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BRIEF REPORT

Candida spp. Deep Sternal Wound Infections: A Consequence of Antibiotic use?

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A cluster of deep sternal wound infections caused by *Candida* spp. occurred at our institution. Investigation did not disclose a common environmental source. We postulate that broad-spectrum antibiotic surgical prophylaxis and liberal use of antibiotics contributed to these infections.

Keywords. antibiotic prophylaxis; antimicrobial stewardship; candida; mediastinitis; sternal infection.

Deep sternal wound infections are thought to originate with the implant of endogenous micro-organisms at the time of surgery. This concept is supported by the fact that infection often occurs within 2 weeks of surgical intervention, with the most common pathogens being *Staphylococcus* spp. [1, 2]. Although *Candida* spp. are rarely associated with deep sternal wound infections postoperatively, the actual frequency of such infections is difficult to establish because of incomplete microbiology data and, historically, a lack of appreciation of their pathogenic potential.

A growing appreciation of the role of *Candida* spp. in deep sternal wound infections occurred in the 1990s [3–5], including their capacity to cause nosocomial outbreaks [6, 7]. Recent series have reported a higher proportion of *Candida* spp. deep sternal wound infections [1, 8]: whether this is due to better recognition or a true increased incidence is uncertain. Here, we describe 7 cases of *Candida* spp. deep sternal wound infections.

CASE SERIES

In late 2022, we recognized an increase in the proportion of deep sternal wound infections involving *Candida* spp. at our institution. A retrospective review of the Flinders Medical Centre SA Pathology microbiology laboratory database for tissue and deep swab specimens yielding *Candida* spp. between 2018 and 2022 was undertaken and specimens from sternal bone or deep tissue were identified. Seven cases occurred in 2022, with 2 cases over the preceding 4 years.

Our public hospital is colocated with a private hospital with all cardiac surgery procedures performed at the private hospital. Six of the cases had index surgery performed, with 4 admitted to the public hospital and 2 in the private hospital. A seventh case had index surgery at a different hospital and was later transferred to the private hospital. The number of cardiac surgeries performed each year for public cases had been relatively stable over the previous decade.

Case notes and microbiological data were manually reviewed for all 7 cases. Surgical and infection control practices were reviewed. Patients undergoing median sternotomy have chlorhexidine bodywash 24 hours before and the morning of surgery and all body hair within the surgical field is clipped. Surgical wound dressings are subject to surgeon preference; however, no changes were noted. Audited hand hygiene compliance rates in the intensive care unit and the surgical wards ranged from 75% to 88%. Routine maintenance of operating theaters including air colony counts were unremarkable and there were no major renovations undertaken.

The details of the cases are summarized in Table 1. All cases had host risk factors for infection: 5 patients had diabetes mellitus and 5 patients were obese. All patients with diabetes were being treated with oral hypoglycemic medications. Five of the 7 patients resided in the Northern Territory. Two of the Northern Territory patients were Indigenous Australians and underwent redo valve replacement surgery for complications of rheumatic heart disease. Most infections occurred within 2 weeks of the index procedure.

In the majority of cases (6/7), a *Candida* spp. was grown from multiple deep specimens on the initial sternal debridement, supporting its role as a primary pathogen. In 1 of the 7 cases, bacteria were also present on the initial debridement (case 2: *Klebsiella aerogenes*). One patient (case 7) developed a bacterial superinfection. One patient (case 3) had *Morganella morganii* cultured from initial sternal debridement, with 2 *Candida* spp. later identified on the fourth debridement, supporting a *Candida* spp. superinfection. *Candida albicans* was the most frequent species isolated (5 cases), with *Candida parapsilosis* (2 cases) and *Candida metapsilosis* isolated as part of a mixed infection (case 3).

All patients were aggressively surgically managed with early debridement and removal of sternal wires and multiple

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Table 1. Clinical Details of Cases of *Candida* spp. Deep Sternal Wound Infection

Case	Demographics	Index Surgery	Time to Infection	Microbiology	Surgery	Antibiotics Prescribed Prior to *Candida* spp. Isolation[a]	Antifungal Treatment	Outcome at 12 mo
1	62 M IHD, BMI 31 DM HbA1c 7.4%[c]	CABG, AVR	14 d	*C albicans* (1)[b] *S epidermidis* (1)	8× surgeries Pectoralis flap	Vancomycin 30 d Meropenem 19 d Cefepime 15 d Ceftriaxone 7 d Rifampicin 7 d Piperacillin/tazobactam 3 d Cefazolin 2 d	Fluconazole 12 mo	Cured
2	60 M IHD, COPD, BMI 30	AVR for aortic stenosis	8 d	*C parapsilosis* (1) *K aerogenes* (1)	9× surgeries Pectoralis flap	Cefazolin 5 d	Fluconazole 2 mo Anidulafungin 3 mo (at time of relapse) Voriconazole ongoing	Relapsed
3	66 M IHD, BMI 29 DM HbA1c 11.8%	CABG	6 d	*M morganii* (1), *S epidermidis* (4), *C albicans* (4), *C metapsilosis* (4)	8× surgeries Pectoralis flap	Meropenem 23 d Vancomycin 3 d Piperacillin/tazobactam 1 d	Anidulafungin 2 wk Fluconazole 6 mo	Cured
4	58 M Indigenous Australian IHD, rheumatic heart disease, BMI 31	Redo AVR	5 d	*C albicans* (1)	10× surgeries Pectoralis flap	Piperacillin/tazobactam 20 d Vancomycin 8 d Amoxycillin/clavulanate 5 d	Anidulafungin 5 wks Fluconazole ongoing	Not known
5	43 M Indigenous Australian COPD, BMI 38 DM HbA1c 5.8%	Redo MVR, TV annuloplasty	15 d	*C albicans* (1)	10× surgeries Omental flap	Piperacillin/tazobactam 6 d	Anidulafungin 2 mo Fluconazole 2 mo Isavuconazole 2 mo Anidulafungin 4 mo	Cured
6	78 F IHD, BMI 38 DM HbA1c 6.3%	CABG, AVR for aortic stenosis	10 d	*C parapsilosis* (1)	2× surgeries Pectoralis flap	Nil	Anidulafungin 4 wk Fluconazole ongoing	Cured
7	71 M IHD No BMI recorded DM, no HbA1c recorded	CABG	Uncertain	*C albicans* (1), *E coli* (3), *E cloacae* (3)	5× surgeries Pectoralis flap	Flucloxacillin 7 d Dicloxacillin	Anidulafungin 3 wk Fluconazole 9 mo	Cured

