



Case report

Candida tropicalis endocarditis on the aortic valve with coexisting meningitis in a patient with multiple risk factors – What to do?

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ARTICLE INFO

Keywords:

Endocarditis
Candida tropicalis
 Aortic valve

ABSTRACT

A 65-year-old female patient with *Candida tropicalis* infective endocarditis on the aortic valve underwent aortic valve replacement. In the postoperative period a head computer tomography revealed a left temporal arachnoid cyst, diagnosed as fungal meningitis. We outline a successful treatment approach for this high-risk patient.

Background

Infective endocarditis (IE) can be caused by various microorganisms. Fungal origin, although relatively rare, exhibit the highest mortality rate reaching up to 50 % [1]. Beside fungal origin, renal insufficiency and diabetes mellitus contribute to increased mortality in IE [2]. *Candida tropicalis* IE is mainly associated with intracardiac electrodes and younger patients [3]. The following case presents patient with fungal endocarditis on a native aortic valve with coexisting fungal meningitis.

Case report

A 65-year-old female patient was admitted for urgent aortic valve replacement due to infective endocarditis. She presented weakness, altered consciousness, and NYHA IV heart failure. Physical examination revealed a deep shank ulceration and grade four sacral bed sore. Her medical history included lower extremity rosacea with ulcers and *Staphylococcus epidermidis* sepsis, treated using long-term antibiotics during previous hospitalization 2 months earlier. Additionally, she had type 2 diabetes with a blood glucose of 46 mmol/L and acute renal insufficiency. Echocardiography found a 24 × 17 mm aortic valve vegetation. Transferred from the Internal Medicine Unit (IMU), her ulcer swab revealed *Acinetobacter baumannii* and *Streptococcus mitis*. IMU administered 7-day broad spectrum antibiotics - colistin (3 × 3 million IU/day) and clindamycin (2 × 300 mg/day). After *Candida tropicalis* was found in blood culture, caspofungin (50 mg/day) was added.

An immediate surgical replacement of the aortic valve with a

biological prosthesis was performed. The degenerated valve along with the vegetation was removed and a perivalvular abscess was excised followed by complex reconstruction of the valve annulus. Postoperatively a permanent atrio-ventricular block grade III occurred with the need for external pacing. After surgery the patient presented quantitative and qualitative consciousness disturbances. Initially, lumbar puncture was abandoned due to extremely low platelet levels and cardiopulmonary failure, which were considered absolute contraindications. A computer tomography (CT) scan of the head uncovered an edematous area with linear post-contrast enhancement in the left parietal area suggesting inflammatory process. Based on this findings, fungal meningitis was diagnosed and therapy with amphotericin B (80 mg in 62 1 dose per day) was initiated. Contemporaneously (after 4 days of use), the caspofungin dosage was increased to 3 × 50 mg and maintained for an additional 8 days. Subsequently, the amphotericin B dosage was increased to 150 mg per day after 5 days and continued for next 8 days. Due to persistent AVB III after surgery a decision to implant a pacemaker was made. Given contraindications to pacemaker implantation due to candidemia, a pacing electrode was implanted in epicardium via left lateral minithoracotomy. On the same day fluconazole was introduced with saturation dose of 600 mg, followed by daily doses of 400 mg for the subsequent 10 days. The patient returned to the Intensive Care Unit and required mechanical ventilation. In the follow-up, a pleurocentesis was performed, yielding 500 ml of straw-colored fluid. Due to signs of malnutrition, enteral high-protein nutrition was initiated. After 15 days, cultures of bronchoalveolar lavage and cerebrospinal fluid showed negative results. However, blood culture revealed the presence of

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<https://doi.org/10.1016/j.idcr.2024.e01949>

Received 17 October 2023; Received in revised form 28 January 2024; Accepted 14 April 2024

Available online 15 April 2024

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methicillin and linezolid-resistant *Staphylococcus hominis*. In response to antibiogram data, therapy with intravenous vancomycin was administered and continued for an additional 13 days, at a daily dose of 1 g per day, with drug concentration monitoring due to renal impairment.

Due to negative results of cerebrospinal fluid on the 10-th post-operative a therapy with caspofungin was ended, amphotericin B was continua for another 5 days and fluconazole for another 10 days. The premature discontinuation of fluconazole was due to the development of liver insufficiency (increase of the aspartate and alanine transaminase, increased levels of bilirubin and international normalized ratio (INR)).

Because of prolonged mechanical ventilation, a tracheotomy was performed, followed by passive oxygen therapy, which was maintained for a further 14 days. The patient underwent intensive rehabilitation, and treatment for the leg ulceration and bed sore was provided, leading to the patient’s improvement. Antibiotic therapy was completed 10 days before the patient’s discharge from the hospital. Ultimately, the patient was hospitalized for 48 days and was discharged home in good condition (Table 1).

Discussion

The provided case is notably uncommon. Fungal endocarditis (FE) constitutes only 1–6 % of all cases of IE [3]. *Candida* is the most frequent cause of FE (50 %), with *C. tropicalis* accounting for around 5 % of FE cases and less than 0.3 % of total IE cases [5]. This species is more prevalent among neonates and young patients [3]. The occurrence of IE on the patient’s native aortic valve was atypical for *Candida* IE, which more commonly targets prosthetic valves. However, *C. tropicalis* has a stronger adhesion to epithelial cells than silicone [3]. Among *Candida* species, *C. tropicalis* generates the highest levels of biofilm, facilitating its frequent attachment to medical devices and valves [4]. Importantly, aortic valve involvement is less common compared to mitral valve infections. In Prabhudas-Strycker’s study, only 3 out of 12 reported native valve *C. tropicalis* endocarditis cases were concerned with aortic valves, and only one required replacement. Additionally, this patient had a history of drug addiction [5].

