J Infect Chemother 25 (2019) 215–217

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic

Case Report

Fungal endocarditis after transcatheter aortic valve replacement (TAVR): Case report and review of literature☆

Hiroshi Morioka [a, *], Yoshiyuki Tokuda [b], Hideki Oshima [b], Mitsutaka Iguchi [a], Yuka Tomita [a], Akihiko Usui [b], Tetsuya Yagi [a]

[a] Department of Infectious Diseases, Nagoya University Hospital, Japan
[b] Department of Cardiac Surgery, Nagoya University Hospital, Japan

ARTICLE INFO

Article history:
Received 1 July 2018
Received in revised form
15 August 2018
Accepted 25 August 2018
Available online 20 September 2018

Keywords:
Transcatheter aortic valve replacement
Transcatheter aortic valve inplacement
Fungal endocarditis
Candida parapsilosis

ABSTRACT

The reported number of transcatheter aortic valve replacement-associated infective endocarditis (TAVR-IE) cases has been increasing worldwide, but information about the incidence and clinical features of fungal TAVR-IE is quite limited. We present a patient who acquired TAVR-IE caused by *Candida parapsilosis* four month after TAVR, who was successfully treated redo-aortic valve replacement and prolonged antifungal therapy.

1. Introduction

Transcatheter aortic valve replacement (TAVR) is a new and less-invasive procedure for aortic stenosis (AS) in patients at high risk for conventional surgical aortic valve replacement (SAVR). The number of TAVRs has been gradually increasing worldwide, and reported cases of TAVR-associated infective endocarditis (TAVR-IE) have also increased accordingly [1,2]. However, the incidence and clinical features of TAVR-IE caused by rare pathogens, including *Candida* spp. and other fungi, remain unknown.

A case of TAVR-IE caused by *Candida parapsilosis* successfully treated by redo-SAVR and antifungal therapy is described along with a review of the literature on the clinical epidemiology and features of fungal TAVR-IE.

2. Case report

An 80-year-old man with a history of type 2 diabetes mellitus, chronic kidney disease, and chronic heart failure was admitted to our hospital for TAVR. A transfemoral TAVR procedure was performed using a 23mm SAPIEN3 transcatheter heart valve (Edwards Lifesciences, Irvine, CA, USA). The TAVR itself was completed with a minor vascular complication, hemorrhage of the right iliac artery. He started complaining abdominal pain since postoperative day (POD) 3, and was finally diagnosed as strangulated ileus on POD 5. Emergent ileus band resection was performed, and he was managed with total parenteral nutrition after the surgery.

On POD 15, he had a high fever and shaking chills. *C. parapsilosis* was isolated from 2 sets of blood cultures and catheter tip cultures. The minimum inhibitory concentrations (MICs) of the antifungals were: fluconazole 1 μg/mL; micafungin 0.5 μg/mL; and amphotericin B 0.5 μg/mL. Endophthalmitis was ruled out by an ophthalmologist. Caspofungin was administered to him at first, and it was then switched to fosfluconazole after identifying the species and drug-susceptibility. He was treated with the antifungals for two weeks from the day on which a negative blood culture result was obtained, and discharged on POD 37.

Two months after discharge, two sets of blood cultures were collected at the outpatient department due to night sweats and low-grade fever. Two days later, *C. parapsilosis* was isolated from both sets of blood cultures. Liposomal amphotericin B (L-AMB) 150 mg/day (≒3 mg/kg) was administered after admission. Transesophageal echocardiography showed mobile vegetations attached to the SAPIEN3 valves without apparent destruction (Fig. 1).

☆ All authors meet the ICMJE authorship criteria.

* Corresponding author. Department of Infectious Diseases, Nagoya University Hospital, 65 Tsurumai-cho, Showa-ku, Nagoya, Aichi 466-8550, Japan.
E-mail address: morioka-hiroshi@med.nagoya-u.ac.jp (H. Morioka).

https://doi.org/10.1016/j.jiac.2018.08.017
1341-321X/

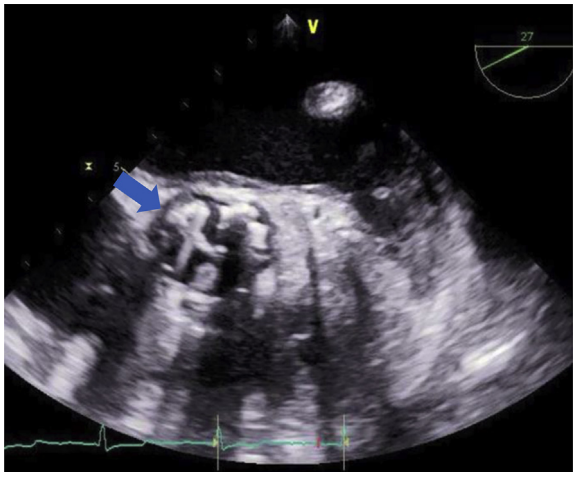

Fig. 1. Transesophageal echocardiography showing vegetation over the transcatheter heart valve (arrow).

