Recurrent *Candida parapsilosis* infective endocarditis aortic root replacement

Introduction

Fungal endocarditis accounts for 1.3–6% of infective endocarditis cases, with *Candida parapsilosis* being the second commonest causative organism. This article discusses a case of a 62-year-old man with a prosthetic aortic root replacement complicated by *C. parapsilosis* endocarditis. The case highlights the most typical presentation of this in adults with the added complication of concomitant *C. parapsilosis* septic arthritis, a presentation that has not been previously reported.

Figure 1. Computed tomography angiogram of the thoracic aorta in 2008 showing a moderate-sized filling defect projecting into the aortic lumen with a possible pedunculated element projecting cranially, identified as a vegetation.

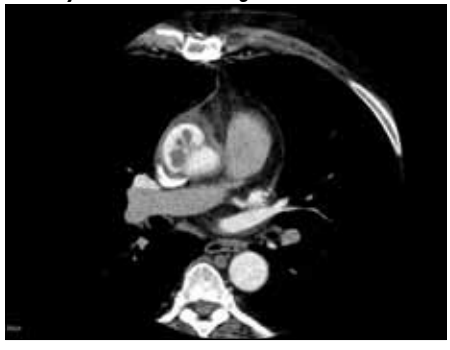

***Figure 2. Standard computed tomography angiogram of the thoracic aorta in early 2011 showing a linear/nodular filling defect anterosuperior to the fold in the mid ascending aortic graft, reduced in size compared to* Figure 1.**

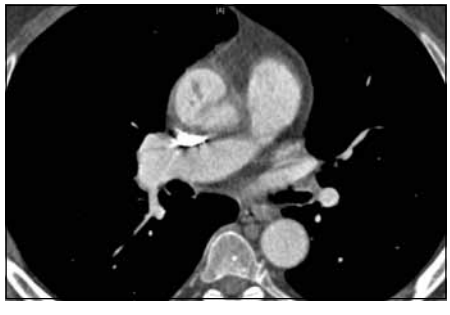

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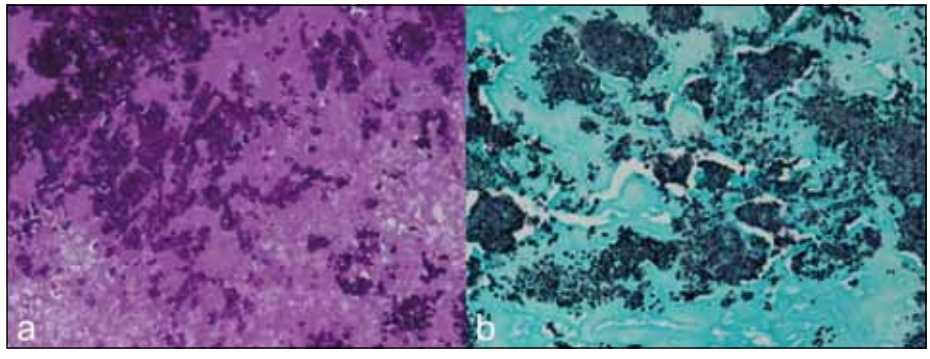
Figure 3. a. Periodic acid–Schiff staining (x40 magnification) and (b) Grocott's staining (x40 magnification) of the explanted vegetation reveal large numbers of predominantly fungal yeast, some budding and fungal hyphae, with morphology in keeping with Candida species.



Case Report

A 62-year-old man was admitted pyrexial for 2 days with acute onset confusion and rigors. He had a leucocyte count of 9.1x10^9/litre, a C-reactive protein of 57 mg/dl and a normal chest X-ray. He was a type 2 diabetic and had a right total knee replacement in 2010 because he had osteoarthritis. In 2006 he had a dilated aortic root with aortic regurgitation (non-Marfan's annulo-aortic ectasia with biscupid aortic valve) detected. He underwent an aortic root with valve and ascending aorta prosthetic replacement without complication that year.

