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A Rare Case of *Aspergillus* Mediastinitis After Coronary Artery Bypass Surgery: A Case Report and Literature Review

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Conflict of interest:

None declared

Patient: Male, 74-year-old
Final Diagnosis: *Aspergillus fumigatus* infection
Symptoms: Anemia • elevated inflammatory marker • fever • mediastinal fluid collection • sternal disruption
Medication: —
Clinical Procedure: —
Specialty: Cardiac Surgery • Infectious Diseases

Objective: Rare disease

Background: Mediastinitis is a serious complication after cardiac surgery; it is a deep sternal wound infection following sternotomy, with clinical evidence and/or microbiological involvement and sternal osteomyelitis. The most common pathogens are *Staphylococcus* spp (*S. aureus*), followed by gram-negative organisms. Establishing an etiological diagnosis of fungal mediastinitis is often a challenging issue, given the nonspecific clinical presentation.

Case Report: A 74-year-old man was diagnosed with a three-vessel coronary artery disease in a university hospital. The patient had as clinical background hypertension, a body mass index (BMI) of 29.78 kg/m², and no diabetes mellitus. After an uneventful coronary artery bypass surgery, he presented clinical and radiological mediastinitis manifestations on the 9th postoperative day. He was treated with a range of antibiotics, with no clinical improvement until the 33rd postoperative day. Then, mediastinal fluid and biopsied tissue were collected and he was started on voriconazole due to growing *Aspergillus* spp. On the 93rd postoperative day, he had clinical improvement and, after several exams, was released from the hospital. We present the first report of *Aspergillus fumigatus* mediastinitis after cardiac surgery in Brazil, successfully treated with voriconazole.

Conclusions: *Aspergillus* infection should be considered in the differential diagnosis of mediastinitis after coronary surgery, especially in a clinical case of unexplained sepsis, negative blood culture, and no clinical improvement despite antibiotic therapy. This case report highlights that the mediastinal fluid and biopsy tissue culture can be useful for the diagnosis of fungal mediastinitis.

Keywords: *Aspergillus* • Mediastinal Diseases • Voriconazole

Abbreviations: BMI – body mass index; WBC – white blood cell; RBC – red blood cells; CRP – C-reactive protein; ICU – Intensive Care Unit; POD – postoperative day; IV – intravenous

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/933193>



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Background

Mediastinitis is a deep sternal wound infection following sternotomy, with clinical evidence and/or microbiological involvement and sternal osteomyelitis, with an incidence varying from 0.5 to 5.6% [1-3].

According to the European Association for Cardio-Thoracic Surgery expert consensus, the diagnosis of mediastinitis after sternotomy requires at least one of the following criteria: 1) a positive culture of fluid or mediastinal tissue; 2) a histopathological lesion compatible and 3) signs and symptoms such as fever, chest pain or sternal instability¹.

Postcardiac surgery wound infections are mostly caused by *Staphylococcus* or *Enterobacteriaceae* species [2,3]. Herein, we report the first case of mediastinitis caused by *Aspergillus* after coronary artery bypass graft surgery in Brazil.

Case Report

A 74-year-old man was admitted to a university hospital in a Brazilian Midwest Region state with precordial pain and typical angina, showing tightness and irradiation to the left upper limb. The patient had hypertension, a body mass index (BMI) of 29.78 kg/m², and no diabetes mellitus. A cardiac catheterization procedure diagnosed three-vessel coronary artery disease, and the patient underwent coronary artery bypass surgery.

Initial laboratory test results revealed no anemia and normal hemogram parameters: white blood cell (WBC) count, $7.2 \times 10^3/\mu\text{L}$ (normal range: 4.5 to $11 \times 10^3/\mu\text{L}$); neutrophils, 66%; red blood cells (RBCs), $5.22 \times 10^6/\mu\text{L}$ and C-reactive protein (CRP), 3.16 mg/L (normal range: 0 to 5 mg/L). Cardiac enzyme levels were normal (creatinine kinase: 13.28 U/L; troponin I: 12.5 pg/mL). The creatinine level was 1.26 mg/dL (0.5-1.2 mg/dL), and blood urea nitrogen was 37.3 mg/dL (16-40 mg/dL). The coagulogram and blood glucose level (88 mg/dL) did not show abnormalities. Blood and urine cultures were negative.

The surgery was uneventful. On the 9th postoperative day (POD), the patient presented with sternal instability, fever (axillary temperature 39.2°C), anemia (hemoglobin, 11 g/dL), leukocytosis (WBCs, $24.8 \times 10^3/\mu\text{L}$) and an elevated inflammatory marker (CRP, 262 mg/L). Chest computed tomography showed sternal disruption, and mediastinal fluid collection suggested mediastinitis (Figure 1). With the diagnosis of infection, therapy with meropenem IV (3000 mg/day) and teicoplanin IV (400 mg/day) was introduced empirically.

No clinical improvement was observed until the 23rd POD, and antibiotic therapy was changed to polymyxin B IV (100 mg/



Figure 1. (A) Computed tomography image of a 3-tesla machine showing areas of mediastinal collections compatible with mediastinitis (arrows). (B) Computed tomography image of a 3-tesla machine showing areas of infection in the sternum (arrows) and mediastinal fluid collections (arrowheads).

day), amikacin IV (500 mg/day) and linezolid IV (1.200 mg/day), due to a negative blood culture. On the 27th POD, owing to persistent fever (axillary temperature 38.8°C) despite antibiotic therapy and suspected candidemia, treatment with micafungin IV (100 mg/day) was introduced empirically.

