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Mediastinitis: Could your case be a candidate for *candida*?

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Summary

Background: *Candida mediastinitis* is rare, but mortality has been reported as high as 50%. There are no clinical trials evaluating treatment of *Candida mediastinitis* and there are only a limited number of reports in the literature.

Case Report: We present two cases of mediastinitis after coronary artery bypass grafting due to *Candida albicans*. Immunosuppression and long surgical procedures were likely risk factors for the infections. After multiple hospitalizations and debridements there was concern for the development of resistance. However, the isolates were determined to be fluconazole-susceptible and the patients were treated with long-term oral fluconazole.

Conclusions: *Candida mediastinitis* is difficult to treat. Even with appropriate treatment, patients may require numerous surgical debridements.

key words: **mediastinitis • *Candida* • treatment**

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Background

Mediastinitis is a life-threatening complication of thoracic surgery in approximately 2% of patient cases [1–5]. It typically develops 2–4 weeks after surgery [4]. Obesity, smoking, duration of surgery, and length of intensive care stay have all been identified as risk factors for postsurgical mediastinitis [5,6]. Staphylococcal species account for the large majority of these infections [4,7]. *Candida mediastinitis* is rare (<10%) but appears to be increasing [4,8]. Antibiotics, which are given as surgical prophylaxis for thoracic surgery, have no coverage against candida. Mortalily rates in *Candida mediastinitis* have been reported as high as 50% [4]. Oftentimes, diagnosis of candida mediastinitis is delayed because intraoperative cultures are not obtained or cultures that are positive for candida are considered contaminants [9]. There are no clinical trials evaluating treatment of *Candida mediastinitis* and very few reports in the literature. Treatment typically involves surgical debridement followed by several months of antifungal therapy [9,10]. We present two cases of mediastinitis after coronary artery bypass grafting due to *Candida albicans*. In both cases, multiple surgical debridements were required.

Case Reports

Patient 1

A 46-year-old Hispanic male presented to the emergency department with purulent drainage from his sternal surgical site. The patient had been hospitalized 15 days earlier for a coronary artery bypass graft (CABG) procedure. The patient had significant past medical history for diabetes (HgA1c 7.6% on admission), end stage renal disease requiring dialysis, hypertension, and Hodgkin's lymphoma (completed last chemotherapy cycle five months earlier). Patient was on therapy for diabetes and hypertension. He was not receiving immunosuppressive therapy and had not received long-term IV antibiotic therapy prior to his admission. The patient received cefazolin as surgical prophylaxis for his CABG procedure. The procedure was approximately 8 hours.

Chest CT with contrast on admission revealed infection of all layers of the incision extending into the anterior mediastinum. Patient underwent surgical debridement of the sternum and resection of chest wall. Cultures were obtained during the procedure. Vancomycin and pipercillin/tazobactam were then initiated empirically. Cultures later revealed *Candida albicans* and therapy was switched to anidulafungin. The patient received fourteen days of IV treatment and was discharged on oral fluconazole 400 mg (~5.5 mg/kg) daily which was to be continued for six months.

Following discharge, the patient was seen in the outpatient antimicrobial treatment (OPAT) clinic for the next two months. During one visit, it was noted that the wound continued to ooze purulent fluid. Patient was placed on doxycycline for ten days for suspected secondary infection with normal skin flora. Two weeks following initiation of doxycyline, the patient appeared to have no improvement. A CT revealed a pocket of pus and osteomyelitis at the head of the clavicle, corresponding to the area of the most superior aspect of the surgical incision. Daptomycin 500 mg (~6 mg/kg) after dialysis and ciprofloxacin 500 mg daily was initiated. There was major concern that the patient needed significant incision and drainage and was scheduled for followup with cardiothoracic surgery three days later. The patient was admitted to the hospital the same week for decreased level of consciousness, sleepiness and generalized weakness. During readmission, the patient underwent additional debridement and resection of sternum and right sternoclavicular joint. Operative cultures were consistent with previous results of *Candida albicans*. There was concern for resistance, so susceptibilities were sent and the patient was started on IV anidulafungin. Results revealed that the organism was susceptible to fluconazole (MIC=1). MICs were also available for voriconazole (MIC=0.06), itraconazole (MIC=0.06), and anidulafungin (MIC=0.12). No bacteria grew on culture after patient was exposed to daptomycin and ciprofloxacin. The patient received fourteen days of IV antifungal therapy and was sent home on oral fluconazole for six months. In addition, the patient was continued on vancomycin and cefepime for six weeks and was followed by the hospital OPAT clinic. At discharge, there was no exudate at the surgical site. At the 3-month follow-up appointment the patient had no signs of surgical site infection.

