CASE REPORT

Rare cause for a common presentation: isolated pulmonary valve endocarditis yet another mimicker

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SUMMARY

Isolated pulmonary valve endocarditis (PVE) is a rare condition. Known risk factors in previous case reports were intravenous drug abuse and congenital heart disease. Epidemiology of PVE has been changing. It is now being reported specially following invasive healthcare-related procedures even in patients with structurally normal heart. Vast majority of patients present with respiratory symptoms and diagnosis of endocarditis may be challenging unless there is high index of suspicion. Various microorganisms had been isolated as aetiological agents; however, *Enterococcus faecalis* is being increasingly isolated. PVE mostly managed conservatively with intravenous antibiotics with option for surgical intervention in specific situations. We present a patient with isolated PVE due to *E. faecalis* following colonoscopy and polypectomy with predisposing risk factor of alcohol excess, mimicking clinically as pneumonia and radiologically as a neoplastic lesion.

BACKGROUND

PVE accounts for 1.5%–2% of infective endocarditis cases¹ and isolated involvement of pulmonary valve is even rarer. Risk factors include male gender, intravenous drug abuse, central venous catheters (including Swan-Ganz catheters), alcoholism, congenital heart disease, pacemaker implantation with subsequent lead infection²; more recent cases are associated with healthcare-related invasive procedures and sometime underlying immunosuppression. The most common pathogens reported in the earlier literature reviews were *Staphylococcus aureus* and coagulase-negative *Staphylococci*. Wide range of other microorganisms including candida had been reported.^{2–3} *Enterococcus faecalis* being increasingly isolated in more recent reports and portal of entry is often invasive procedures in hospital.^{2–3} Reported invasive procedures are also quite varied. PVE due to *E. faecalis* had been described in patient with blood transfusion-dependent aplastic anaemia,⁴ in myelodysplastic syndrome patient on immunosuppressive therapy for relapsing polychondritis with *Histoplasma capsulatum*,⁵ even following normal vaginal delivery in hospital with no organism isolated in blood culture.⁶ There are reported cases of isolated PVE in patient undergoing chronic haemodialysis⁷ and in patient with orthotopic liver transplantation.⁸ Clinical presentation of PVE is mostly with fever, respiratory symptoms including dyspnoea,

cough, haemoptysis and pleuritic chest pain due to septic pulmonary emboli. Chest X-ray may show pulmonary consolidation. These patients tend to get treatment for chest infection often delaying blood culture and echocardiogram unless there is high index of suspicion.

CASE PRESENTATION

A 63-year-old previously healthy retired businessman was transferred from a regional hospital to our tertiary centre with history of intermittent fever for 4 weeks, lethargy, dyspnoea and pleuritic chest pain. He had colonoscopy organised by his general practitioner as a part of screening for colorectal cancer after having a positive immunochemical faecal occult blood test 3 weeks prior to the onset of symptoms. Colonoscopy identified four polyps which were excised and were benign on histopathology. His blood test before colonoscopy showed haemoglobin of 152 g/L, iron studies showed serum ferritin of 472 mcg/L, transferrin saturation of 32%, excluding significant iron deficiency. His vitamin B12 and serum folate levels were also normal. It was thought his positive faecal occult blood test was due to minor haemorrhoidal bleed. He had 50 pack-year smoking history and alcohol consumption of 12–14 standard drinks per day with no history of intravenous drug abuse, immunosuppression or underlying structural heart disease. Patient received initial treatment in the regional hospital with combination of intravenous benzylpenicillin, gentamicin and oral clarithromycin for 3 days but continued to have febrile episodes. On physical examination, his heart rate was 102/min, blood pressure 100/60 mm Hg; respiratory rate was 24/min and temperature of 38°C. He had crackles in the right lower zone of his chest and had no peripheral stigmata of infective endocarditis. Auscultation of his heart did not reveal any murmur or pericardial rub.

INVESTIGATIONS

His blood test on admission showed haemoglobin of 118 g/L with white cell count of 9.3×10^9 /L and absolute neutrophil count of 7.59×10^9 /L, raised gamma-glutamyl transferase of 226 U/L and mildly elevated transaminases likely reflecting alcohol excess. His C-reactive protein was markedly raised (258 mg/L). X-ray of chest showed right lower zone patchy infiltrate (figure 1). CT pulmonary angiogram was performed for pleuritic chest pain and initial poor antibiotic response. It showed

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Figure 1 Chest radiography showing right lower zone patchy infiltrate.

background paraseptal emphysema with upper lobe predominance and a right hilar central mass, measuring up to 61 mm in maximum, measured in anteroposterior dimension. This mass extended posteroinferiorly surrounding the right intralobar artery and was continuous with the right hilar node. This mass resulted in complete obstruction of the anterior branch of right upper pulmonary artery and effacement of the corresponding airway. Other findings included bilateral lower lobe partial atelectasis and mediastinal and bilateral hilar adenopathy with nodes up to 18 mm short axis. The radiologist in his report strongly suggested primary bronchogenic carcinoma with no evidence of pulmonary embolism (figure 2). Three sets of blood cultures were positive for *E. faecalis*, including initial blood culture taken in the regional hospital. Transthoracic echocardiogram showed moderate pulmonary regurgitation but failed to show any clear vegetation (figure 3). The transthoracic echocardiographic image quality was affected by patient's obesity and underlying obstructive airway disease limiting optimal visualisation of the pulmonary valve. Transoesophageal echocardiogram showed a mobile mass arising from thickened pulmonary valve (figure 4) causing moderate pulmonary regurgitation. This confirmed diagnosis of PVE based on modified Duke's criteria.

