**Candida tropicalis** defibrillator endocarditis: A case report and review of current literature

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**A R T I C L E  I N F O**

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**A B S T R A C T**

We provide a review of current literature and report on a case of electronic device infective endocarditis with *C. tropicalis*. A 64-year-old man presented for revision of his implantable cardioverter defibrillator. Echocardiography revealed extensive vegetations attached to the Eustachian valve and in the right ventricular apex. Microbiological findings presented *C. tropicalis* on the explanted material. The patient refused additional surgical intervention. We successfully treated the patient with liposomal Amphotericin B and Flucytosine for 8 weeks.

1. Introduction

Endocarditis is a severe infectious disease with a high proportion of fatal cases [1–7]. In-hospital mortality ranges from 12% to 17% for native valve endocarditis, 23%–26% for prosthetic valve endocarditis, 10% for cardiac implantable electronic device infective endocarditis (CIED-IE), and 8% for right-sided endocarditis. There are numerous factors known to increase mortality, such as heart failure, renal failure, diabetes, male sex, and higher age. Moreover, hospital-acquired endocarditis, endocarditis location, cardiac resynchronization therapy as well as persistent infection, and cardiac, hemodynamic and neurological complications are relevant risk factors [3,5–11].

Around 70% of endocarditis cases are native valve endocarditis and 21%–25% are prosthetic valve endocarditis. Other than that, CIED-IE accounts for about 5% of all endocarditis cases. Likewise, right-sided endocarditis, mainly caused by CIED-IE, accounts for 8.5% [3,4,8]. In recent decades, the number of CIED-IE has increased in a more progressive manner than the number of device implantations [12,13]. This highlights the healthcare burden of CIED-IE [14]. Certain risk factors such as renal insufficiency, male sex, anticoagulant use, long-term corticosteroid treatment, number of pacing leads, device revision and prior device procedures are associated with the incidence of CIED-IE. Perioperative antibiotic use has a protective effect [15–19]. Regarding aetiology, *S. aureus*, coagulase-negative staphylococci, and viridans group streptococci are the most common pathogens for endocarditis. However, about 2% account for fungal endocarditis [3–6,10,20]. The majority of fungaemia cases are contributed to *C. albicans* (52.1%) and *C. glabrata* (28.0%) whereas *C. tropicalis* only accounts for about 4.1% [21]. Thus, Candida species are the most common cause of fungal endocarditis. In particular, *C. tropicalis* causes up to 9% of Candida endocarditis and up to 13% of Candida CIED-IE [22,23]. Nevertheless, *Aspergillus* species may also account for 11–24% of fungal endocarditis cases [20,24]. The sensitivity of blood cultures to detect *Candida* is 50–70% [25] which may result in blood culture negative infective endocarditis and thus in a postponed start for optimal therapy. *Candida* endocarditis is difficult to treat and often associated with a poor outcome. Baddley et al. showed a significant difference in mortality among *Candida* patients and patients with non-fungal endocarditis of 30.3% vs. 17.0%, respectively [22]. Others described mortality rates of 33.3% in fungal endocarditis compared to 14.8% in non-fungal endocarditis and 46.6% in *Candida* endocarditis compared to 16.1% in non-*Candida* endocarditis [3,26].

In this case report we present a rare case of *C. tropicalis* implantable cardioverter defibrillator endocarditis combined with an endocarditis affecting the right ventricular lead, the right ventricle and the Eustachian valve.

2. Case

The patient, a 64-year-old man with one vessel coronary artery disease, chronic kidney disease and paroxysmal atrial fibrillation presented for a right ventricular lead revision of his single chamber...
implantable cardioverter defibrillator due to loss of sensing.

