Title

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CLINICAL VIGNETTE

Late Prosthetic Pulmonary Valve Infective Endocarditis in a 25-Year-Old Male with Repaired Tetralogy of Fallot

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Case Presentation

A 25-year-old male presented with 3 weeks of intermittent fevers, gross hematuria, and left gluteal muscle pain. He had a past history of intravenous (IV) drug use, hepatitis C virus infection, and Tetralogy of Fallot status post an uncharacterized repair in childhood. At presentation he was afebrile but tachycardic with heart rates in the 110s and without any respiratory symptoms nor chest pain. His physical exam was notable for a V/VI holosystolic murmur loudest at the left upper sternal border and lungs with bibasilar crackles.

The initial laboratory findings were remarkable for a mild leukocytosis (white blood cell count of 10 K/cumm), low normal platelets (188 K/cumm), anemia (hemoglobin 8.5 g/dL), elevated BUN (91 mg/dL), elevated creatinine (9.65 mg/dL), and elevated inflammatory markers (ESR and CRP). Additionally, urinalysis was supportive of a glomerulonephritis.

Imaging was significant for multiple thin-walled pulmonary cavitary lesions and subcentimeter nodules throughout both lungs suspicious for septic emboli.

The initial evaluation included transthoracic echocardiogram (TTE) which was suspicious for a pulmonic valve vegetation (Figures 1 and 2).

Both the initial blood cultures, in 6/6 bottles and urine culture grew *Enterococcus faecalis (E. faecalis)*. The patient was empirically treated with vancomycin, ceftriaxone, and daptomycin which were narrowed to ampicillin and ceftriaxone following antimicrobial sensitivity.

Transesophageal echocardiography (TEE) was consistent with Tetralogy of Fallot status post repair of a ventricular septal defect. It also revealed a 16-17mm bioprosthetic pulmonic valve with severe, wide open pulmonary regurgitation due to two flail bioprosthetic leaflets. There was also severe calcification of the annulus/prosthetic valve struts (13 mm in height) extending into the main pulmonary artery causing moderate prosthetic valve stenosis with a peak velocity of 3.1 meters/second (m/s) with main pulmonary artery post-stenotic dilation of 33 mm. The TEE also revealed multiple, linear mobile echodensities measuring up to 21 mm (Figure 3).

The patient was diagnosed with bioprosthetic pulmonary valve endocarditis and a multidisciplinary team created a treatment plan. The Cardiology Consult service recommended surgical pulmonic valve replacement with possible annular reconstruction given the patient's severe pulmonary regurgitation with flail bioprosthetic leaflets. However, the need for surgery was not considered urgent because the patient was asymptomatic. The Cardiothoracic (CT) Surgery Consult service recommended that the patient be referred to an adult congenital CT surgeon. Lastly, the Infectious Disease (ID) Consult service recommended a 6-week course of IV antibiotics in addition to a colonoscopy to rule-out a gastrointestinal source for the *E. faecalis*.

Clinical Follow-up

Given the patients stable vital signs, surgery was considered non-urgent and he was managed with IV antibiotics with inpatient substance abuse counseling and rehabilitation. Surgical pulmonary valve replacement by a congenital CT surgeon was planned after treatment.

Introduction

Prosthetic valve endocarditis (PVE) generally involves the deposition of microthrombi, comprised of platelets and fibrin to endothelialized prosthetic valve surfaces which serve as foci for circulating bacteria to adhere and lead to infected vegetations.[1,2] About 2.5% of the US population has valvular heart disease and over 120,000 valvular surgeries are performed each year in the US. The incidence of PVE varies by subgroups between 0.3-1.2% per year with high overall mortality, 20-85%.[3-5] Adults with congenital heart disease with prosthetic valves, such as the patient in our case, are at increased risk of developing PVE compared to other subgroups, but have lower overall mortality (6%) compared to all patients with PVE.[6,7]

Risk Factors

Common risk factors for infective endocarditis (IE) include recent dental procedures, male sex, IV drug use, structural heart disease, chronic hemodialysis, history of cardiac surgery, skin trauma, and other infections.[8-12] However, specific risk factors for PPV endocarditis are harder to identify in the research literature because the pulmonary prosthesis is considered the least commonly infected prosthesis in PVE cases (about 5.6% of all cases of PVE).[13] There are no large registries of PPV patients to help identify specific risk factors for IE. One small retrospective cohort study of 17 adult patients at the Mayo Clinic characterized PPV and right ventricle to pulmonary artery conduit (RVPAC) endocarditis between January 2000 and May 2015. It reported the following risk factors associated with PVE: a relatively young median age of 34.4 years, 12/17 patients were male and a history of bacteremia (88%).[14] A minority of these patients had a previous episode of IE (24%) and none had IV drug use.[14] Our patient had all of the risk factors noted in the Mayo Clinic study, including a history of IV drug use.