Figure 2 CT scan of the chest showing right hilar central mass mimicking neoplastic lesion.

Figure 3 Transthoracic echocardiogram showing moderate pulmonary regurgitation.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses before the positive blood culture and the transoesophageal echocardiographic finding of vegetation would include both infective and non-infective aetiologies. Infective aetiology would include possibility of hospital-acquired pneumonia with resistant organism considering history of prior hospitalisation for colonoscopy and polypectomy. Considering patient's heavy smoking history with mediastinal and hilar adenopathy bronchogenic carcinoma would be high in the differential diagnoses list. Subacute infections like infective endocarditis or its complications such as septic emboli and abscess formation may continue to show initial poor response despite appropriate antibiotics. Mycobacterial and other granulomatous infections including fungal infection can also cause hilar adenopathy with similar clinical picture. Unusual organisms according to local infectious disease prevalence also need to be considered. Melioidosis is one such possibility based on the patient's geographical location in North Queensland Australia. Excess alcohol intake is one of the risk factors for this infection. Non-infective differential diagnoses apart from primary bronchogenic carcinoma would include metastatic malignancy, lymphoma, sarcoidosis, Wegener's granulomatosis, extrinsic allergic alveolitis and pulmonary embolism. Differential diagnoses of pulmonary valve mass apart from vegetation due to

Figure 4 Transoesophageal echocardiogram showing pulmonary valve vegetation. AV: Aortic valve, MPA: Main pulmonary artery, RV: Right ventricle, VEG: Vegetation.

Figure 5 Repeat CT scan of the chest after 1 month of intravenous antibiotic therapy showed interval decrease in the size of the right hilar mass.

infective endocarditis would include possibility of marantic endocarditis and thrombus.

TREATMENT

Patient was on combination of intravenous benzylpenicillin, gentamicin and oral clarithromycin from the regional hospital. Initial use of gentamicin was not indicated for treating a respiratory infection; therefore, it was ceased and benzylpenicillin and clarithromycin were continued at the tertiary hospital. However, combination of benzylpenicillin and gentamicin was started soon as the sensitivity of *E. faecalis* became available. This combination was later changed to ceftriaxone because of worsening renal function. Antibiotic therapy was guided by our infectious disease team and patient received total 6 weeks of intravenous antibiotics. The patient improved and became asymptomatic with antibiotic therapy. Measures to prevent alcohol excess and smoking cessation programme was initiated.

OUTCOME AND FOLLOW-UP

Follow-up transoesophageal echocardiogram after 6 weeks showed marked reduction in vegetation size and pulmonary regurgitation. The patient had serial CT scan of the chest with close follow-up in the respiratory clinic. CT scan a month later showed interval decrease in the size of right hilar mass to 20.6 mm in largest diameter as well as reduction in size of mediastinal lymphadenopathy (figure 5). However, there were new findings of a pleural-based left lingular segment nodule, measuring 22×23 mm and three spiculated cavitary nodules in the anterior segment of the right upper lobe with the largest measuring 14×18 mm. The impression from radiologist was possible ongoing infection with septic emboli, other differentials proposed were possibility of malignancy and pulmonary tuberculosis. The patient was still on his intravenous antibiotic at the time of this scan which was continued to complete the 6-weeks course. Infectious disease team followed up his progress in their clinic. Follow-up scan after 5 months showed complete resolution of right hilar mass with some subcentimetre mediastinal lymph nodes remaining. The nodular lesion including the cavitary ones showed marked reduction in size suggestive of resolving infective aetiology. Patient continues his follow-up in the cardiology and respiratory clinic. In regard to patient's anaemia, it was likely secondary to combination of the infection

causing anaemia of chronic disease and bone marrow suppressive effect of alcohol excess. His haemoglobin level improved to 135 g/L at the end of 6 weeks of antibiotic therapy.