14 months earlier, the patient underwent cardiopulmonary resuscitation due to ventricular tachycardia. He was treated on the intensive care unit in an external hospital for 42 days. He was mechanical ventilated for the first 28 days and catecholamine therapy was required for the first 13 days. Continuous venovenous hemodiafiltration was performed from day 3 to day 14 due to sepsis with multiple organ failure. The patient developed a prolonged pneumonia, which was caused by chlamydia (Serological testing day 24) and treated with Piperacillin/Tazobactam, Ciprofloxacin and Clarithromycin. Due to colonic diverticular bleeding eight erythrocyte concentrates were transfused. The patient developed a C. tropicalis sepsis. C. tropicalis was detected in faecal and blood cultures 17 days after the survived sudden cardiac death and was treated with Caspofungin for 2 weeks. Following the antifungal therapy, blood cultures were negative. An implantable cardioverter defibrillator was implanted for secondary prevention. One appropriate shock was applied due to ventricular fibrillation 5 weeks after implantation. 7 months later, the right ventricular lead showed a loss of sensing and was replaced. At that time, a transthoracic echocardiography showed no abnormalities.

On admission, 14 months after the survived sudden cardiac death and 7 months after the first replacement of the ICD, there was a moderate rise in the C-reactive protein level (2.0 mg/dl) and a slightly reduced glomerular filtration rate (71 ml/min). Otherwise, laboratory findings and clinical examination as well as chest X-Ray were inconspicuous. Surprisingly, a pus-filled ICD pocket was observed during surgery. The extracted lead was covered with thin vegetations. Implantation of a new internal cardio defibrillator was postponed. A large floating mass on the Eustachian valve measuring 40 × 17 mm (Fig. 1) and a smaller floating mass located in the right ventricular apex measuring 22 × 15 mm (Fig. 2) was detected by echocardiography (day 0).

To detect C. tropicalis on the ICD and its lead the matrix-assisted laser desorption ionization-time of flight mass spectrometry (Bruker...
Table 1

| Reference | Age/ Gender | Medical history | Symptoms | Diagnostics | Complications | Therapy | Outcome |
|-----------|-------------|-----------------|----------|-------------|---------------|---------|---------|
| Bauer et al. 2019 | 64/M | IDA, S. aureus IE and PV replacement | Fever, chest pain | Pericardial effusion | 2 weeks | Liposomal Amphotericin B 5 mg/kg/d and Flucytosine 25 mg/kg (q.i.d.). | No follow up |
| [61] | 53/M | IDA, intravenous drug abuse | Fever, chest pain | Transoesophageal and transthoracic echocardiography revealed floating masses on the Eustachian valve | 2 weeks | Liposomal Amphotericin B 5 mg/kg/d and Flucytosine 25 mg/kg (q.i.d.). | No follow up |