On the 33rd POD, the patient underwent a new surgical procedure for sternal resuscitation. Mediastinal fluid and biopsied

tissue were collected. In the culture of both materials, there was growth of *Aspergillus* section *Fumigati*. The fungus was identified through its phenotypic characters, such as macro- and micro-morphology and growth temperature [4]. The patient was treated orally with voriconazole (400 mg/day) for 30 days (until the 77th POD), and after the surgical scar healed and laboratory parameters improved, he was discharged from the ICU. Unfortunately, at our hospital galactomannan tests are not available.

Thereafter, *Serratia marcescens*, but no *Aspergillus*, was isolated from a secretion drained through the surgical scar. The second infectious episode was treated with oral levofloxacin (750 mg/day) until the patient was discharged on the 93rd POD. After a week, the patient returned to the hospital, showing that the surgical wound healed well after 4 months of follow-up.

Discussion

Postoperative *Aspergillus* mediastinitis is a rare event, mostly associated with heart transplants, valve surgery, and tetralogy of Fallot repair surgery [5-8].

The diagnosis of invasive aspergillosis is a major challenge. This condition can mimic other diseases, and the diagnosis is often delayed. Diagnostic dilemmas can delay appropriate therapy of mediastinitis and influence the outcome [9].

Postsurgical invasive aspergillosis may occur as a result of host susceptibility and may be caused by *Aspergillus* spores from the air during surgery. However, postoperative contamination due to a high number of spores in the environment, contaminated grafts, paranasal sinuses and hematogenous dissemination is also possible [10,11]. Intrahospital outbreaks caused by *Aspergillus* species were also described [12,13]. Risk assessment and implementation of preventive measures (eg, environmental control strategies, air surveillance, inpatients, immunocompromised patients in high-efficiency particulate air filter rooms, and antifungal prophylaxis in high-risk patient groups) showed that this reduces the incidence of invasive fungal infection [12,14].

Mediastinal infections are usually indolent and, in some cases, occur several months after heart surgery [6,15]. Previous studies have shown that patients with mediastinitis are hospitalized longer than patients without this complication [3,4].

In our case, the diagnosis of mediastinitis was readily suspected, but fungal culture was not requested at the onset of the symptoms. Because of the persistent signs and symptoms of infection and considering that the classical postcardiac surgery wound infections are mostly caused by *Staphylococcus*

or *Enterobacteriaceae* species [1,2], several classes of antibiotics were administered.

Of note, cardiovascular infection by *Aspergillus* is difficult to diagnose, considering that this fungus is infrequently isolated from blood cultures and some surgical specimens are not sent to the laboratory for fungal culture [8,16].

Micafungin was ineffective in our patient because echinocandins are not recommended as first-line agents and are reserved for the salvage setting or in combination with another antifungal class. Voriconazole is most suitable for the treatment of invasive aspergillosis [17]. In the present case, the use of voriconazole was effective. However, it is important to remember that due to the non-linear pharmacokinetics of this drug, it is poorly soluble in water and may cause renal toxicity. An alternative to this problem would be the use of a liposomal solution that increases solubility, reduces toxicity, and enhances the antifungal action [18]. Unfortunately, this pharmaceutical formulation was not available in our institution.

The main risk factors for mediastinitis include diabetes mellitus, chronic obstructive pulmonary disease, obesity, bilateral internal mammary artery use, advanced age, smoking, mechanical ventricular assist devices, and prolonged ICU stay [1,2,19]. In our case, the preoperative risk factors for *Aspergillus* mediastinitis were obesity and advanced age, and the postoperative risk factor was prolonged use of ventilator support in the ICU.

Invasive aspergillosis occurs more frequently in severely immunocompromised patients; however, cases of surgical site infection have been reported in both immunocompetent and immunocompromised individuals [9,16].

Some tools are very important and help diagnoses. Procalcitonin levels seem to be able to distinguish between fungal and bacterial infection [20]. Galactomannan is another biomarker used for clinical suspicion of invasive fungal infections. However, they were not available at our hospital due to lack of reagents.

In reviews based on PubMed (<http://www.ncbi.nih.gov/>) and SciELO (<https://scielo.org/>) database searches using the keywords “mediastinitis,” “*Aspergillus*” and “coronary artery bypass,” only 3 cases of *Aspergillus* mediastinitis were reported from 2000 to July 2020 after coronary artery bypass graft surgery [8,12,13]. All these cases were of immunocompetent patients, aged over 50 years, of which 2 patients had diabetes mellitus. Among them, 2 patients progressed well, even without antifungal treatment; the third patient died, despite caspofungin treatment. The good outcome of our case might have been partly due to the correct treatment with voriconazole, which proved to be effective.

Conclusions

Aspergillus infection should be considered in the differential diagnosis of mediastinitis after coronary surgery, especially in a clinical case of unexplained infection and negative blood culture. This case report highlights that the mediastinal fluid and biopsy tissue culture can be useful for the diagnosis of fungal mediastinitis and helps reduce mortality. In addition, it highlights how the indiscriminate use of antifungal and antibiotic without defining the etiological agent can prolong hospitalization and contribute to microbial resistance.

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Ethics Approval

The study was approved by the local Research Ethics Committee – Plataforma Brasil (CAAE: 95838818.0.0000.0021).

Declaration of Figures' Authenticity

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