Clinical Manifestation

The Mayo Clinic patients with PPV endocarditis presented with fever (94%) and a grade III/VI or higher systolic murmur (88%).[14] A minority of the patients had a diastolic murmur (35%), hypotension or septic shock (29%), abnormal CXR (38%), and evidence of a pulmonary embolism (35%).[14] Six of 17 of the patients had Tetralogy of Fallot and 1 of these 6 had *E. faecalis* bacteremia, as observed in our case.[14]

Microbiology

The pathogens observed in the Mayo Clinic PPV endocarditis series are consistent with general PVE, with the most common pathogens being *Staphylococcus aureus* (MSSA), coagulase-negative staphylococci, and viridans group streptococci.[14-16] *E. faecalis*, is a much rarer pathogen—though there is increasing isolation reported, particularly in patients with prosthetic heart valves.[17,18] In our patient both the urine cultures and the blood cultures grew *E. faecalis*. *E. faecalis* bloodstream infections in IE typically arise from the gastrointestinal and urogenital tracts where they reside as commensal bacteria.[19] While uncommon, there is an association of enterococcal endocarditis and undiagnosed colorectal cancer, though *Streptococcus bovis* is more commonly isolated[19] with recommendation for a colonoscopy. The source of *E. faecalis* in the majority of IE cases is unidentified—but when it is identified, the source is usually the GU tract.[19] Despite initiation of appropriate antimicrobial therapy for our patient, the blood cultures remained persistently positive highlighting the virulence of *E. faecalis* for prosthetic valves.

Diagnosis

The modified Duke Criteria are used to define and diagnose IE.[20] Our patient fulfilled two major criteria positive blood cultures and evidence of endocardial involvement and three minor criteria, predisposition, vascular and immunological phenomena. PPV can be difficult to diagnosis even with optimal echo imaging.[21] In one study TTE was diagnostic for PPV/RVPAC IE in only 62% of cases while TEE was diagnostic in only 57%. Combined, TTE and TEE were diagnostic in 88% of cases.[14]

Treatment

The decision of whether to proceed with surgical versus medical therapy for PPV IE is supported by a number of factors including recurrent/continuous bacteremia, heart failure, recurrent fever, cardiogenic shock, and severe PPV regurgitation.[14] We found only one study citing treatment success of PPV endocarditis with medical therapy alone.[22] Our patient's severe valvular dysfunction will ultimately need surgical correction of the infected PPV. However, surgical intervention of the infected PPV is not without significant morbidity and mortality. One study reported death occurring in 17% of patients with PPV/RVPAC IE.[14] Management of patients with PPV IE is both complex and challenging, requiring a multidisciplinary approach to treatment.

Conclusion

The literature exploring infective endocarditis of surgically implanted prosthetic pulmonary valves is very limited. This report illustrates how PPV endocarditis can present atypically, highlighting need for increased vigilance, particularly in lower health literacy populations with incomplete awareness of surgical and medical history. PPV endocarditis remains a rare condition associated with a significant morbidity and a high likelihood of requiring surgical intervention. In order to improve evidence-based decision-making in patients with PPV endocarditis, future reporting and structured epidemiological analyses are needed.