Abbreviations: AVR, aortic valve replacement; BMI, body mass index; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; IHD, ischemic heart disease; MVR, mitral valve replacement; TV, tricuspid valve.

[a]Antibiotics prescribed in hospital up to the isolation of *Candida* spp. (excluding surgical prophylaxis).

[b]The bracketed number represents the number of surgeries after the index procedure from which the organism was first isolated.

[c]HbA1c taken 0–2 mo before index surgery.

procedures culminating in reconstructive flap surgery with either pectoralis major or omental transposition. Patients were treated with prolonged antifungal therapy, in most cases anidulafungin, followed by fluconazole 400–800 mg by mouth daily. All patients survived to hospital discharge. Long-term follow-up data was available for 6 of the 7 cases: 3 patients were cured after courses of 6, 9, and 12 months of fluconazole, respectively; 1 case was cured but remained on fluconazole with a planned duration beyond 12 months. Two patients had relapsed infection: 1 with associated candidemia (case 2) and 1 with persistent sternal wound induration who was eventually cured after 10 months of antifungal therapy (case 5).

DISCUSSION

The cause of this cluster of *Candida* spp. deep sternal wound infections was investigated by the infection prevention and control unit and surgical quality and safety team. Unlike previously described outbreaks by Isenberg and Pertowski, no common staff or environmental source could be identified [6, 7]. The difference in *Candida* spp. also argued against a point source outbreak. No change in wound dressings, surgical equipment or postoperative care were implicated.

In response to increasing rates of deep sternal wound infection caused by gram-negative bacteria, antimicrobial prophylaxis for cardiac surgery was revised in 2017 at our institution: gentamicin was added to cefazolin and teicoplanin. Routine glycopeptide use was rationalized by the large numbers of patients from the Northern Territory with difficulties in methicillin-resistant *Staphylococcus aureus* screening before surgery. All patients received this surgical prophylaxis with the exception of 1 who did not receive gentamicin because of renal impairment. In addition, 6 of 7 cases received antibiotic therapy before the isolation of *Candida* spp. from deep surgical specimens, in many cases with broad-spectrum agents for durations longer than 1 week (Table 1). In some cases, this was necessary to treat concomitant bacterial infection.

Antibiotic use has long been recognized as an important risk factor for *Candida* spp. infection through the loss of "colonization resistance" provided by endogenous microbiota [9]. Patients undergoing cardiac surgery have been found to have higher perioperative *Candida* spp. colonization with greater exposure to antibiotics [10]. Higher intensity of *Candida* spp. colonization has been shown, in turn, to precede invasive *Candida* spp. infections in surgical patients [11, 12]. There are no previous studies clearly linking *Candida* spp. sternal wound infections with antibiotic use; however, 1 study provides circumstantial evidence of an association. Modrau et al, who reported the highest proportion of *Candida* spp. deep sternal infections at 20.5%, did so in the setting of broad-spectrum antibiotic surgical prophylaxis with cefuroxime and gentamicin, administered for a minimum of 48 hours and up to 5 days, which is longer than the usual recommendation of 24 hours [8, 13]. They were not able to provide an alternate explanation for the high number of *Candida* spp. infections in their study.

Across various settings, the use of antibiotics has been associated with subsequent *Candida* spp. infections. In hospitalized patients, antibiotic exposure is a risk factor for invasive *Candida* spp. infection and has been incorporated into predictive scoring systems, both in the intensive care unit and in general wards [14, 15]. In patients with liver cirrhosis, receipt of antibiotics in the previous 7 days is an independent risk factor for candidemia [16]. A case control study comparing fungal and bacterial prosthetic joint infections found antibiotic use in the previous 90 days was significantly associated with *Candida* spp. infection [17].

The outcomes of patients in our series compare relatively favorably with those in earlier series of *Candida* spp. sternal wound infections that report high mortality and high relapse rates [4, 5]. This likely reflects several factors: the prompt recognition of the significance of *Candida* spp. isolated from deep sternal wound specimens, advances in surgical techniques, and early and prolonged antifungal treatment. The difficulty of managing *Candida* spp. sternal wound infections is illustrated by the number of surgical debridements required to control the infection, the prolonged intensive care and hospital admissions, and that 2 patients developed relapsed infection. Limited experience supports a long duration of antifungal therapy, in the order of 6–12 months, to avoid relapses that have been seen with shorter treatments [18].

The limitations of this case series are that it is observational in nature, involving a small number of patients. The lack of a control group does not allow firm conclusions to be drawn about the influence of antibiotic use on these infections relative to other variable such as comorbidities and host factors. For a more definitive conclusion, a case control study is required.

SUMMARY

A cluster of complicated deep sternal wound infections caused by *Candida* spp. occurred in the setting of broad-spectrum antimicrobial surgical prophylaxis and liberal use of antibiotics. The lack of an alternative explanation and the recognized association between antibiotic use and *Candida* spp. infection supports antibiotic use as a driver of these infections.

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