It’s crucial to highlight that the patient survived despite an extremely

high mortality risk. The surgical procedure carried a 43 % mortality risk according to the EuroSCORE II – a surgical risk score. The species of *Candida* was another risk factor. In Saiprom’s study, *C. tropicalis* emerged as the most virulent among *Candida* species, exhibiting the highest hydrophobicity, protease activity, and true hyphae formation, all contributing to greater host cell damage [5]. Candidemia itself presents a substantial mortality rate, as Mazzi reported, reaching 42.2 % [6]. This report delves into the simultaneous presence of *C. tropicalis* IE and meningitis, a combination that had not been reported previously. Untreated *Candida* meningitis poses a mortality risk of 57 % [7]. Goldani’s analysis classified *C. tropicalis* as an emerging pathogen in meningitis, with a 30 % mortality rate despite appropriate amphotericin B and 5-fluorocytosine therapy [8]. Risk factors for *Candida* IE include female prevalence, transmission from external medical devices, association with aortic valve pathology, hemodialysis, cerebrovascular disease, neutropenia, and alcohol abuse [9]. Ojha also added risk factors such as immunosuppression, presence of a central line, long-term antibiotic therapy, history of open-heart surgery, prosthetic grafts, and drug addiction [10]. This patient presented several conventional risk factors for candidemia and fungal IE, including a history of hemodialysis and long-term antibiotic therapy. Moreover, persistent ulceration could feasibly serve as an additional risk factor, providing an entry point for fungal invasion.

The patient’s swift neurological assessment and the decision to proceed with a CT scan, with contraindications to lumbar puncture, led to a modification in the fungal pharmacotherapy, transitioning to liposomal amphotericin B with patients’ significant neurological state improvement. While echinocandins are typically recommended as first-line therapy for invasive candidemias, liposomal amphotericin B is the suggested treatment for *Candida* meningitis [11]. Notably, this anti-fungal agent is considered safe for use in patients with renal insufficiency [12]. The efficacy of amphotericin over echinocandins as the initial therapy for *Candida tropicalis* was substantiated in a study involving adult patients with neutropenia [13].

Colomba described coexisting *Candida glabrata* endocarditis and meningitis successfully treated with liposomal amphotericin B (3 mg/kg/daily) for 4 weeks and then oral fluconazole [14].

Patients’ recovery proved that combination therapy with

Table 1
Dosages and time frames of administrated antibiotics.

Medical preparation	day 1	day 2	day 3	day 4	day 5	day 6	day 7	day 8	day 9	day 10	day 11	day 12	day 13	day 14	day 15	day 16	day 17	day 18	day 19	day 20	day 21	day 22	day 23	day 24	day 25	day 26	day 27	day 28	day 29	day 30	day 31	day 32
Colistin [mln IU]	9																															
Clindamycine [mg]	600																															
Caspofungin [mg]			50				150																									
Amphotericin B [mg]							80					150																				
Fluconazole [mg]														600	400																	
Vancomycine [g]																			1.5	+1	1											

Day of the surgery.

casposungin and liposomal amphotericin B was effective for coexisting endocarditis and meningitis.

The success of the treatment was also influenced by the use of step-down therapy to fluconazole. In Husni multi-center study among non-neutropenic patients, those who had a stepdown therapy had more favorable outcomes (78 % survival) as compared to those with no stepdown (56 % survival) [15].

Another challenge involved overcoming perioperative complications, such as third-degree atrioventricular block (AV III block). Klapkowski reported that permanent third-degree AV III block requiring pacemaker implantation occurred in 6.9 % of patients after aortic valve replacement. Among those patients, 18.2 % developed infective endocarditis [16]. In this specific case, AV III block was associated with an abscess communicating with the right atrium. It was assumed that AV block would occur during abscess evacuation and reconstruction of the aortic valvular annulus.

It is estimated that 0.5–4.8 % of implantations of cardiac electrotherapy devices are complicated by infection. It seems prudent to implant epicardial electrodes instead of endocavitary electrodes to avoid infection in high-risk patients [17]. This technique had been considered before implantation to avoid early CDRIE (Cardiac Devices Related Infective Endocarditis) since fungemia was still present.

Conclusion

It seems that the decision to provide salvage surgical intervention in patients with fungal endocarditis and meningitis. Despite the extremely high perioperative risk, the prompt diagnostics, as well as the correct antifungal pharmacotherapy and intensive care management can improve patient survival. This particular case shows that comprehensive diagnosis, surgical and medical treatment, work of multidisciplinary Heart-Team give hope for patients with the highest procedural risk.

Ethical approval statement

All data were anonymized, and individual patient consent and ethics committee approval were not required.

Consent

Individual patient consent was waived because of the study's retrospective design and the data collection from routine care.

Funding Source

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author Statement

All authors of this paper declare that this manuscript is original, has not been previously published in print or electronic form, is not under consideration by another editorial board, and there are no ethical issues or conflicts of interest. The manuscript has been read and approved by all named authors. The order of the author listed in the manuscript has been approved by all authors. All authors declare no conflict of interest regarding this manuscript.

CRedit authorship contribution statement

Michał Kapalka: Data curation, Formal analysis, Investigation, Writing – original draft. **Grzegorz Hirnle:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project

administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Tomasz Hrapkowicz:** Conceptualization, Supervision, Writing – review & editing. **Michał Krawiec:** Data curation, Formal analysis, Investigation, Writing – original draft.

Conflict of Interest

All authors of this paper declare that the case report has not been previously published in print or electronic form, is not under consideration by another editorial board, and there are no ethical issues or conflicts of interest. All authors declare no conflict of interest regarding this manuscript.

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