

Original article:

Candida parapsilosis endocarditis in a patient with Patent Ductus

Arteriosus

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Abstracts:

PDA-related endocarditis is a very rare entity and *Candida* as its etiological agent in itself is infrequent. Nonspecific symptoms make diagnosis of fungal endocarditis extremely difficult. This report presents a case of a woman with PDA who came for surgical repair and diagnosed with suffering from *Candida parapsilosis* endocarditis which was suspected on echocardiography and confirmed with its isolation in repeated blood cultures. Timely diagnosis and appropriate antifungal therapy in form of liposomal Amphotericin B for 3 weeks led to the resolution of infection. Owing to the greater risk of fatal complications associated with fungal endocarditis, it is imperative to have a high index of suspicion in patients with known risk factors to reach to an accurate diagnosis as soon as possible.

Key Words: Patent ductus arteriosus, *Candida parapsilosis*, fungal endocarditis.

Introduction:

Incidence of infective endocarditis caused by fungal species accounts for 1.3% to 6% of all cases. Whereas *Candida* species alone account for 94.1% of fungal endocarditis cases,^{1,2,3} *Candida albicans* is the most common causative agent followed by *Candida parapsilosis* (17%).¹ *C. parapsilosis*, a commensal of human skin is known for its capacity to grow in total parenteral nutrition and forms biofilms on catheters and other implanted devices. The nosocomial spread is by hand carriage which leads to its persistence in the hospital environment.⁴ Risk factors for *C. parapsilosis* endocarditis include, previous valvular disease, presence of prosthetic valves, intravenous drug use and parenteral nutrition, abdominal surgery, immunosuppression and treatment with broad-spectrum antibiotics.¹ Intravenous catheters, bone marrow transplant and abdominal surgery are

additional risk factors for *Candida* infections.^{5,6,7}

Candida endocarditis is associated with a high rates of mortality even with aggressive treatment.⁶ This report presents a case of *C. parapsilosis* endocarditis involving right ventricular outflow tract.

Case report:

A 29 years old female patient, known case of PDA was admitted for surgical repair in a Superspeciality hospital in May 2016. She had history of fever off and on for last 1 month. She had no other symptoms besides fever. Her physical examination was unremarkable except for a continuous pansystolic murmur on CVS examination. On day 2 of admission, a two dimensional echocardiography was performed which revealed a moderate sized PDA with a large mobile vegetation in the Right ventricular outflow tract. The same day blood samples were sent for complete hemogram and

leucocyte counts. The results are as follows: Hemoglobin-11.1 g/dl, Total Leucocytes Counts-4300/mm³, Differential Leucocyte Counts= P64 L29 E01 M06. After sending the first set of blood cultures, the patient was started empirically on Ceftriaxone, Amikacin, and Vancomycin. Repeated Blood culture samples collected at different intervals over the next 4 days showed growth in 3 blood samples while other four were sterile.

Positive blood culture samples grew smooth pasty cream coloured colonies on Sabourauds dextrose agar. Gram stain showed oval budding gram positive yeast like cells (figure 1). The infective organism was identified as *Candida* species which was germ tube negative (figure 2).⁸ On Corn Meal Agar, fine and coarse pseudomycelium (giant forms) were seen. Blastospores were seen at the septa and terminal ends either singly or in short chains (figure 3). Creamy white to pale pink colored colonies were seen on CHROM Agar (figure 4).

Further speciation and Antifungal susceptibility testing was done at the Microbiology Department, AIIMS, New Delhi. Here it was identified as *Candida parapsilosis* which was sensitive to Amphotericin B, Caspofungin and Micafungin and resistant to Fluconazole, Voriconazole and Posaconazole {determined by Microbroth Dilution technique (CLSI M27-S4)}⁹ (Table 1).

On day 5, Liposomal Amphotericin B 150mg in 500 ml 5% dextrose was started with serial monitoring of renal function tests which was continued for 21 days. ECHO repeated on Day 18 showed findings similar to the ECHO done on Day 2. A set of Blood culture samples sent two weeks after the initiation of antifungal therapy were found to be sterile. Patient was afebrile throughout her stay in hospital. She was discharged on day 25 on Oral Fluconazole 400mg

OD for 1 month without undergoing PDA repair surgery. Repeat ECHO done 1 month after the discharge showed disappearance of vegetation with blood cultures being sterile. The patient was readmitted in July 2016 for PDA closure surgery which was successfully performed and the patient was discharged the next day. Follow up Blood cultures sent after a week also showed no growth.