As demonstrated earlier, *Candida* IE in particular and fungal IE in general present very severe infectious diseases with poor outcome and multiple complications. Leof et al. indicated a rate for embolic complications in 73% of *Candida* IE [27] whereas Baddley et al. did not observe an increased risk for embolization in fungal IE [22]. In CIED-IE lead, vegetation size and mobility do not correlate with the occurrence of pulmonary embolism. Only systemic embolism increases the overall mortality [28]. Nevertheless, large vegetations, as described in our case, may increase the risk for fulminant pulmonary embolism [28]. Yet, there is a significant number of silent pulmonary as well as systemic embolisms [19,29–31]. The risk for an embolism reduces continuously over time after initiation of medical treatment with having the lowest risk 2 weeks following the initiation of causative medical treatment with liposomal Amphotericin B 5 mg/kg/d and Flucytosine 25 mg/kg (q.i.d.). Due to an acute infusion-related reaction to liposomal Amphotericin B associated with leg and lower back pain, we successfully administered Clemastine 2 mg and Ranitidine 50 mg prior to infusion. The patient refused an operative revision of the vegetations.
| Reference | Age/Gender | Medical history | Device | Symptoms | Diagnostics | Complications | Therapy | Outcome |
|-----------|------------|-----------------|--------|----------|-------------|---------------|---------|---------|
| [62]      | 71/M       | DM, CHF, obstructive uropathy, recurrent urinary tract infections, complete heart block | 9 months VVI-PM | Fever, confusion | UC: Yeast Autopsy: 20 × 20 mm vegetation on lead, involved RA, TV, IVC. Consolidation in left lower lung Microscopic: Many colonies of Candida organisms in vegetation, myocardium, lung BC: C. albicans TTE: 50 × 20 × 20 mm mass attached to pacer wire extending from RA to RV | CHF | Broad-spectrum antibacterials | Patient deceased |
| [63]      | 65/M       | CVA, IV catheter-related C. albicans fungaemia 6 months before device infection | 8 years PPM | Fever, confusion, urine/faecal incontinence | Gastrointestinal bleeding, hypotension, pulmonary embolism | | | |
| [64]      | 56/M       | Heart block | 5 years PPM | Fever, cough, dyspnoea | Subtotal occlusion of left PA | Right atriotomy and pulmonary arteriotomy, removed PPM leads and fungus ball from left main PA | 2 years follow up without relapse |
| [65]      | 75/M       | DM, sick sinus syndrome | 2 years PPM | Blurred vision | Endophthalmitis, multorgan failure | Amphotericin B + Flucytosine Refused surgery to remove PPM | Patient deceased with multorgan failure |
| [66]      | 56/M       | Chronic bronchitis, sinus dysfunction | 4 years PPM 3 months PPM/wire (pouch infection) | Fever, dyspnoea | Left PA occlusion | Right atriotomy – removed vegetation, wires and PPM Amphotericin B 0.5 mg/kg/d + Flucytosine for 18 days, followed by oral Fluconazole 400 mg/d, followed by 200 mg/d for 7 months | 7 months follow up without relapse |
| [67]      | 56/M       | Sick sinus syndrome | PPM | Fever, dyspnoea | – | Antibiotic (not defined) Surgical removal of PPM | Survived |
| [68]      | 72/M       | Brady cardia – tachycardia syndrome | < 1 month DDD-PM | – | TOE: Vegetation on TV Lead: C. glabrata | Endovascular extraction of PPM C. glabrata infection uncontrolled | Patient deceased after 2 months with active Candida endocarditis |
| [69]      | 77/M       | DM, CAD, sick sinus syndrome | 5 months PPM | Fever, dyspnoea, lethargy | Multiorgan failure | Thoracotomy – vegetation on TV, interatrial septum and on PPM lead, removed vegetation and lead Lipoosomal Amphotericin B 3 mg/kg/d due to renal failure | Patient deceased with multorgan failure after surgery |
| [70]      | 87/M       | CML, renal neoplasm, prosthetic AV | 16 years PPM | Fever, renal insufficiency | Fatal stroke on day 63 | Fluconazole 5 mg/kg/d, then 10 mg/kg/d Not a surgical Candidate | Patient deceased with fatal stroke |
| [71]      | 49/M       | DM, CAD, CHF, VT | 1 year ICD | Fever, dyspnoea, cough | – | Amphotericin B 8 weeks followed by Fluconazole 400 mg/d p.o. Thoracotomy | 6 months follow up without relapse |
| [72]      | 63/M       | CAD, CHF, VT | 10 months ICD | Fatigue | Vegetation: C. albicans | | | |