Patient 2

A 59-year-old female was admitted to the hospital after presenting with fever, chills, chest wall pain, and purulent drainage from her sternal incision site. She had undergone a CABG procedure six weeks earlier. Approximately two weeks after surgery the patient saw her primary care provider in for bloody discharge from the sternal incision. The provider at that time gave the patient a prescription for cephalexin and the patient reported that it appeared to get a little better, but did not resolve completely.

The patient's past medical history was significant for tobacco use, diabetes mellitus (HgA1c 5.5% on admission), obesity, hypertension, hyperlipidemia, two previous MIs and idiopathic thrombocytic purpura (ITP), for which she was receiving prednisone. The patient had not received long-term IV antibiotic therapy prior to her admission. The patient received cefazolin as surgical prophylaxis for her CABG procedure. The procedure was approximately 5.5 hours.

Upon admission to the medical intensive care unit, vancomycin and pipercillin/tazobactam were started empirically for suspected deep sternal wound infection with possible osteomyelitis. A CT without contrast revealed subcutaneous air bubbles suggesting infection deep in the subcutaneous tissue. The patient was taken to the operating room for surgical exploration and sternal wound debridement. During the procedure sternal osteomyelitis and mediastinal infection were confirmed, requiring subtotal sternectomy. Initial cultures obtained during the procedure revealed *Candida albicans* and *Staphylococcus epidermidis* (vancomycin susceptible, MIC=1) and anidulafungin was added to her antimicrobial regimen. The patient was taken for a second debridement and chest wall reconstruction on post-operative day (POD) 5. Followup cultures from surgery showed no growth. Pipercillin/tazobactam was discontinued and the anidulafungin was changed to fluconazole 400 mg IV daily (~4.2 mg/kg). The patient remained febrile with elevated WBCs. The wound was debrided for the third time on POD 10.

Over the next 3 weeks the wound was debrided an additional 4 times. Fluconazole was switched to oral therapy on POD 30, with the plan to continue therapy for at least 6 months. At this time superficial necrosis was observed and concern for pseudomonal infection was noted. Cultures were drawn at the next debridement on POD 38 and were positive for *Proteus mirabilus (*susceptible to piperacillin/tazobactam by disk diffusion), VRE (susceptible to linezolid, MIC=2), MRSA (susceptible to vancomycin, MIC=1), *Pseudomonas aeruginosa* (susceptible to cefepime and piperacillin/tazobactam, MIC=8 and 8/4, respectively) and *Klebsiella pneumonia* (susceptible to piperacillin/tazobactam MIC=8/4). Linezolid and cefepime were initiated. The wound was debrided once more over the next week (POD 43) and began to show good granulation tissue. Antibacterials were continued for four weeks. Oral fluconazole was continued for a total of 6 months. The last available follow-up note at 1 year indicated that the patient discontinued fluconazole 1 month after discharge, 4 months earlier than planned. It was noted that the incision was healing well although patient did complain of bilateral tenderness in her rib cage. Imaging from 1-year follow-up visit revealed no evidence of infection.

Discussion

While *Candida* is the leading cause of invasive fungal infections in hospitals, with *Candida albicans* being the most prevalent, *Candida mediastinitis* is rare. We have described two cases of *Candida mediastinitis.* Both patients had previously undergone a coronary artery bypass graft procedure, which is a risk factor for mediastinitis. Hospital Infection Control reviewed both patient cases and determined that the patients were high-risk for such infections due to their immunocompromised state and their long duration of surgery.

In both cases, the infecting organism was *Candida albicans*. Prompt diagnosis and treatment of *Candida mediastinitis* plays an important role in treatment success and decreasing mortality. Delays in treatment, such as dismissal of cultures as contaminants, increases the risk of mortality in these patients. Both patients were treated appropriately once cultures returned.

The guidelines currently recommend several months of treatment, similar to treatment of osteomyelitis. There have been reports about vertebral osteomyelitis due to *Candida* being successfully treated with amphotericin B and fluconazole [11,12]. Both patients initially received intravenous antifungal therapy, but were able to be switched to oral therapy. Fluconazole is an acceptable agent in these cases and may be preferable due to ease of administration and good tolerability.

Another component of treatment success is the proper dosing of fluconazole. There have been reports regarding sternal osteomyelitis showing failure with 200 mg daily of fluconazole; consequently, treatment is successful when the dose is increased to 400 mg daily and continued for six months [13]. Currently duration of treatment is unclear with publications ranging from weeks to several months. One report showed relapse in patients who had initially undergone treatment for two and three months [14]. These patients were subsequently re-treated for nine and twelve months and cured.

Another major component of treatment success appears to be surgery. Even in cases where the organism is susceptible multiple debridements may be required. Patients initially treated with only antifungals have been shown to need additional surgery [12].

Conclusions

Both of our patients required multiple debridements, even with infections with susceptible organisms. There was concern for fluconazole failure in both of these patients. However, susceptibility testing showed that fluconzazole was appropriate and that proper debridement was key to treatment.

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