In 2008 he presented similarly with confusion and rigors. His blood cultures grew *Candida parapsilosis* and successive transthoracic and transoesophageal echocardiograms showed no evidence of endocarditis. He was treated as having fungal prosthetic endocarditis with 4 weeks of culture-sensitive intravenous flucytosine and amphotericin B after which his symptoms resolved and his blood cultures were negative. He was discharged but returned with the same symptoms and positive blood cultures 2 weeks later. Computed tomography angiogram showed a vegetation within the ascending aortic lumen (*Figure 1*). He was treated for 8 weeks with intravenous flucytosine and amphotericin B. Redo aortic valve surgery was deemed too risky. He was discharged having negative blood cultures with lifelong fluconazole 200 mg twice daily and regular follow up. Repeat computed tomography angiogram 6 months later showed the vegetation to have resolved.

On admission in 2011 it was revealed he had not been compliant with his medications. Blood cultures confirmed *C. parapsilosis*, yet successive transthoracic and transoesophageal echocardiograms showed no vegetations. Cranial magnetic resonance imaging showed evidence of septic emboli with multiple ischaemic infarcts of the left temporal region and evidence of cerebritis. He scored 5 minor criteria on his modified Dukes score and was treated as having infective endocarditis with culture-sensitive intravenous fluconazole for 6 weeks. His C-reactive protein normalized to <3 mg/dl. Repeat computed tomography angiogram showed a linear/nodular filling defect in the mid ascending aorta graft, yet not as large as in 2008 (*Figure 2*).

Early in the admission he complained of acute onset right knee pain. His right knee was hot on palpation and mildly swollen. Right knee aspiration grew *C. parapsilosis* sensitive to fluconazole. Orthopaedic input treated his septic arthritis non-operatively with intravenous fluconazole. His right knee pain and swelling subsided and he has been symptom free since then.

He underwent a redo aortic valve with aortic root and ascending aorta replacement 1 month later. Culture and histology of the explanted graft was positive for *C. parapsilosis* (*Figure 3*). Postoperatively he received 6 weeks of amphotericin B and 4 weeks of flucytosine. On follow-up 1 year later he remained asymptomatic with negative blood cultures.

Discussion

This article describes a case of prosthetic fungal endocarditis complicated with concomitant prosthetic fungal septic arthritis. Concomitant *C. parapsilosis* joint prosthetic infection caused by *C. parapsilosis* endocarditis has not previously been reported.

Fungal endocarditis accounts for 1.3–6% of all infective endocarditis cases and carries a mortality of >41.7% (Garzoni et al, 2007). Its incidence has increased over the past two decades. Fungal endocarditis has a higher probability than bacterial endocarditis of inducing embolic events, and can be a diagnostic challenge because of the lack of typical clinical signs and symptoms such as murmur development (Garzoni et al, 2007).

The most common causative species is Candida, *C. albicans* accounting for 46%, followed by *C. parapsilosis* (17%) (Trofa et al, 2008). *C. parapsilosis* endocarditis is commonly associated with intravenous drug abusers (20% of cases), yet growing evidence has shown 87% of Candida endocarditis cases to be associated with nosocomial infections by forming a biofilm on vascular devices and catheters (Garzoni et al, 2007; Gould et al, 2012). Outbreaks of *C. parapsilosis* endocarditis were associated with intraoperative contamination (such as cardiac bypass equipment and surgical glove tears). Moreover, *C. parapsilosis* is the most prevalent fungal pathogen on health-care workers' hands (Baddley et al, 2008). Cardiovascular surgical procedures generally involve prophylactic antibiotics, which may also promote commensal candidal growth.

The cause of the initial *C. parapsilosis* endocarditis here is speculative. Although there was no episode of candidaemia during the initial replacement, the combination of potential intraoperative contamination, the patient's diabetic status and issues with medication compliance may have contributed to successive episodes of candidaemia.

Modified Dukes criteria can guide the clinician towards a diagnosis of fungal endocarditis when imaging is not conclusive. *C. parapsilosis* has a rapid virulence and echocardiography must be repeated every 7–10 days as vegetations may initially be difficult to demonstrate (Gould et al, 2012). Differences in patient morphology, transducer location, operator issues and artefacts from acoustic shadowing of the metallic prosthetic heart valve may lead to echocardiography showing no demonstrable evidence of endocarditis.

Feuchtner et al (2009) showed that multislice computed tomography could detect vegetations, abscesses and pseudoaneurysms caused by endocarditis with the same accuracy and superior anatomical information than transoesophageal echocardiography.