Figures

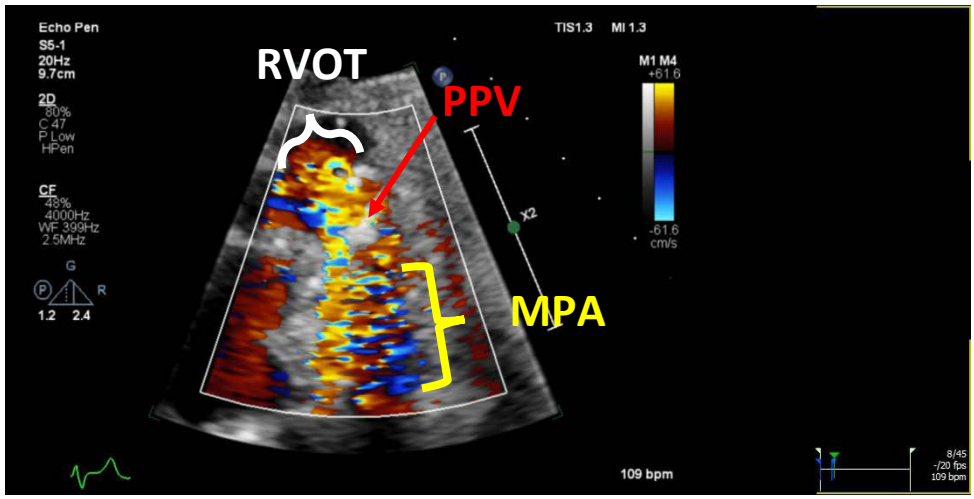

Figure 1: TTE Color doppler image showing reversal of flow through the prosthetic pulmonary valve (red arrow) during diastole. Normally during diastole the prosthetic pulmonary valve (PPV) is closed, with no blood flow going across the PPV, which is characterized by little to no color flow using color doppler during this phase of the cardiac cycle. However, here we see extensive, turbulent color flow during diastole across the PPV originating from the main pulmonary artery (MPA) going into the RVOT characterized by the red/yellow jets in the RVOT across the PV.

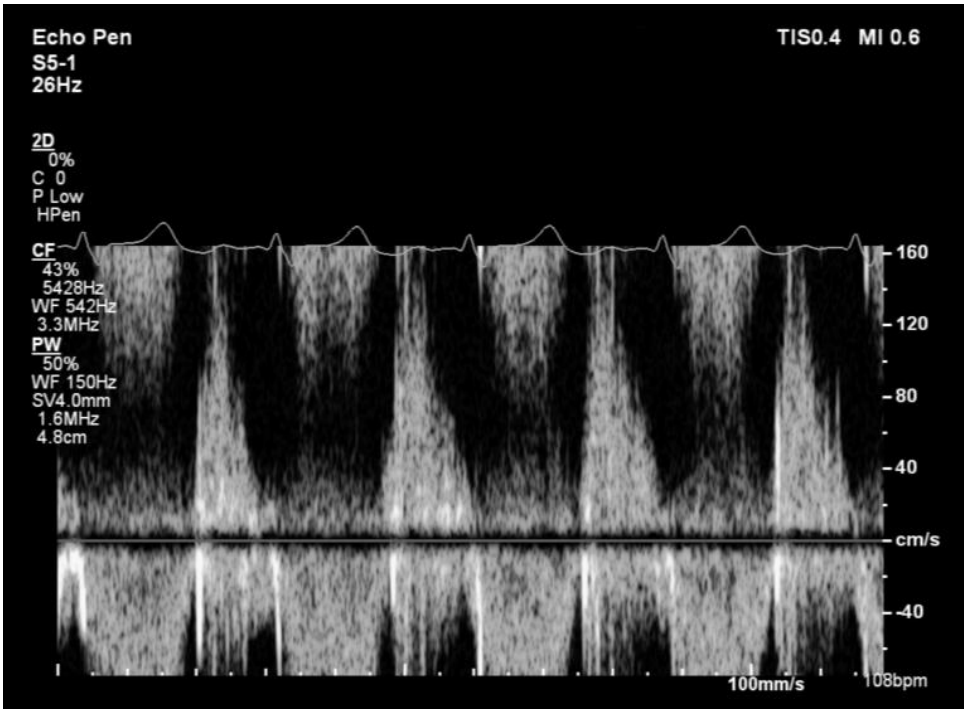

Figure 2: TTE continuous wave doppler image showing flow reversal across the prosthetic pulmonary valve throughout diastole. The pulse wave doppler provides information about the gradient between the RVOT and PA and here suggests severe pulmonary regurgitation.