Discussion:

PDA-related endocarditis (whether infective or Non-infective) is a very rare entity with an estimated annual risk of <0.25% in patients with PDA.¹⁰ *Candida* endocarditis in itself is an uncommon but often a fatal entity. There is paucity of epidemiologic data regarding its incidence. Whatever little known is derived from small case series or case reports.¹¹ Literature contains around 80-90 reported cases of *Candida parapsilosis* endocarditis. Around 20 cases have been published in the last 10 years alone.¹² The diagnosis of *Candida* endocarditis is extremely difficult because its signs and symptoms are nonspecific and often identical to those of bacterial endocarditis. In a review of patients with *Candida* endocarditis, 77% of them were diagnosed post mortem.¹³ Fungal endocarditis generally results in larger vegetation than bacterial endocarditis, and tends to be more invasive to the valves, destroying the adjacent tissues, and thus promoting embolism formation.¹⁴ Therefore, it is imperative to have a high index of suspicion in patients with known risk factors to reach to an accurate diagnosis as soon as possible so that the treatment can be initiated without delay. Treatment for *Candida* endocarditis consists of Amphotericin B plus Flucytosine and early surgery. Oral azoles can be taken for long term suppression. Role of Echinocandins has not been established though these have been effective in sporadic cases.¹⁵

In vitro sensitivity to Amphotericin B, 5-Fluorocytosine, Fluconazole, Ketoconazole, and Itraconazole has been shown by *Candida parapsilosis*.¹⁶ However, there are different schools of thought regarding treatment options because there are cases including ours where endocarditis was successfully treated with antifungal agents alone and no surgery was required.^{5,6,17,18,19} on the other hand there are

some guidelines that mandate surgery to be performed as early as possible in the majority of cases.²⁰ We suggest here to keep the fungal etiology of infective endocarditis on list when Echocardiography findings show large vegetations and thereby send patient's blood for fungal cultures along with the bacterial ones on time so that the appropriate management can be done accordingly.

Acknowledgement:

The authors would like to thank Dr. Immaculata Xess, Department of Microbiology, A.I.I.M.S, New Delhi for species identification and antifungal susceptibility testing of the *Candida* isolates.

Table:1 ANTIFUNGAL SENSITIVITY PATTERN OF THE ISOLATE:		
DRUG	MIC(µg/ml)	INTERPRETATION
FLUCONAZOLE	32	RESISTANT
VORICONAZOLE	2	RESISTANT
POSACONAZOLE	0.125	RESISTANT
AMPHOTERICIN B	0.5	SENSITIVE
CASPOFUNGIN	0.125	SENSITIVE
MICAFUNGIN	0.25	SENSITIVE

Table 1: Cut-off for susceptibility:

For all drugs CLSI M27-S4⁹ guidelines followed except for posaconazole

For posaconazole, EUCAST²¹ guidelines were followed.

Control strains used: *C. parapsilosis* ATCC 22019 and *C. krusei* ATCC 6258

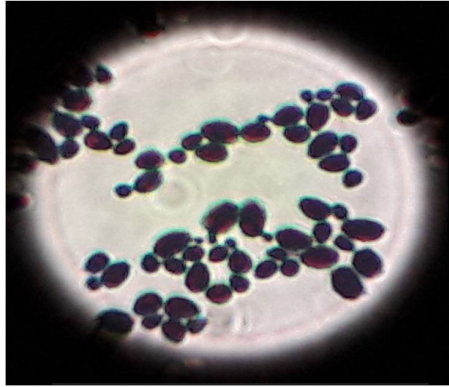


Figure 1

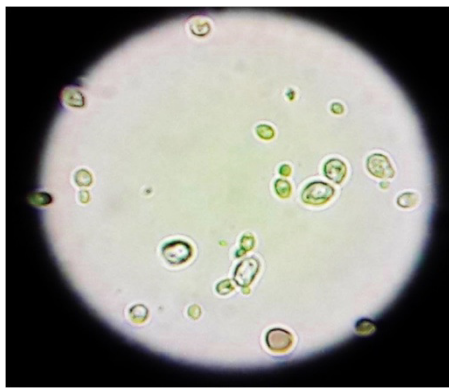


Figure 2

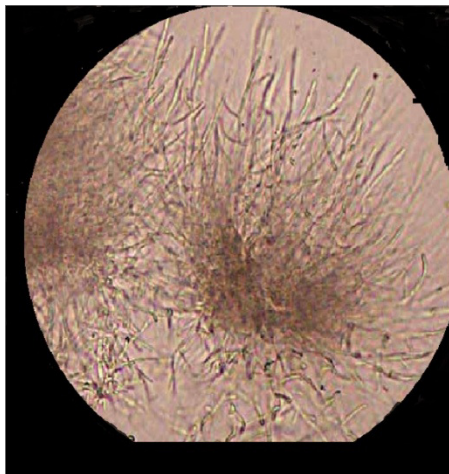


Figure 3

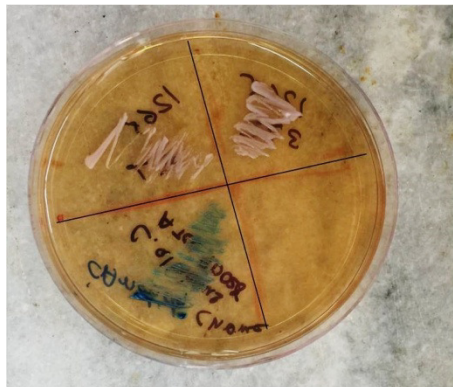


Figure 4

References:

