

Sternectomy for *Candida albicans* sternal osteomyelitis after left ventricular assist device implantation

Mathias van Hemelrijck¹, Michelle Frank¹, Annelies Zinkernagel¹, Ronny Buechel¹, Juri Sromicki¹, Markus Wilhelm¹, Holger Klein¹, Barbara Hasse¹, and carlos mestres¹

¹University Hospital Zurich

July 22, 2020

Abstract

Fungal osteomyelitis is uncommon after cardiac surgery. A case of *Candida albicans* and *S. epidermidis* osteomyelitis with device infection after implantation of a left ventricular assist device in a male patient is presented. After confirmation with microbiological and radiological examinations, debridement was performed. Surgical specimens grew *C. albicans* and *S. epidermidis*. Fluconazole, daptomycin and negative pressure wound therapy failed to achieve healing. Total sternectomy and pectoralis muscle flap reconstruction were performed. There was no recurrent infection for *C. albicans* on a prolonged antifungal regime. The combination of antifungal therapy and aggressive surgical debridement may be useful to control fungal osteomyelitis.

Sternectomy for *Candida albicans* sternal osteomyelitis after left ventricular assist device implantation

Running title: Debridement for fungal osteomyelitis

Mathias Van Hemelrijck, MD¹, Michelle Frank, MD², Annelies S. Zinkernagel, MD, PhD, MSc³,

Ronny Buechel⁴, MD⁴, Juri Sromicki, MD¹, Markus J. Wilhelm, MD, PhD¹, Holger Klein, MD⁵, Barbara Hasse, MD³, Carlos - A. Mestres, MD, PhD¹

¹Clinic for Cardiac Surgery, ²Clinic for Cardiology, ³Division of Infectious Diseases and Hospital Epidemiology, ⁴ Department of Nuclear Medicine, Cardiac Imaging, ⁵Department of Plastic Surgery and Hand Surgery, University Hospital Zurich, Zurich, Switzerland

Presented in part at the 15th Symposium of the International Society of Cardiovascular Infectious Diseases, Lausanne, Switzerland, June 2 - 4, 2019

Word count (total): 1427

Word count (abstract): 100

Correspondence to:

Carlos – A. Mestres MD PhD FETCS

Department of Cardiac Surgery

University Hospital Zürich

Rämistrasse 100

CH-8091 Zürich (Switzerland)

Tel.: +41 44 255 95 82

Fax: +41 44 255 44 67

E-mail: Carlos.Mestres@usz.ch

Abstract

Fungal osteomyelitis is uncommon after cardiac surgery. A case of *Candida albicans* and *S. epidermidis* osteomyelitis with device infection after implantation of a left ventricular assist device in a male patient is presented. After confirmation with microbiological and radiological examinations, debridement was performed. Surgical specimens grew *C. albicans* and *S. epidermidis*. Fluconazole, daptomycin and negative pressure wound therapy failed to achieve healing. Total sternectomy and pectoralis muscle flap reconstruction were performed. There was no recurrent infection for *C. albicans* on a prolonged antifungal regime. The combination of antifungal therapy and aggressive surgical debridement may be useful to control fungal osteomyelitis.

Introduction

Fungal osteomyelitis is a serious albeit uncommon condition after cardiac surgery. It requires aggressive therapy and is associated with high mortality. Treatment strategy includes prolonged antifungal therapy and surgical debridement, whereas the extent of excision is still a matter of debate. A case of *Candida albicans* and coagulase negative staphylococci sternal osteomyelitis and concomitant left ventricular assist device (LVAD) infection, its therapy and outcome are discussed.

Case report

A 60-year-old male patient underwent LVAD (HeartWare®) implantation in November 2017 as a bridge-to-transplantation due to ischemic cardiomyopathy. He required 6 mediastinal re-explorations due to recurrent bleeding. After bleeding control, he subsequently was discharged from the hospital two months postoperatively. Three months later he was readmitted due to pulmonary decompensation and sternal wound infection (SWI). Fluorodeoxyglucose-positron emission tomography-(FDG-PET)-scan confirmed sternal uptake (Figure 1). Surgical debridement of the sternum was performed. *C. albicans* and *Staphylococcus epidermidis* grew in the intraoperative samples. Negative pressure wound therapy (NPWT) was initiated. The antimicrobial therapy included Caspofungin 50mg/24h IV and Daptomycin 10 mg/kg body weight/24h IV. Sequential samples of sternal tissue, taken during repetitive wound revisions, were persistently positive for *C. albicans* and *S. epidermidis*. Blood cultures were negative, and a subsequent FDG-PET-scan suggested persistent sternal infection and a new abscess-like-formation around the LVAD. We scheduled the patient for surgical resection and dead space filling with an adjacent muscle flap. LVAD exchange was not an option since the new device would have had to be implanted in an already infected area. Heart transplantation could not be offered to the patient due to his poor condition. LVAD explantation was not an option because of severely reduced left ventricular function. Total sternectomy and pectoralis muscle flap closure of the chest were successfully performed (Figure 2). After a complicated in-hospital course, which included pneumonia requiring temporary veno-venous extracorporeal membrane oxygenation (ECMO) and add-on of an antimicrobial therapy with Meropenem 2x1g/d i.v. (nosocomial pneumonia) and Clarithromycin 2x500mg/d p.o. The patient was discharged, after almost nine months in the hospital.

