrophils. With the exception of the initial MSSA-positive cultures on presentation, all subsequent blood cultures were negative.

INVESTIGATIONS

Despite the normal echocardiograms at presentation, we maintained a high suspicion for IE and thus repeated TTE and TOE after several weeks of persistent fevers. The two studies had evidence of neither valvular vegetation, nor abscess, nor

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regurgitation (video 1). Given the negative echocardiograms, we initiated an extensive work up for FUO. Comprehensive review of the patient's travel and social history was unremarkable. Basic laboratory work up and review of blood peripheral smear were normal. Infectious work up, including blood cultures, HIV testing and *Clostridium difficile* PCR stool testing, was negative, with the exception of the above mentioned *S. aureus* blood cultures. The patient underwent several imaging studies including brain and spinal MRI and X-ray CT of the abdomen, all of which were normal. A tagged-white blood cell (WBC) scan was then obtained, which demonstrated intense tracer uptake in lungs and upper extremities, consistent with presumed septic emboli visualised on prior CT, and known upper extremity DVTs; it did not provide an explanation for the patient's persistent high fevers. All non-essential medications were sequentially discontinued to exclude possibility of drug fever. Almost 1 month into his hospitalisation, we performed a PET-CT scan, which demonstrated circumferential fluorodeoxyglucose (FDG)-avidity involving the right ventricular outflow tract (RVOT), concerning for prosthetic valve IE (figure 1).

DIFFERENTIAL DIAGNOSIS

When the patient's fevers persisted despite appropriate antibiotic therapy, we began an extensive work up for other aetiologies of fever, with basic laboratory work, microbiology studies and extensive imaging tests, as outlined above. Given the acuity of his presentation, we favoured an infectious source, including either IE or an occult infection. His vasculitis rash and renal dysfunction also led us to consider possible rheumatological conditions, although his rash and kidney function improved with the cessation of β -lactam therapy.

TREATMENT

Based on the findings of his PET-CT, the patient was taken to the operating room where he underwent median sternotomy. He was found to have extensive vegetative involvement of his RVOT and prosthetic pulmonic valve, which was also partially dehiscenced (figure 2). He underwent redo pulmonic valve replacement and reconstruction of his RVOT. The debrided material was cultured and did not grow any organisms. However, PCR analysis of the vegetative material detected *S. aureus*.

OUTCOME AND FOLLOW-UP

The patient had excellent recovery and was discharged home to complete a 6-week course of vancomycin. At his follow-up appointment 1 month after discharge, he was doing very well, with no manifestations of heart failure and no infection.

Video 1 Parasternal short-axis view with transthoracic echocardiogram of patient's pulmonic valve. There is evidence of neither valvular regurgitation nor vegetations, however, the valve and right ventricular outflow tract are poorly visualised.

Figure 1 A coronal section of the patient's positron emission tomography scan, demonstrating fluorodeoxyglucose-avidity in the area of the pulmonic valve and right ventricular outflow tract.

DISCUSSION

We present a rare case of prosthetic pulmonic valve and outflow tract IE. Although the epidemiology is not well-described, in a recent 6-year cohort study in New Zealand, of 35 patients presenting with right-sided IE, only four had involvement of the pulmonic valve.¹ Known risk factors for pulmonary valve IE include intravenous drug use, alcohol abuse, congenital heart disease and prior cardiac surgery.^{3 4}

Establishing the diagnosis of IE was hindered by concomitant development of HSP. This patient's case of HSP was most likely

Figure 2 The patient's excised bioprosthetic pulmonic valve, with extensive vegetation.

associated with the use of ceftriaxone, given its temporal association, and the resolution of the patient's rash and arthralgias with discontinuation of this medication; however, HSP has also rarely been associated with IE, including a case of pulmonic valve endocarditis in Korea.⁶

The soft murmur of pulmonic regurgitation can be missed, and TTE has a sensitivity for detection of pulmonic valve IE of 70%. TOE often identifies cases missed by TTE.^{2–4} However, even with TOE, diagnosis of a pulmonary valve lesion is limited due to its anterior position, and among all the cardiac valves, the pulmonic valve is the least well visualised by TOE.⁷ The sensitivity and specificity of TTE and TOE are both further reduced in structural heart disease and prosthetic heart valves, due to acoustic shadowing and complex viewing windows.⁸ Furthermore, bioprosthetic degeneration and infective lesions may manifest similarly on echocardiography.⁹

We were unable to visualise the extensive vegetation involving the pulmonary valve and RVOT. Because of his unusual presentation and negative imaging, the patient subsequently had a protracted hospital course with an extensive work up for his persistent fevers.

