Dizziness Found to Be *Candida Parapsilosis* Prosthetic Valve Endocarditis

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ABSTRACT

Candida parapsilosis is an opportunistic pathogen with a propensity for biofilm formation and adhesion to medical devices. Although rare, fungal prosthetic valve endocarditis (PVE) is a feared complication of disseminated candidemia or direct intraoperative contamination from fungal adherence to prosthetic valves. *C. parapsilosis* is one of the most common species underlying fungal endocarditis. We present a 78-year-old male patient 2 months after transcatheter aortic valve replacement with persistent dizziness and a cerebellar stroke found to be secondary to treatment-resistant disseminated candidemia and fungal PVE. This case highlights the diagnostic challenges of source identification in fungal endocarditis and reinforces the importance of considering prosthetic valve involvement early in the evaluation of persistent fungemia. Optimal management of *C. parapsilosis* endocarditis requires prolonged antifungal therapy as well as definitive source control.

KEYWORDS: Candidemia; candida parapsilosis; TAVR; infective endocarditis; infectious diseases

BACKGROUND

Candida parapsilosis is an opportunistic pathogen with a propensity for adhesion to medical devices via biofilm formation.[1,2] The organism has a particular predilection for colonizing prosthetic devices such as implanted cardiac valves, although most *C. parapsilosis* infections arise from underlying intestinal colonization with subsequent fungal translocation to the blood and possible dissemination to solid organs.[3,4] Along with *C. albicans*, *C. parapsilosis* is the most common species underlying fungal endocarditis,[5] a life-threatening condition with reported mortality rates approaching 60%.[6-11] It should be noted, however, that fungal endocarditis is rare, accounting for only 1–2% of all infective endocarditis cases.[11,12] More specifically, *Candida parapsilosis* accounts for approximately 0.61% (5/822) of infective endocarditis cases.[11] A subset of fungal infective endocarditis is fungal prosthetic valve endocarditis (PVE), a condition in which an implanted cardiac valve serves as a nidus for fungal colonization. *Candida parapsilosis* as the source of PVE is similarly rare, accounting for approximately 0.84% (2/237) of all PVE cases.[11] Fungal PVE may either arise as a complication of disseminated candidemia or serve as the primary source of bloodstream infection, the latter most often due to direct intraoperative contamination with fungal adherence to prosthetic valves. Bacterial and fungal organisms, including *Candida* spp., can be introduced during valve surgery in both children[13] and adults[11] and often manifest as clinical infection within 60 days to over a year post-operatively.

We present the case of a patient with persistent candidemia 2 months after a transcatheter aortic valve replacement. We outline the diagnostic complexities associated with a nonspecific initial presentation with minimal symptom progression despite fungemia and discuss the optimal management of prosthetic valve endocarditis.

CASE REPORT

A 78-year-old male presented to the emergency department with urinary frequency and acute dizziness, ongoing for the past day. His past medical history included type 2 diabetes mellitus, atrial fibrillation, heart failure with reduced ejection fraction ([EF] 25–30%), and stage D2 aortic stenosis (symptomatic severe low-flow, low-gradient aortic stenosis with reduced left ventricular ejection fraction). The patient presented 2 months after a transcatheter aortic valve replacement (TAVR) and three-vessel coronary artery bypass grafting (CABG) with post-operative EF of 40%. Notably, the patient was hospitalized 3 weeks prior for *Serratia marascens* urinary tract infection (UTI) that evolved into *Serratia marascens* bacteremia and eventually septic shock requiring vasopressor support. Blood and urine cultures at that time did not detect fungal species. The patient also had an unrelated unilateral ureteral stent placed for an obstructive renal calculus in the mid-ureter.

On presentation, the patient was afebrile, normotensive, and breathing comfortably on room air. Physical exam revealed a non-toxic appearance, a grade II/VI systolic ejection murmur best heard at the right upper sternal border, and mild suprapubic tenderness. The neurologic exam was notable only for an unsteady gait. Labs were notable for hemoglobin 8.9 g/dL (baseline 8–9 g/dL); leukocytosis was not present. Urinalysis was significant for pyuria (>180

WBC/HPF), hematuria (>180 RBC/HPF), and 4+ bacteriuria. Computed tomography (CT) of the abdomen and pelvis was largely unremarkable with no evidence of pyelonephritis or intrabdominal abscesses. Treatment for UTI was initiated with trimethoprim/sulfamethoxazole following urine culture growing *Serratia marascens* >100,000 col/mL. Blood cultures speciated as *Candida parapsilosis*, prompting initiation of caspofungin therapy. Transesophageal echocardiography demonstrated two mobile densities on the bioprosthetic aortic valve with trace intravalvular leak suggestive of fungal endocarditis. Magnetic resonance imaging (MRI) of the brain on hospital day (HD) 7 revealed acute ischemia of the superior right cerebellum consistent with septic emboli [**Figure 1**]. Per the patient's goals of care and concern for high surgical risk, the patient declined urgent valve replacement surgery. Therapy was changed to liposomal amphotericin B (AmphoB) for treatment of disseminated candidemia with endocarditis. The patient was switched to fluconazole and micafungin in the setting of acute kidney injury (AKI) secondary to AmphoB toxicity. Blood cultures were negative for yeast on HD 19. Fluconazole was transitioned to isavuconazole due to QTc prolongation. The patient was discharged on HD 32 with an additional 4 weeks of micafungin treatment and long-term suppressive therapy with isavuconazole. Unfortunately, the patient succumbed to disseminated infection with multiorgan involvement 48 days after hospital admission [**Figure 2**].