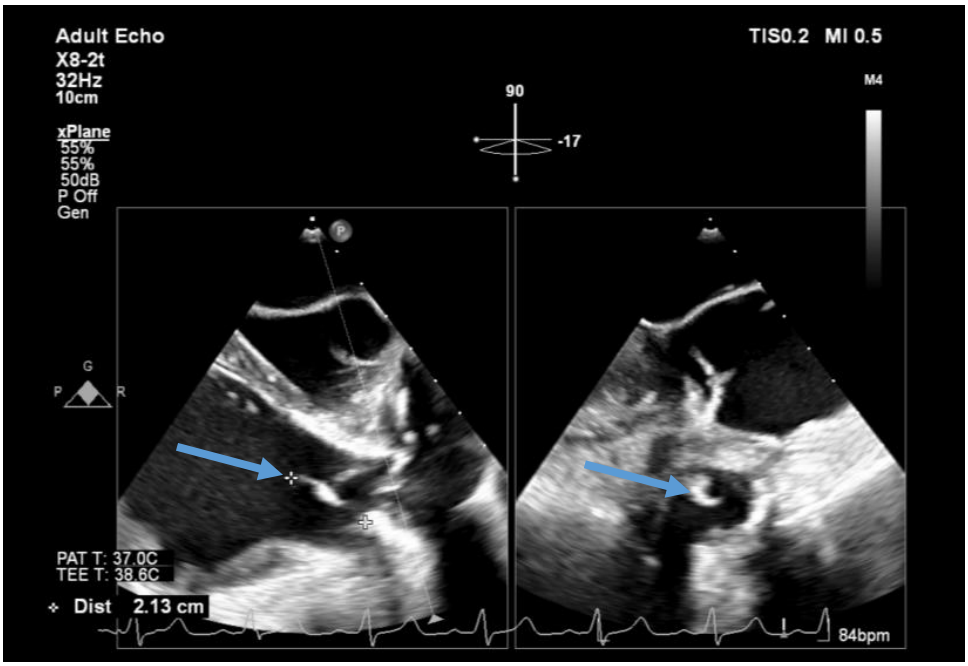

Figure 3: TEE image of prosthetic pulmonary valve showing vegetations (blue arrows).

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REFERENCES

1. **Sullam PM, Drake TA, Sande MA**. Pathogenesis of endocarditis. *Am J Med*. 1985 Jun 28;78(6B):110-5. doi: 10.1016/0002-9343(85)90373-0. PMID: 4014276.
2. **Jung CJ, Yeh CY, Shun CT, Hsu RB, Cheng HW, Lin CS, Chia JS**. Platelets enhance biofilm formation and resistance of endocarditis-inducing streptococci on the injured heart valve. *J Infect Dis*. 2012 Apr 1;205(7):1066-75. doi: 10.1093/infdis/jis021. Epub 2012 Feb 21. PMID: 22357661.
3. Centers for Disease Control and Prevention. 2020. Valvular Heart Disease. CDC.gov. [online] Available at: <https://www.cdc.gov/heartdisease/valvular_disease.htm> [Accessed 15 November 2020].
4. **Matiasz R, Rigolin VH**. 2017 Focused Update for Management of Patients with Valvular Heart Disease: Summary of New Recommendations. *J Am Heart Assoc*. 2018 Jan; 7(1): e007596.
5. **Rekik S, Trabelsi I, Znazen A, Maaloul I, Hentati M, Frikha I, Ben Jemaa M, Hammami A, Kammoun S**. Prosthetic valve endocarditis: management strategies and prognosis: A ten-year analysis in a tertiary care centre in Tunisia. *Neth Heart J*. 2009 Feb;17(2):56-60. doi: 10.1007/BF03086218. PMID: 19247467; PMCID: PMC2644380.
6. **Gersony WM, Hayes CJ, Driscoll DJ, Keane JF, Kidd L, O'Fallon WM, Pieroni DR, Wolfe RR, Weidman WH**. Bacterial endocarditis in patients with aortic stenosis, pulmonary stenosis, or ventricular septal defect. *Circulation*. 1993 Feb;87(2 Suppl):I121-6. PMID: 8425318.
7. **Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, Veen G, Stappers JL, Grobbee DE, Mulder BJ**. Turning 18 with congenital heart disease: prediction of infective endocarditis based on a large population. *Eur Heart J*. 2011 Aug;32(15):1926-34. doi: 10.1093/eurheartj/ehq485. Epub 2011 Jan 8. PMID: 21217144.
8. **Lockhart PB, Brennan MT, Thornhill M, Michalowicz BS, Noll J, Bahrani-Mougeot FK, Sasser HC**. Poor oral hygiene as a risk factor for infective endocarditis-related bacteremia. *J Am Dent Assoc*. 2009 Oct;140(10):1238-44. doi: 10.14219/jada.archive.2009.0046. PMID: 19797553; PMCID: PMC2770162.
9. **Hill EE, Herijgers P, Claus P, Vanderschueren S, Herregods MC, Peetermans WE**. Infective endocarditis: changing epidemiology and predictors of 6-month mortality: a prospective cohort study. *Eur Heart J*. 2007 Jan;28(2):196-203. doi: 10.1093/eurheartj/ehl427. Epub 2006 Dec 7. PMID: 17158121.
10. **McKinsey DS, Ratts TE, Bisno AL.** Underlying cardiac lesions in adults with infective endocarditis. The changing spectrum. *Am J Med*. 1987 Apr;82(4):681-8. doi: 10.1016/0002-9343(87)90001-5. PMID: 3565426.
11. **Nucifora G, Badano LP, Viale P, Gianfagna P, Allocca G, Montanaro D, Livi U, Fioretti PM.** Infective endocarditis in chronic haemodialysis patients: an increasing clinical challenge. *Eur Heart J*. 2007 Oct;28(19):2307-12. doi: 10.1093/eurheartj/ehm278. Epub 2007 Jul 26. PMID: 17656347.
12. **Robinson DL, Fowler VG, Sexton DJ, Corey RG, Conlon PJ**. Bacterial endocarditis in hemodialysis

patients. *Am J Kidney Dis*. 1997 Oct;30(4):521-4. doi: 10.1016/s0272-6386(97)90311-5. PMID: 9328367.