When prior work up with echocardiography and tagged-WBC scan was likewise unrevealing, we elected to utilise an alternate diagnostic study with superior spatial resolution to confirm and further characterise IE in our patient. Cardiac MRI, cardiac CT and PET-CT are considered second-line tools in the work up of IE, with roles that are still evolving.¹⁰ Cardiac MRI is effective in the diagnosis of IE through direct visualisation of vegetations and detection of inflammatory extension into surrounding tissues via delayed contrast enhancement, and this modality has excellent sensitivity for detecting complications of IE including aortic root pseudoaneurysms or embolic lesions.^{11–12} However, cardiac MRI lacks the spatial resolution to detect small vegetations.¹² Cardiac CT similarly lacks resolution to detect small vegetations, but it has gained an emerging role in detecting IE complications and is useful for preoperative planning.¹³ Ultimately, we chose to perform PET-CT, given the patient's history of prior surgeries and potential for chronic, postinflammatory findings confounding the acute presentation.

Although not traditionally used for the evaluation of IE, given its limited availability and study, PET-CT has recently been shown to be a very effective diagnostic tool in situations for which standard echocardiography has been unsuccessful in detecting IE. PET-CT allows for localisation of infectious processes with the injection of FDG that is taken up by inflammatory cells and accumulates in areas of infection. This allows for visualisation of infective processes prior to the subsequent development of morphological changes that would be detected by other imaging modalities.^{14–15} Utilisation of PET-CT has been particularly useful in diagnosis of IE involving prosthetic valves, as this type of endocarditis is often a much more inflammatory process than native valve IE, with infection that extends into the valve annulus and periannular tissue.¹⁶ A prospective cohort study by Saby *et al*¹⁷ showed that PET-CT offers a sensitivity of 73% and specificity of 80% in patients with suspected prosthetic valve IE; however, this study also found that the sensitivity of the modified Duke criteria rises to 97% when PET-CT is included in addition to the traditional determinants of clinical presentation, culture data and echocardiographic findings.

The majority of studies and reported cases describing use of PET-CT for diagnosis of prosthetic valve IE report aortic and mitral valve disease, and the utility of PET-CT for detection of endocarditis involving the prosthetic pulmonary valve, is not clearly established.^{18–20} Given the rarity of prosthetic

pulmonary valve IE, relatively little has been published about the use of PET-CT for diagnosing such disease and is limited to case reports. Similar to our reported case, Yamasaki *et al*²¹ describe a patient with a history of Tetralogy of Fallot who presented with fever of unknown origin and was found by PET-CT to have prosthetic pulmonary valve endocarditis. Another case report describes use of PET-CT in diagnosis of prosthetic pulmonary valve endocarditis in a patient with a history of supra-valvular aortic stenosis and subvalvular stenosis, who had undergone percutaneous pulmonary valve implantation.²²

Pulmonic valve IE, which is uncommon, and IE in congenital heart disease patients can be challenging to diagnose. A high index of suspicion, particularly in patients with known risk factors, must be maintained to allow for prompt diagnosis and appropriate management. Utilisation of PET-CT in cases of high clinical suspicion but with equivocal echocardiogram findings may allow for more rapid diagnosis and appropriate management (often high-risk surgical procedures) of IE.

Learning points

- ▶ Pulmonic valve infective endocarditis is a rare cause of infective endocarditis.
- ▶ Transthoracic echo has only 70% sensitivity for diagnosing infective endocarditis. Owing to its anterior position, the pulmonic valve is poorly visualised on transoesophageal echo, making pulmonic valve infective endocarditis diagnostically challenging.
- ▶ Positron emission tomography-CT can be used to diagnosis infective endocarditis in cases in which there is a high index of suspicion but persistently negative echocardiograms.

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