1. Garzoni C, Nobre VA, Garbino J. *Candida parapsilosis* endocarditis: a comparative review of the literature. *Eur J Clin Microbiol Infect Dis* 2007;26:915–26.
2. Pierrotti LC, Baddour LM. Fungal endocarditis, 1995–2000. *Chest* 2002;122:302–10.
3. Otaki M, Kawashima M, Yamaguchi A, Kitamura N. A case report of *Candida* prosthetic endocarditis: an autopsy review. *Kyobu Geka* 1992;45:335–8.
4. Clark TA, Slavinski SA, Morgan J, Lott T, Arthington-Skaggs BA, Brandt ME, et al. Epidemiologic and molecular characterization of an outbreak of *Candida parapsilosis* bloodstream infections in a community hospital. *J Clin Microbiol* 2004;42:4468–72.
5. Kaloterakis A, Rizos I, Goumas G, Filiotou A, Barbetseas J, Papathanasiou S, et al. Isolated native tricuspid valve *Candida* endocarditis in a non-drug-addicted patient: case report and review of the literature. *J Heart Valve Dis* 2003;12:652–8.
6. Saito Y, Takahashi M, Sato A, Katsuki T, Ikeda U, Shimada K. Isolated tricuspid valve endocarditis due to *Candida parapsilosis* associated with long-term central venous catheter implantation. *Intern Med* 2001;40:403–4.
7. Cancelas JA, Lopez J, Cabezudo E, Navas E, Garcia Larana J, Jimenez Mena M, et al. Native valve endocarditis due to *Candida parapsilosis*: a late complication after bone marrow transplantation-related fungemia. *Bone Marrow Transplant*. 1994;13:333–4.
8. Milne LJR. Fungi. In: Collee JG, Fraser AG, Marmion BP, Simmons A, editors. *Mackie & McCartney Practical Medical Microbiology*, 14th ed. Chichester: Churchill Livingstone; 2012. p. 699-700.
9. CLSI. Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Fourth Informational Supplement. CLSI document M27-S4. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.
10. Kovacina B, Beaudoin J, Sidhu M, Hui G, Hassani C, Agrawal R, et al. Patent Ductus Arteriosus Endarteritis. Massachusetts General Hospital, Cardiovascular images- a joint publication of the Department

of Radiology and Heart Center Newsletter [Internet]. 2012 May;47. Available from: http://www.massgeneral.org/imaging/news/cv-newsletter/may_2012.htm

11. Baddley JW, Benjamin DK Jr, Patel M, Miro J, Athan E, Barsic B, et al. International Collaboration on Endocarditis-Prospective Cohort Study Group (ICE-PCS). Candida infective endocarditis. *Eur J Clin Microbiol Infect Dis* 2008; 27(7):519-29.
12. Silva-Pinto A a,b,n, Ferraz R a,b, Casanova J c, Sarmiento A a,b, Santos L a,b. Candida parapsilosis prosthetic valve endocarditis. *Medical Mycology Case Reports* 9. 2015;37-38.
13. Seelig MS, Speth CP, Kozinn PJ, Taschdjian CL, Toni EF, Goldberg P. Patterns of Candida endocarditis following cardiac surgery: Importance of early diagnosis and therapy (an analysis of 91 cases). *Prog Cardiovasc Dis* 1974;17(2):125–60.
14. Muehrcke DD, Lytle BW, Cosgrove 3rd DM. Surgical and long-term antifungal therapy for fungal prosthetic valve endocarditis. *Ann Thorac Surg* 1995;60:538–43.
15. Karchmer AW. Infective endocarditis. In: Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson JL, Loscalzo J, editors. *Harrison's Principles of Internal Medicine*, 19th ed. New York: McGraw-Hill Education; 2015. p. 816-26.
16. Trizna Z, Chen SH, Lockhart S, Lundquist KF, Smith EB, Wagner RF. Candida parapsilosis chondritis successfully treated with oral fluconazole. *Arch Dermatol* 2000;136:804.
17. Lejko-Zupanc T, Kozelj M. A case of recurrent Candida parapsilosis prosthetic valve endocarditis: cure by medical treatment alone. *J Infect* 1997;35:81–2.
18. Baddour L M. Long-term suppressive therapy for Candida parapsilosis- induced prosthetic valve endocarditis. *Mayo Clin Proc* 1995;70:773–5.
19. Zahid MA, Klotz SA, Hinthorn DR. Medical treatment of recurrent candidemia in a patient with probable Candida parapsilosis prosthetic valve endocarditis. *Chest* 1994;105:1597–8.
20. Cornely OA, Bassetti M, Calandra T, Garbino J, Kullberg BJ, Lortholary O, et al. ESCMID* guideline for the diagnosis and management of Candida diseases 2012: non-neutropenic adult patients. *Clin Microbiol Infect* 2012;18(suppl. 7):19-37
21. Arendrup MC, Cuenca-Estrella M, Lass-Flörl C, Hope W, EUCAST-AFST. EUCAST technical note on the EUCAST definitive document EDef 7.2: method for the determination of broth dilution minimum inhibitory concentrations of antifungal agents for yeasts EDef 7.2 (EUCAST-AFST). *Clin Microbiol Infect* 2012;18:E246-7.