13. **Nagpal A, Sohail MR, Steckelberg JM**. Prosthetic valve endocarditis: state of the heart. *Clinical Investigation*. 2012;2(8):803-817.
14. **Miranda WR, Connolly HM, Bonnichsen CR, DeSimone DC, Dearani JA, Maleszewski JJ, Greason KL, Wilson WR, Baddour LM**. Prosthetic pulmonary valve and pulmonary conduit endocarditis: clinical, microbiological and echocardiographic features in adults. *Eur Heart J Cardiovasc Imaging*. 2016 Aug;17(8):936-43. doi: 10.1093/ehjci/jew086. Epub 2016 May 8. PMID: 27161836.
15. **Nataloni M, Pergolini M, Rescigno G, Mocchegiani R**. Prosthetic valve endocarditis. *J Cardiovasc Med (Hagerstown)*. 2010 Dec;11(12):869-83. doi: 10.2459/JCM.0b013e328336ec9a. PMID: 20154632.
16. **Murdoch DR, Corey GR, Hoen B, Miró JM, Fowler VG Jr, Bayer AS, Karchmer AW, Olaison L, Pappas PA, Moreillon P, Chambers ST, Chu VH, Falcó V, Holland DJ, Jones P, Klein JL, Raymond NJ, Read KM, Tripodi MF, Utili R, Wang A, Woods CW, Cabell CH; International Collaboration on Endocarditis-Prospective Cohort Study (ICE-PCS) Investigators**. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. *Arch Intern Med*. 2009 Mar 9;169(5):463-73. doi: 10.1001/archinternmed.2008.603. PMID: 19273776; PMCID: PMC3625651.
17. **Reza AS, Anand D, Cheng SH, Anand D**. Rare cause for a common presentation: isolated pulmonary valve endocarditis yet another mimicker. *BMJ Case Rep*. 2018 Jul 18;2018:bcr2018224703. doi: 10.1136/bcr-2018-224703. PMID: 30021734; PMCID: PMC6058097.
18. **Dahl A, Rasmussen RV, Bundgaard H, et al.** Enterococcus faecalis Infective Endocarditis. *Circulation*. 2013;127(17):1810-1817. doi:10.1161/circulationaha.112.001170
19. **Khan Z, Siddiqui N, Saif MW.** *Enterococcus Faecalis* Infective Endocarditis and Colorectal Carcinoma: Case of New Association Gaining Ground. *Gastroenterology Res*. 2018;11(3):238-240. doi:10.14740/gr996w
20. **Baddour LM, Wilson WR, Bayer AS, Fowler VG Jr, Tleyjeh IM, Rybak MJ, Barsic B, Lockhart PB, Gewitz MH, Levison ME, Bolger AF, Steckelberg JM, Baltimore RS, Fink AM, O'Gara P, Taubert KA; American Heart Association Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young, Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and Stroke Council**. Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications: A Scientific Statement for Healthcare Professionals From the American Heart Association. *Circulation*. 2015 Oct 13;132(15):1435-86. doi: 10.1161/CIR.0000000000000296. Epub 2015 Sep 15. Erratum in: *Circulation*. 2015 Oct 27;132(17):e215. Erratum in: *Circulation*. 2016 Aug 23;134(8):e113. Erratum in: *Circulation*. 2018 Jul 31;138(5):e78-e79. PMID: 26373316.
21. **Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, Vilacosta I, Moreillon P, de Jesus Antunes M, Thilen U, Lekakis J, Lengyel M, Müller L, Naber CK, Nihoyannopoulos P, Moritz A, Zamorano JL; ESC Committee for Practice Guidelines**. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. *Eur Heart J*. 2009 Oct;30(19):2369-413. doi: 10.1093/eurheartj/ehp285. Epub 2009 Aug 27. PMID: 19713420.
22. **Irving CA, Kelly D, Gould FK, O'Sullivan JJ**. Successful medical treatment of bioprosthetic pulmonary valve endocarditis caused by methicillin-resistant Staphylococcus aureus. *Pediatr Cardiol*. 2010 May;31(4):553-5. doi: 10.1007/s00246-009-9631-y. Epub 2010 Jan 10. PMID: 20063157.