(continued on next page)
| Reference | Age/Gender | Medical history | Device | Symptoms | Diagnostics | Complications | Therapy | Outcome |
|-----------|------------|----------------|--------|----------|-------------|---------------|---------|---------|
| [73] 56/M | Rheumatic heart disease, cardiomyopathy, VT | 12 years ICD 1 week Generator | Fever, sweat, hypotension, ICD pocket dehisced | atrial ICD lead (largest 16 mm) Lead and pocket: C. albicans | Hypotension, atrial lead fracture with embolization into left PA, septic shock | – | Percutaneous explantation Received Fluconazole, then liposomal Amphotericin B | After improvement patient deceased with P. aeruginosa sepsis No follow up |
| [74] 76/M | Colorectal cancer, CVC, parenteral nutrition, abdominal surgery before CIED-IE | PPM | – | BC: C. parapsilosis Echo: Vegetation on lead | Possible cerebral embolus | – | PPM removal Fluconazole for 42 days | Patient deceased secondary to abdominal surgery complications 14 months follow up without relapse |
| [26] 38/M | Mechanical AV replacement | 3 months PPM | Fever | BC: C. albicans | Multiple pulmonary embolisms, sepsis | – | PPM removal Caspofungin for 6 weeks, followed by 12 weeks oral Fluconazole and Posaconazole | 3 months follow up without relapse |
| [75] 19/M | Complete heart block with epicardial PPM age 5, endocardia replacement due to car accident and following long lasting intensive care unit stay | 1 year PPM | Fever, cough, haemoptysis | BC: C. albicans TTE: Mass on PPM lead | – | Thoracotomy, explanation and epicardial reimplantation of PPM Caspofungin and Fluconazole for 8 weeks | 3 months follow up without relapse |
| [76] 69/F | COPD Gold IV, DM, hypertension, paroxysmal AF, pulmonary hypertension, sick sinus syndrome, sepsis and mechanical ventilation (20 days on ICU) after 2 weeks DDD-PM implantation | 2 weeks DDD-PM | Fever | BC: P. mirabilis and C. albicans CVC tip: C. albicans TOE: With vegetation on PM lead during 2nd Anidulafungin therapy | Pneumonia, pericardial infusion, respiratory insufficiency and mechanical ventilation, flaccid tetraparesis | – | Anidulafungin (200 mg day 1, then 100 mg/d) for 3 days followed by Fluconazole 800 mg/d for 2 weeks 6 days later positive blood cultures Anidulafungin (200 mg day 1, then 100 mg/d) followed by Fluconazole Anidulafungin (200 mg day 1, then 100 mg/d) after TOE findings until 16 days after negative BC | Follow up (time frame not given): no relapse |
| [23] 80/M | CAD, COPD, AF, complete heart block | 12 years PPM 8 years Generator | Chills, confusion | BC: C. parapsilosis TOE: 5 × 5 mm mobile mass on lead, fibrinous strands on TV Vegetation: C. parapsilosis Vegetation and lead: C. albicans TTE/TOE: 20 mm vegetation on the atrial lead Intra-cardiac echocardiography: 50 mm vegetation in the RA | Left main PA embolus and left lower lung infarct | – | Amphotericin B, maintained for 3 weeks after percutaneous explantation | 1 year follow up without relapse |
| [77] 75/F | Gallbladder removal and gut perforation 34 months earlier | 62 months DDD-PM | Fever | BC: C. albicans Vegetation and lead: C. albicans TTE/TOE: 20 mm vegetation on the atrial lead Intra-cardiac echocardiography: 50 mm vegetation in the RA | Complete obstruction of the SVC | – | Fluconazole 400 mg q.d. for 40 days Micafungin 100 mg/d for 45 days Percutaneous explantation Reimplantation 10 days later (BC negative) and Micafungin for further 15 days | 6 months follow up without relapse |
| [78] 62/M | CHF, DM, CAD, HCV infection | 11 months ICD | Fever, dysnea on exertion, chest pressure | BC: Candida albicans TOE: 40 mm mass on ICD lead | – | Fluconazole 400 mg q.d. 10 days Micafungin 100 mg/d for 45 days Percutaneous explantation | 6 months follow up without relapse |
