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# Cardiovascular implantable electronic devices fungal infections: unpredicted frequency and challenging management

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**Background:** Fungal infections (FIs) of cardiovascular implantable electronic devices (CIED) are uncommon but show often a poor prognosis. Due to their rarity, their characteristics and optimal management are not clearly defined. The aim of our study was to describe the characteristics and outcome of a series of CIED-FIs.

**Material/methods:** In this prospective, observational, single-centre study, over a 48-months period (November 2012 – November 2016), we enrolled all consecutive patients with CIED infection observed at our Centre from whom clinically significant fungal isolates were obtained from either blood, CIED-pocket samples, leads. Patients (pts) were co-managed with Cardiology and Microbiology Units. Demographic, clinical, microbiological, treatment and outcome data were recorded.

**Results:** We observed 84 pts with CIED infection, 7 of whom (8,3% vs. 2% from the literature), were CIED-FIs (Figure 1: 5 males, median age 76,5 years, range 50-86). The infection involved pacemakers in 2 pts and implantable cardioverter defibrillators in 5. Median number of leads/patient was 3 (range 1-3). All pts had undergone ≥1 prior device revision (median 2; range 1-4). Regarding risk factors for infections, 6 out of 7 pts showed chronic heart failure, two diabetes mellitus and one a myeloperoxidase deficiency. Three patients showed fever at presentation, one of them sepsis and all of them had endocarditis. Local signs of infection were present in the majority of pts, including pocket erosion (6) and purulent discharge (5). Candida spp. was identified in all cases: C. albicans (4), C. tropicalis (2), C. parapsilosis (1). All fungal isolates were pansensible to antifungals except for one C. albicans strain resistant to fluconazole. All pts showed an associated bacterial infection. Pts received an initial combination antimicrobial therapy, either empirical or consistent with pre-extraction isolates when available, which was re-assessed according to further microbiological investigations. Antifungal

treatment consisted of echinocandins in 4 pts and fluconazole in 3, with a median duration of 3 weeks (range 1-5). Five pts underwent a complete CIED extraction with both clinical and microbiological success; one of them, however, showed a non-fungal relapse of CIED infection after 5 months. The CIED was not removed due to critical clinical conditions in 2 pts, who experienced a clinical failure in absence of further fungal isolate. All the latter 3 subjects (1 relapse, 2 failures) were subsequently re-managed with device extraction and antimicrobial treatment, thus obtaining successful outcome. The remaining 4 pts showed no relapse after a median follow-up of 14,5 months (range 6-18).

**Conclusions:** In our experience, CIED-FIs were more frequent than previously reported, and represented a severe clinical event, requiring a complex management. An echinocandin-based regimen, in addition to device extraction, may represent a successful treatment approach.

| Patient | Age / sex | Comorbidities | Type of infection | Clinical findings | Echocardiography | Culture results | Complications | Antifungal therapy, Device Management | Outcome / Follow-up |
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| **Pt. 1** | 83 / M | Parkinson's disease, CHF | Pocket infection + endocarditis | Pocket erosion and purulent discharge | 8 mm filamentous vegetation on RA lead tip, a smaller one along the RV lead | PC, LC: *C. Albicans + MSSA*<br><br>BC: *MSSA* | None | Caspofungin for 4 wks<br>Complete CIED removal | Clinical success<br>No relapse after 18 months |
| **Pt. 2** | 83 / M | Anemia | Endocarditis | Sepsis | 30 mm round vegetation over tricuspid valve and lead loop | BC from CVC: *C. Albicans + S. epidermidis* | Confusion, metastatic abscesses | Fluconazole for 5 wks<br>No CIED removal | Failure* |
| **Pt. 3** | 79 / M | Essential hypertension, dyslipidemia, CHF, myeloperoxidase deficiency | Pocket infection + endocarditis | Fever, pocket erosion and generator exposure | 7 x 4 mm vegetation along the RV lead | PC, RA-LC: *C. tropicalis + S. epidermidis* | Acute heart failure, sepsis, pneumonia | Micafungin for 1 wks, then fluconazole for 2 wks<br>Complete CIED removal | Clinical successful<br>No relapse after 18 months |
| **Pt. 4** | 50 / F | Marfan's syndrome, mental retardation, CHF | Pocket infection + endocarditis | Pocket erosion and purulent discharge | 4 x 2 mm vegetation on RA lead tip | PC: *C. parapsilosis + S. epidermidis* | None | Fluconazole for 5 wks<br>No CIED extraction | Failure* |
| **Pt. 5** | 86 / M | Essential hypertension, Parkinson's disease, arteriopathy, CHF | Pocket infection | Pocket erosion and purulent discharge | No vegetations | BC, RA-LC: *MSSA*<br><br>PC: *C. albicans + MSSA* | None | Micafungin for 1 wk<br>Complete CIED removal | Clinical success<br>No relapse after 11 months |
| **Pt. 6** | 74 / M | Type I mellitus diabetes, CKD, essential hypertension, CHF, dyslipidemia, multinodular goiter | Pocket infection | Pocket erosion and purulent discharge | No vegetations | PC: *C. tropicalis*<br><br>RV-LC: *C. tropicalis + P. aeruginosa* | Pocket hematoma, anemia, diabetes decompensation | Micafungin for 3 weeks<br>Complete CIED removal | Relapse* after 5 months |
| **Pt. 7** | 73 / F | Type II diabetes, COPD, essential hypertension, CHF, hypotiroidism | Pocket infection + endocarditis | Fever, pocket erosion with generator exposure and purulent discharge | No vegetations | PC: *C. Albicans + MSSA*<br><br>LC: *MSSA* | Diabetes decompensation, AKI, pocket hematoma, anemia | Fluconazole for 2 weeks<br>Complete CIED removal | Clinical success<br>No relapse after 6 months |

***Figure 1. Characteristics, management and outcome of the 7 patients with CIED FIs.***

*Legend: M, male; F, female; CHF, chronic heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; RA, right atrium; RV, right ventricle; PC, pocket culture; LC, lead culture; BC, blood culture; CVC, central venous catheter; MSSA, methicillin-sensible Staphilococcus aureus; AKI, acute kidney injury; IV, intra-venous.*

***Pts 2, 4 and 6 were furtherly re-managed with device extraction and antimicrobial treatment, obtaining successful outcome***