Six months later under suppressive antifungal therapy with oral Fluconazole 400mg/24h, no signs of fungal growth could be observed. However, a mechanical skin perforation above the LVAD outflow cannula was documented and subsequent debridement with LVAD coverage by a myo-cutaneous *latissimus dorsi* muscle flap was performed (Figure 3). Cultures of the excised ulcerated tissue and all collected blood cultures did not show fungal or antimicrobial growth, furthermore aspergillus antigen was negative (index 0.04). After an initially satisfactory postoperative course, the patient developed bilateral pneumonia and died nine days after flap coverage. Postmortem examination disclosed respiratory failure with diffuse alveolar damage as the immediate cause of death. Further findings showed a chronic left-sided pleural empyema with pus surrounding the LVAD-driveline. However, there were no persistent signs of osteomyelitis.

Comment

Deep sternal wound infection (DSWI) after cardiac surgery has an incidence of around 2% (1). With a reported mortality of 55% (2), *Candida* osteomyelitis represents a severe and uncommon condition that requires combined surgical debridement and prolonged antifungal treatment. Re-sternotomies due to non-infective causes, prolonged use of antibiotics, colonization of the respiratory and urinary tracts and the use of percutaneous dilatational tracheostomy devices, have been identified as risk factors facilitating *Candida* infections (2). Fungal osteomyelitis represents a treatment challenge for which a number of surgical strategies have been suggested (1, 2, 3). The optimal treatment strategy is still not clear (2, 3). There are no significant outcome differences between the different surgical approaches, although more promising results have been confirmed with omental flaps in a recent review by Arikan and colleagues (3). But omental flaps require the opening of the abdominal cave, harshly increasing the patient's mortality. The use of a NPWT and a muscle flap is recommended by the European Association of Cardiothoracic Surgery (EACTS) as Class I and IIb recommendation, respectively, with a level of evidence B in DSWI. However, there is no clear treatment strategy regarding fungal osteomyelitis (3). On the other hand, Pappas et al. recommend surgical debridement and an antifungal regime of 6 to 12 months (4). These recommendations are based on case reports and small series (5, 6). In terms of timing of secondary wound closure, there is still a gap of knowledge among current guidelines and recommendation reports.

The implicated patient suffered from a combination of DSWI and LVAD associated infection. In a recent multicentric study, Tattevin and colleagues reported 30% of infections after LVAD implantation with 4% being cannula or pump related. *Candida*- associated LVAD infections were found in 6% of the patients. In this prospective study, the mortality rate among infected patients was 10% (7). Regarding treatment strategies, it has been suggested that persistent infections under a suppressive antibiotic regime might require device explantation and subsequent heart transplantation (8). In the case reported herein, an initial debridement with NPWT was unsuccessful. The patient therefore underwent total sternectomy and muscle flap closure. Since neither device explantation nor heart-transplantation were possible in our case, we decided that long-term suppressive antifungal therapy was mandatory. We achieved control of fungal osteomyelitis in this exceedingly uncommon case of infection in a patient under long-term mechanical circulatory support.

Authors contributions:

MVH: Concept and design, drafting article, revision of article

MF, AZ, RB, JS, MW and HK critical revision of article, approval of article

BH and CAM: drafting article, critical revision of article, approval of article

References

1. Modrau IS, Ejlertsen T, Rasmussen BS. Emerging role of *Candida* in deep sternal wound infection, *Ann Thorac Surg* 2009; 88:1905-1909
2. Arikan AA, Omay O, Kanko M, Horuz E, et al. Treatment of *Candida* sternal infection following cardiac surgery - a review of literature. *Infect Dis* 2019; 51:1-11
3. Abu-Omar Y, Kocher GJ, Bosco P, Barbero C, et al. European Association for Cardio-Thoracic Surgery expert consensus statement on the prevention and management of mediastinitis. *Eur J Cardiothorac Surg* 2017; 51:10-29.
4. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, et al. Clinical practice guideline for the management of candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis* 2016; 15:e1-50
5. Clancy CJ, Nguyen MH, Morris AJ. Candidal Mediastinitis: An emerging clinical entity. *Clin Inf Dis* 1997; 3:608-613
6. Malani PN, McNeil SA, Bradley SF, Kauffman CA. *Candida albicans* Sternal Wound Infections: A chronic and recurrent complication of median sternotomy, *Clin Inf Dis* 2002; 11:1316-1320
7. Tattevin P, Flecher E, Auffret V, Leclercq C, et al. Risk factors and prognostic impact of left ventricular assist device-associated infections. *Am Heart J* 2019; 214:69-76.

8. O'Horo JC, Abu Saleh OM, Stulak JM, Wilhelm MP, et al. Left ventricular assist device infections: A systematic review. *ASAIO J* 2018; 64:287-294.

Figure legends

Figure 1

Sternal uptake in an FDG-PET-scan. The arrow points towards it.

Figure 2

A: mediastinum after sternectomy, the arrow points to the caudal portion of the outflow cannula B: pectoralis flap covering the mediastinum

Figure 3

Latissimus dorsi muscle flap

A: Before incision, B: After skin demarcation C: Before covering the mediastinum and LVAD (circle) with a *latissimus dorsi* muscle flap (star), D: Final result. The arrow points in all images to the mediastinum.

Hosted file

Sternectomysequence.pptx available at <https://authorea.com/users/314230/articles/471436-sternectomy-for-candida-albicans-sternal-osteomyelitis-after-left-ventricular-assist-device-implantation>

Hosted file

Sternaluptakecasereport.pptx available at <https://authorea.com/users/314230/articles/471436-sternectomy-for-candida-albicans-sternal-osteomyelitis-after-left-ventricular-assist-device-implantation>

Hosted file

Latdorsiflap.pptx available at <https://authorea.com/users/314230/articles/471436-sternectomy-for-candida-albicans-sternal-osteomyelitis-after-left-ventricular-assist-device-implantation>