| [79] 68/F | Not given | 2 years DDD-PM 1 year Generator and lead | Fever | BC: MRSA and C. tropicalis TOE: With vegetations on atrial and ventricular leads (largest 25 × 8 mm) | – | Fluconazole 400 mg/d Thoracotomy, ICD explantation Discharged day 3 Procedure: 6 weeks of Fluconazole 200 mg before reimplantation | No follow up |
| [80] 60/F | Sarcoïdosis, DM, CKD, reduced LV-EF, episodes of non-sustained VT, 9 months | 26 months single lead ICD | Fever, cough, chest pain | BC: C. albicans Vegetation: C. albicans | – | Thoracotomy, Micafungin 2 weeks followed by Fluconazole for 6 weeks | Relapse after 7 months; successfully treated with Caspofungin and Fluconazole | (continued on next page)
| Reference | Age/Gender | Medical history | Device | Symptoms | Diagnostics | Complications | Therapy | Outcome |
|-----------|------------|----------------|--------|----------|-------------|---------------|---------|---------|
| [81] 86/M DM | Earlier several abdominal surgeries with infection and positive BC for C. albicans | TTE: 20,9 × 44,9 mm | Vegetation on ICD lead | Relapse of fungaemia and vegetation on the TV after 7 months | Relapse: Vancomycin and Ceftriaxone for 6 weeks (BC negative) 4 weeks later | 20 days follow up without relapse |
| | | TTE/TOE: Multiple vegetations on the PM electrode | | | | |
| | | More weeks of Liposomal Amphotericin B/Caspofungin added (70 mg day 1, 50 mg/d) | | | | |
| | | | | | | No follow up |
| [82] 70/F | Prior day hospital for 1 week due to urinary tract infection with septic shock (Vancomycin 1 day, Piperacillin/Tazobactam 3 days, followed by Ciprofloxacin p.o.), DM, CKD, CHF, survived SCD | TTE/TOE: Multiple vegetations on ICD, AV vegetation, new tricuspid regurgitation | Septic shock, bilateral pulmonary emboli | Liposomal Amphotericin B 5.5 mg/kg/d for 28 days and 3 mg/kg/d due to nephrotoxicity for 28 days, Caspofungin 70 mg day 1, 50 mg/d | 56 days follow up without relapse |
| | | | | | | |
| [83] 65/F | Hypertension, CKD, hemodialysis, DVT, NICM, NYHA IV, LV-EF 10%, obesity, hypertension, DM, DVT, pulmonary embolism, palliative inotrope therapy via Hickmann catheter: multiple bloodstream infections | TOE: 23 mm vegetation on ICD electrode | Septic shock, bilateral pulmonary emboli | Liposomal Amphotericin B and Caspofungin 70 mg day 1, 50 mg/d | 6 months follow up without relapse |
| | | | | | | |
| [41] 25/F | NICM, NYHA IV, LV-EF 10%, obesity, hypertension, DM, DVT, pulmonary embolism, palliative inotrope therapy via Hickmann catheter: multiple bloodstream infections | TOE: 61,3 × 16,5 mm in the RA from SVC + 21 × 16 mm RA part of RV electrode | Septic shock, bilateral pulmonary emboli | Liposomal Amphotericin B 5.5 mg/kg/d for 28 days and 3 mg/kg/d due to nephrotoxicity for 28 days, Caspofungin 70 mg day 1, 50 mg/d | 14 months follow up without relapse |
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**Abbreviations:** AF = Atrial fibrillation; CAD = Coronary artery disease; CHP = congestive heart failure; CVD = Chronic kidney disease; CVA = cerebrovascular accident; DM = Diabetes mellitus; DVT = Deep vein thrombosis; EV = Eustachian valve; F = female; HP = histopathology; ICM = Ischemic cardiomyopathy; IDA = intravenous drug abuse; M = male; PA = Pulmonary artery; PM = pacemaker; PV = Pulmonary valve; RA = Right atrium; RV = Right ventricle; SCV = SVC; SCD = Sudden cardiac death; TTE/TOE = transthoracic echocardiography/transoesophageal echocardiography; TTE = transthoracic echocardiography; TV = Tricuspid valve; UC = Urine culture; VF = Ventricular fibrillation; VP = Ventricular pacemaker; VR = Ventricular rhythm; W = white; Y = young.
treatment [2,29,32,33].

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