Figure 1. [**A**] MRI imaging acquired on hospital day 7 depicting a 17 x 13 mm wedge-shaped lesion in the superior right cerebellum, visualized as hyperintense with restricted diffusion on DWI, [**B**] with a corresponding hypointensity on ADC, consistent with acute ischemic infarct.

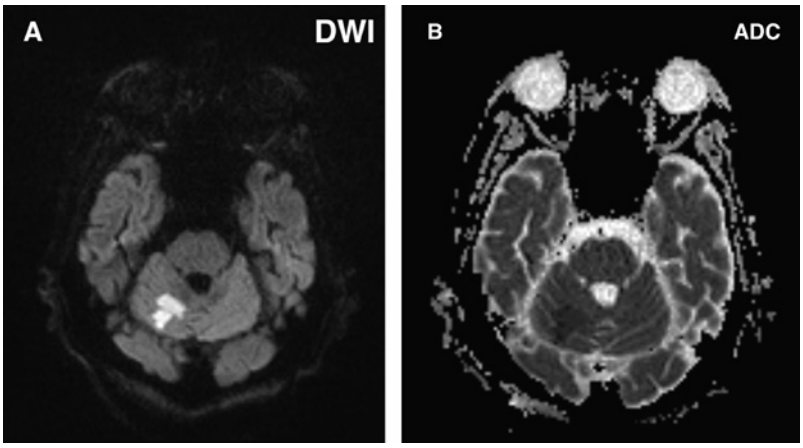
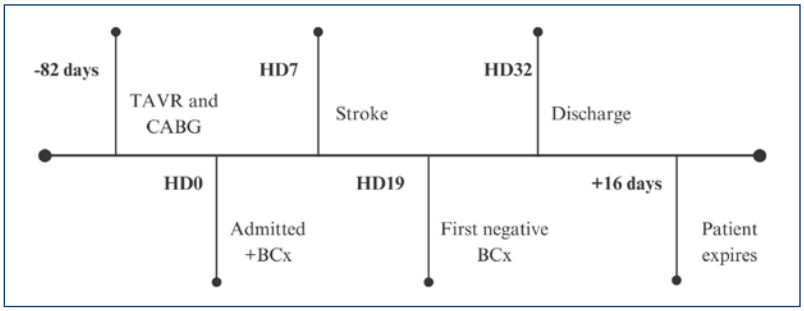


Figure 2. Timeline of events.



DISCUSSION

This case is an example of post-TAVR *Candida parapsilosis* endocarditis complicated by septic embolic stroke, overall illustrating the importance of a thorough history and physical examination in determining the source of fungal endocarditis. Although fungal PVE can be a sequela of candidemia from another source, the infected prosthetic valve itself can also be the primary source of infection. In our patient, the absence of a clear extracardiac infectious focus ultimately pointed to the prosthetic valve itself as the likely nidus of infection. Biofilm formation on the prosthetic surface likely enabled continuous microbial shedding into the bloodstream, contributing to persistent fungemia despite appropriate antifungal therapy.

It is important to recognize that embolic and/or hemorrhagic complications, most commonly as cerebral thromboembolic events, have been found to occur in greater than 40% of patients with *Candida parapsilosis* endocarditis.[14] Our patient's mild but persistent dizziness was ultimately found to be the manifestation of cerebellar infarct, likely caused by septic emboli originating from the infected valve. This complication highlights the importance of thoroughly investigating unexplained symptoms, even when they are mild or nonspecific, especially in the context of systemic infection. Although stroke was not initially suspected, the combination of fungal endocarditis and ongoing dizziness warranted advanced neuroimaging, which proved essential in identifying the full extent of disease.

Previous reports of *C. parapsilosis* endocarditis within a year after TAVR have established that source control is elusive with medical treatment alone given the propensity for biofilm formation,[9,15,16] a hallmark of *C. parapsilosis* pathogenicity that underlies fluconazole resistance.[4] The latest guidelines from the Infectious Diseases Society of America (IDSA) and the American Heart Association recommend treatment of *C. parapsilosis* endocarditis with antifungal therapy (ie, echinocandins, triazoles, polyenes) combined with adjuvant surgical intervention.[17,18] The combination of medical and surgical therapy confers increased survival in patients with fungal endocarditis compared to medical therapy alone. A 2005 meta-analysis of *Candida* endocarditis cases reported a prevalence odds ratio of 0.56

for mortality in patients undergoing adjunctive surgery in addition to medical therapy when compared to medical therapy alone.[5,19] Regardless of surgical intervention, the IDSA recommends chronic suppressive antifungal therapy with a triazole agent to prevent disease recurrence.[17] Although our patient was discharged with chronic antifungal suppression, he succumbed to the infection in the context of goals of care precluding valve replacement surgery.

CONCLUSION

In summary, we describe a unique presentation of *Candida parapsilosis* endocarditis complicated by embolic cerebellar infarction. This case highlights the diagnostic challenges of source identification in fungal endocarditis and reinforces the importance of considering prosthetic valve involvement early in the evaluation of persistent fungemia. Prior reports and our experience emphasize that optimal management of *C. parapsilosis* endocarditis requires not only prolonged antifungal therapy but also timely surgical valve replacement to achieve definitive source control.

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Disclosures

None to report.

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