To date no prospective randomized controlled trial has been performed to formulate the ideal treatment for fungal endocarditis. Guidelines from the American College of Cardiology and the American Heart Association currently indicate a class I recommendation for surgical intervention in the case of fungal endocarditis, followed by antifungal therapy (Bonow et al, 2006). The Infectious Diseases Society of America guidelines on Candida endocarditis advocate treatment with valve replacement irrespective of native or prosthetic valve involvement (Pappas et al, 2009). Multivariate analysis showed a marked reduction in mortality in patients who underwent adjuvant surgery, irrespective of native or prosthetic involvement, age or gender (Garzoni et al, 2007). Despite this, the guidelines recognize that medical therapy alone can at times be curative, and hence treatment should be guided on a case-by-case basis with long-term follow up for several years as a result of high relapse rates.

Guidelines recommend dual therapy of *C. parapsilosis* endocarditis with amphotericin B with or without 5-flucytosine (Pappas et al, 2009; Gould et al, 2012). Lifelong fluconazole 400–800 mg daily for susceptible organisms is advised in patients with no surgical intervention. If valve replacement occurs, antifungal treatment is recommended for at least 4–6 weeks afterwards.

No other case in the literature demonstrates concomitant *C. parapsilosis* septic arthritis. Roughly 1% of prosthetic joint infections are thought to be caused by *Candida* spp., of which most are caused by *C. albicans* (Dutronc et al, 2010). Treatment of joint prosthetic infections can include long-term antibiotics, debridement with the retention of the prosthesis, arthrodesis, and one or two stage re-implantation (Macheras et al, 2011). Optimal management is guided by patient characteristics.

Conclusions

This case summarizes the characteristic signs and symptoms in a patient with endocarditis caused by *C. parapsilosis*. The diagnostic challenge should not deter the clinician from having a high index of suspicion of fungal endocarditis, particularly in a patient with known valve prosthesis. The virulence of *C. parapsilosis* should encourage the clinician to manage the patient aggressively. The complication of concomitant prosthetic septic arthritis highlights the clinical challenges. **BJHM**

Baddley JW, Benjamin Jr DK, Patel M et al (2008) Candida infective endocarditis. *Eur J Clin Microbiol Infect Dis* **27**(7): 519–29

Bonow RO, Carabello BA, Chatterjee K et al (2006) ACC/AHA 2006 guidelines for the management of patients with valvular heart disease. *J Am Coll Cardiol* **48:** 1–148

Dutronc H, Dauchy FA, Cazanave C et al (2010) Candida prosthetic infections: case series and literature review. *Scand J Infect Dis* **42:** 11–12

Feuchtner GM, Stolzmann P, Dichtl W et al (2009) Multislice computed tomography in infective endocarditis: comparison with transesophageal echocardiography and intraoperative findings. *J Am Coll Cardiol* **53:** 436–44

Garzoni C, Nobre VA, Garbino J (2007) *Candida parapsilosis* endocarditis: a comparative review of the literature. *Eur J Clin Microbiol Infect Dis* **26:** 915–26

Gould FK, Denning DW, Elliott ASJ et al (2012) Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy. *J Antimicrob Chemother* **67:** 269–89

Macheras GA, Kateros K, Galanakos SP et al (2011) The long-term results of a two-stage protocol for revision of an infected total knee replacement. *J Bone Joint Surg Br* **93**(11): 1487–92

Pappas PG, Kauffman CA, Andes D et al (2009) Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis* **48**(5): 503–35

Trofa D, Gácser A, Nosanchuk JD (2008) *Candida parapsilosis*, an emerging fungal pathogen. *Clin Microbiol Rev* **21**(4): 606–25

LEARNING POINTS

- This is the first reported case of concomitant *Candida parapsilosis* infective endocarditis and septic arthritis.
- Fungal endocarditis presents atypically and has a higher embolic complication rate than bacterial endocarditis.
- The incidence of fungal prosthetic infections are increasing as a result of improving diagnostic techniques and a greater exposure to medical interventions predisposing towards fungal infection.
- A combined medical and surgical approach is recommended.
- Antifungal combination therapy is recommended to treat fungal biofilms which act as a nidus of infection and resistance.