DISCUSSION

Patient described in the case, presented to our hospital with febrile illness with respiratory symptoms and chest X-ray findings suggestive of pneumonia. Patient's initial poor response to antibiotic therapy and pleuritic chest pain lead to CT scan of the chest, the finding of which was not typical of pneumonia rather it mimicked a neoplastic lesion. It was after his positive blood culture with the growth of *E. faecalis* lead to more focused investigation into the possibility of infective endocarditis. His transthoracic echocardiogram, however, failed to show any definite vegetation. It is worth mentioning that sensitivity for the diagnosis of native valve endocarditis with transthoracic echocardiogram is around 70% and with transoesophageal echocardiogram about 96%. This is generally true for aortic and mitral valve; however, this may not be applicable while imaging pulmonary valve because of its anterior location and furthest from the transoesophageal probe. Miranda *et al* reviewed nine patients with confirmed PVE. Transthoracic and transoesophageal echocardiograms were done in six and seven patients, respectively. Four patients underwent both procedures. Transthoracic echocardiogram was diagnostic in all cases, but transoesophageal echocardiogram failed to detect pulmonary valve involvement in one patient.⁹ Same author in a different paper published the yield of transthoracic and transoesophageal echocardiography as diagnostic tools for prosthetic pulmonary valve or right ventricle to pulmonary artery conduit infective endocarditis in total 17 patients. Transthoracic echocardiogram was diagnostic for infective endocarditis in 62% and transoesophageal echocardiogram was diagnostic in 57% patients; when both modalities combined, it were diagnostic in 15 of 17 (88%) cases. Authors concluded that either modality alone was not sensitive enough in these cases. Both modalities should complement each other in the evaluation of patients with suspected prosthetic pulmonary valve or right ventricle to pulmonary artery conduit infective endocarditis.¹⁰ With either imaging modality pulmonary valve may be difficult to visualise properly in certain patients, also unlike other valves, pulmonary valve often not interrogated sufficiently unless specified to the sonographer. In our patient, the transthoracic echocardiogram although showed moderate pulmonary regurgitation but failed to show clear vegetation, the transoesophageal echocardiogram finally revealed the vegetation confirming the complementary nature of these two modalities of imaging. Clinically, pulmonary regurgitation has a low-pitched murmur and is often missed, and taking into consideration of the non-specific nature of presentation, isolated PVE remains to be clinically challenging to diagnose. As a general rule, pulmonary valve needs to be carefully interrogated during echocardiographic examination in all suspected endocarditis cases.

Nosocomial infective endocarditis incidence is on the rise, and incidence as high as 34% of all infective endocarditis cases had been described. Staphylococcus and Enterococcus species found as the most common causative agents in this setting. Staphylococci in nosocomial infective endocarditis had higher methicillin-resistance rates than in community-acquired cases with affected population being older with comorbidities and poorer prognosis.^{11 12} With increasing healthcare-related invasive procedures and more patients on immunosuppression, PVE incidence likely to rise in future. However, nosocomial infective endocarditis is not a pulmonary valve specific phenomenon

rather it follows similar trend as community-acquired infective endocarditis with mitral and aortic valve involved in majority of cases and pulmonary valve being the least involved.^{11 12}

Majority of patients with pulmonary or tricuspid valve endocarditis are managed conservatively. Right-sided endocarditis has a better prognosis and is more likely to respond to medical therapy than infection of the left-sided valves. Parenteral antibiotic is generally administered for 4–6 weeks. Results of retrospective studies suggest that vegetation less than 1–2 cm long in right-sided endocarditis usually responds to medical treatment.^{13 14} A review of the published clinical experience indicates that the role of surgery in isolated PVE is unclear and the current infective endocarditis guidelines do not mention specifically regarding indication for surgery in isolated PVE. In general, surgery is indicated when there is persistent bacteraemia despite appropriate antimicrobial therapy, progressive valve destruction and incompetence, locally invasive infection including abscess formation or relapsing infection after completion of a full course of antibiotic therapy or recurrent pulmonary emboli. It is recommended that infection with *Staphylococcus*, the presence of vegetation larger than 2 cm long or cardiovascular instability should prompt consideration of early surgical intervention in patients with PVE.¹⁴ Surgical options include debridement of the infected area, vegetation excision with either valve preservation or valve repair with homologous or autologous pericardium avoiding artificial material whenever possible or valve replacement. The most commonly used strategy for valve replacement involves stentless xenografts and pulmonary homografts.^{15 16}

Learning points

- Isolated pulmonary valve endocarditis is rare. Majority of patients present with respiratory symptoms and unless there is high index of suspicion the diagnosis of endocarditis may be delayed or missed.
- Apart from conventional risk factor like intravenous drug abuse, invasive healthcare-related procedures are emerging as a predisposing risk factor.
- Majority of patients are managed conservatively with intravenous antibiotics; however, surgical treatment is considered in specific situations.

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Contributors ASR was involved in the concept and design of the work, drafting the article, corrections, data collection, analysis, literature review and overall coordination. DA was responsible for the conception, data acquisition of TOE, follow-up review and revising the paper critically. SHC and DA were responsible for the conception, data acquisition and review. SHC was also responsible for the consent taking. All authors contributed to the final approval of the paper and agreed to be accountable.

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