C. parapsilosis was still detected from blood cultures on the 6th day despite the administration of L-AMB. Since the serum creatinine was increased to 1.8 mg/dL on the 8th day, the L-AMB was switched to micafungin 150 mg/day plus oral fluconazole 200 mg/day (loading dose: 400 mg). Because of uncontrollable candidemia, redo-SAVR was performed on the 11th day of the admission. Intraoperative inspection showed fragile vegetations attached to the prosthetic valves, and no perivalvular abscess (Fig. 2). The transcatheter valve was removed en bloc, and the native aortic valve leaflets were subsequently excised. A Carpentier-Edwards Magna Ease aortic valve bioprosthesis (Edwards Lifesciences, Irvine, CA, USA), which was soaked with L-AMB, was then implanted with single interrupted suture technique. The use of felt pledgets was avoided to minimize artificial materials.

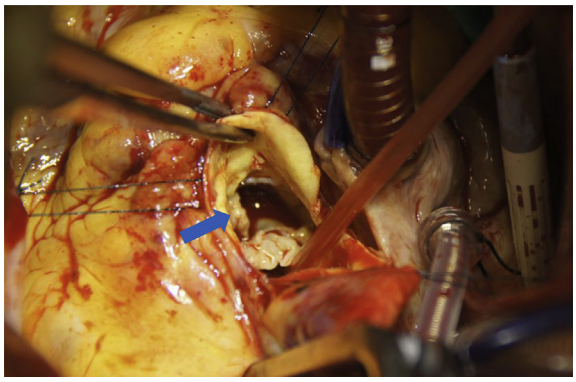

Fig. 2. Vegetation seen above SAPIEN3 transcatheter heart valve (arrow).

C. parapsilosis was grown from cultures of the prosthetic valve and the stent.

Intravenous antifungal therapy (micafungin, following L-AMB due to a suspected drug eruption) combined with oral fluconazole were continued for 6 weeks after surgery, and oral fluconazole is still being continued over 6 months.

3. Discussion

Fungal IE is known to be rare but associated with a high mortality rate (56.6%). *Candida* spp. and *Aspergillus* spp. are predominant organisms among fungal IE [3]. The incidence, mortality rate at 1 year of *Candida* IE are reported to be from 1 to 2% among total IE and 59%, respectively [4]. Risk factors for *Candida* IE have been reported to be prosthetic valves, injection drug use, cancer chemotherapy, central venous catheters, and prior bacterial endocarditis [5]. A combination therapy of valve replacement and antifungal therapy, regardless of native or prothetic valve, is strongly recommended for fungal IE [6,7].

C. parapsilosis has a notorious pathogenetic mechanism involving biofilm formation on indwelling devices, including prosthetic valves [4,8]. Lipid-based amphotericin B is the drug of choice for *Candida* IE due to its fungicidal activity and penetration into biofilms. Echinocandins have the same characteristics of fungicidal activity and biofilm penetration, besides excellent drug tolerability compared to amphotericin B [5]. However, echinocandins are generally not recommended for the treatment of *C. parapsilosis* infection because of the higher MIC than other *Candida* spp. and potential treatment failure [8].

We might have needed to consider biofilm formation on the prosthetic valves at the first episode of candidemia; however, L-AMB could not be used due to the patient's chronic kidney disease, and neither could echinocandins due to their potential therapeutic failure. As for the second episode of candidemia, the blood cultures were not negative following L-AMB monotherapy. Medication alone was insufficient treatment for the *C. parapsilosis* TAVR-IE; thus, redo-SAVR should have been considered even for a patient who was previously judged not candidates for SAVR. More importantly, it is essential to prevent catheter-associated blood stream infection in patients after TAVR.

Large multicenter registries have demonstrated the overall picture of TAVR-IE. Regueiro and Santos reported TAVR-IE in 250 of 20,006 and 53 of 7944 patients, respectively. The incidence of TAVR-IE ranged from 0.50 to 0.89% within the first year, and 1.1% per person-year. They also reported the incidence of fungal TAVR-IE as 2/250 (0.8%) −1/53 (1.9%) within the follow up periods [1,2]. The clinical features of fungal TAVR-IE were not mentioned in these registry reports. To the best of our knowledge, only total 4 cases of fungal TAVR IE cases have been reported already, including our case (Table 1). The mortality rate of fungal TAVR-IE is 50%: 2 patients who received surgical redo-AVR survived, but the others died during their hospital stay [9–11]. Ironically, TAVR itself is usually performed for patients who are at high risk of SAVR, but redo-SAVR

Table 1
Reported cases of TAVR-IE.

Reference	Reported year	Age/Gender	Approach	Valve	Duration since TAVR	Blood culture	Organisms	Antifungal therapy	Re-do surgery	Outcome
This case		80/M	TF	SAPIEN 23mm	4 months	Positive	*Candida parapsilosis*	L-AMB, MCFG + FLCZ	Y	Survived
[7]	2016	ND/ND	DA	SAPIEN 23mm	2 months	ND	*Aspergillus* spp.	ND	N	Expired
[8]	2011	91/M	TA	SAPIEN 23mm	54 days	Positive	*Candida albicans*	ND	N	Expired
[9]	2011	78/M	TF	ND	9 months	Negative	*Histoplasma capsulatum*	ND	Y	Survived

Abbreviations: TAVR, transcatheter aortic valve replacement; IE, infective endocarditis; M, male; TF, transfemoral; DA, direct aorta; TA, transapical; L-AMB, liposomal amphotericin B; MCFG, micafungin; FLCZ, fluconazole; ND, no data.

is may be the cornerstone of treatment of fungal TAVR-IE, similar to conventional fungal IE [6,7].

In conclusion, fungal TAVR-IE itself seem to be a rare complication so far. The more TAVRs are performed, the more fungal TAVR-IE may occur. To prevent TAVR-IE caused by any pathogen is a top priority, however, establishing case accumulation system of rare complications is also necessary to determine the real epidemiological and clinical features, as well as to suggest the appropriate treatment of fungal TAVR-IE to improve the survival rate.

Meeting presentation

None.

Conflicts of interest

None.

Financial disclosure

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgement

None.

This case report was approved by the institutional review board of Nagoya University Graduate School of Medicine (No. 13414).

References

[1] Regueiro A, Linke A, Latib A, Ihlemann N, Urena M, Walther T, et al. Association between transcatheter aortic valve replacement and subsequent infective endocarditis and in-hospital death. JAMA 2016;316:1083–92.
[2] Amat-Santos IJ, Messika-Zeitoun D, Eltchaninoff H, Kapadia S, Lerakis S, Cheema AN, et al. Infective endocarditis after transcatheter aortic valve implantation: results from a large multicenter registry. Circulation 2015;131:1566–74.
[3] Pierrotti LC, Baddour LM. Fungal endocarditis, 1995-2000. Chest 2002;122:302–10.
[4] Arnold CJ, Johnson M, Bayer AS, Bradley S, Giannitsioti E, Miro JM, et al. *Candida* infective endocarditis: an observational cohort study with a focus on therapy. Antimicrob Agents Chemother 2015;59:2365–73.
[5] Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the infectious diseases society of America. Clin Infect Dis 2016;62:e1–50.
[6] Baddour LM, Wilson WR, Bayer AS, Fowler Jr VG, Tleyjeh IM, Rybak MJ, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American heart association. Circulation 2015;132:1435–86.
[7] Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. 2015 ESC guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the European society of cardiology (ESC). Endorsed by: European association for cardio-thoracic surgery (EACTS), the European association of nuclear medicine (EANM). Eur Heart J 2015;36:3075–128.
[8] van Asbeck EC, Clemons KV, Stevens DA. *Candida parapsilosis*: a review of its epidemiology, pathogenesis, clinical aspects, typing and antimicrobial susceptibility. Crit Rev Microbiol 2009;35:283–309.
[9] Nelson AJ, Montarello NJ, Roberts-Thomson RL, Montarello N, Delacroix S, Chokka RG, et al. Fungal obstruction of transcatheter aortic valve replacement valve. Circ Cardiovasc Interv 2016;9.
[10] Santos M, Thiene G, Sievers HH, Basso C. *Candida* endocarditis complicating transapical aortic valve implantation. Eur Heart J 2011;32:2265.
[11] Head SJ, Dewey TM, Mack MJ. Fungal endocarditis after transfemoral aortic valve implantation. Cathet Cardiovasc Interv 2011;78:1017–9.