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Case Report

Aspergillus mediastinitis after cardiac surgery

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SUMMARY

Background: Mediastinitis is a serious complication after cardiac surgery. While bacteria are the more common pathogens, fungal infections are rare. In particular, several cases of postoperative Aspergillus mediastinitis have been reported, the majority of which had an extremely poor outcome.
Methods: A case of mediastinitis in a 42-year-old patient due to *Aspergillus fumigatus* after cardiac surgery is described. Two main risk factors were found: cardiogenic shock requiring veno-arterial extracorporeal life support and failure of primary closure of the sternum. A full recovery was attained after surgical drainage and antifungal therapy with liposomal amphotericin B, followed by a combination of voriconazole and caspofungin. The patient was followed for 18 months without relapse.
Results: This is an extremely rare case of postoperative Aspergillus mediastinitis exhibiting a favourable outcome. Based on a systematic review of the literature, previous cases were examined with a focus on risk factors, antifungal therapies, and outcomes.
Conclusion: The clinical features of postoperative Aspergillus mediastinitis may be paucisymptomatic, emphasizing the need for a low index of suspicion in cases of culture-negative mediastinitis or in indolent wound infections. In addition to surgical debridement, the central component of antifungal therapy should include amphotericin B or voriconazole.
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1. Introduction

Mediastinitis is a feared complication of open heart surgery. Most commonly due to *Staphylococcus spp* or *Enterobacteriaceae*, non-bacterial pathogens are rare. Several cases of postoperative Aspergillus mediastinitis have been described in the literature in immunocompetent patients or after heart transplantation. The patient outcome after such a complication is extremely poor despite antifungal therapy and surgery.[1]

The third reported case of postoperative Aspergillus mediastinitis in an immunocompetent adult patient who had a favourable outcome is described herein. A review of the literature showed that successful treatment is exceedingly rare and that the optimal antifungal therapy needs to be determined.

2. Case report

A 42-year-old woman with a history of three open heart surgeries for mitral and aortic valve replacements was admitted to the intensive care unit (ICU) after her fourth double valve replacement. Anaesthetic interventions were uneventful, including antibiotic prophylaxis with cefamandole. Veno-arterial extracorporeal life support (ECLS) was initiated immediately after surgery due to biventricular failure. The patient's postoperative course was complicated by cardiac tamponade on postoperative day (POD) 1, requiring surgical drainage; primary closure of the sternum was not possible due to significant myocardial oedema, necessitating a latex patch sutured to the skin. She received a 7-day course of imipenem for ventilator-associated pneumonia due to extended-spectrum beta-lactamase-producing *Enterobacter cloacae* . After a week, she was successfully weaned off ECLS, and sternal closure was achieved on POD 16, under imipenem and vancomycin prophylaxis. During this procedure, samples from the surgical site were systematically

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sent for bacteriological and mycological analyses (POD 16); however there were no clinical or biological signs of an underlying infectious process.

All surgical samples including sternal and pericardial tissues were positive for hyphae under direct visualization, compatible with *Aspergillus spp*. Cultures returned positive for several colonies of *Aspergillus fumigatus*; no bacteria were isolated. An extensive search for possible environmental contamination did not reveal any source in the operating room or in the ICU. An external fan that was used to cool the patient during a summer heat wave was suspected to be the source of contamination. The fan was not cultured due to the delay from the time it was used for the patient. No other patient undergoing cardiac surgery since the year prior to this case and to date has developed postoperative mediastinitis or another invasive Aspergillus infection.

Intravenous (IV) liposomal amphotericin B at 3 mg/kg daily was started on POD 17 for 7 days, followed by IV voriconazole at 2.5 mg/kg twice daily (POD 23), adjusted according to plasma levels. Ten days after the initiation of treatment (POD 27), cultures from the surgical drains were still positive for fungi, therefore IV caspofungin (70 mg on the first day followed by 50 mg daily) was added to IV voriconazole (POD 28) for an additional period of 21 days.

A whole body computed tomography scan showed no sign of secondary localization of invasive aspergillosis; endocarditis was

Table 1
Main characteristics of patients with mediastinitis due to *Aspergillus spp* after cardiac surgery

Ref.	Age (years) and sex	Surgical procedure	Immuno-deficiency	Risk factors	Delay between surgery and diagnosis	*Aspergillus* species	Antifungal treatment and duration	Outcome (Time between diagnosis and death/cure)
[8]	51, M	Heart transplantation	Yes	Immunosuppressive agents	NA	*A. fumigatus*	None	Death (Unknown)
[9]	64, M	Valvular surgery	No	Urgent surgery, COPD	12 days	*A. flavus*	Amphotericin B	Death (19 days)
[10]	46, M	Valvular surgery	No	-	NA	*A. fumigatus*	NA	Death (Unknown)
	72, F	Coronary artery bypass graft	No	-	NA	*A. flavus*	NA	Cure (Unknown)
[11]	61, M	Heart transplantation	Yes	COPD, immunosuppressive agents	5 weeks	*A. fumigatus*	Voriconazole 200 mg twice daily indefinitely	Cure (13 months of treatment)
[12]	51, F	Heart transplantation	Yes	Multiple redo-surgeries, immunosuppressive agents	2 months	*A. fumigatus*	Liposomal amphotericin B 5 mg/kg daily + caspofungin 35 mg daily Then voriconazole 400 mg daily 6 months total	Cure (6 months)
[13]	3, F	Repair of congenital cardiomyopathy	No	Multiple redo-surgeries	5 months	*A. fumigatus*	IV caspofungin 6 months + oral voriconazole 8 months	Cure (14 months)
	6 mo, F		No	Multiple redo-surgeries, ECMO, delayed sternal closure	<1 month	*Aspergillus spp*	None (post-mortem diagnosis)	Death (16 days)
	1 mo, M		No	Multiple redo-surgeries, delayed sternal closure	1 month	*A. fumigatus*	Liposomal amphotericin B + caspofungin 1 week after	Death (23 days)
[14]	60, M	Coronary artery bypass graft	No	Diabetes mellitus	2 months	*A. fumigatus*	NA	Cure (4 weeks)
[15]	61, M	Heart transplantation	Yes	Redo-surgery, septic shock, immunosuppressive agents	1 month	*A. fumigatus*	NA	Death (Unknown)
[16]	63, M	Aortic dissection	No	Delayed sternal closure, hemodynamic instability	34 days	*A. fumigatus*	NA	Death (43 days)
[17]	68, M	Pulmonary endarterectomy	No	Pulmonary hypertension, candidemia prior to surgery	8 days	*A flavus*	Liposomal amphotericin B 3 mg/kg daily + voriconazole 4 mg/kg daily	Death (26 days)
[18]	57, M	Coronary artery bypass graft	No	Diabetes mellitus, redo-surgery	6 days	*A. fumigatus*, *A. flavus*	Caspofungin	Death (Unknown)
	57, F	Heart transplantation	Yes	Immunosuppressive agents, haemodialysis, COPD	49 days	*A. fumigatus*, *A. terreus*	Caspofungin + voriconazole	Cure (Unknown)
[19]	55, F	Heart transplantation	Yes	Redo-surgery, immunosuppressive agents, haemodialysis, cardiogenic shock	5 weeks	*A. calidoustus*	Posaconazole 11 days + voriconazole 10 days + amphotericin B 42 days	Cure (4 months)
Present case	42, F	Valvular surgery	No	Multiple redo-surgeries, delayed sternal closure, cardiogenic shock	16 days	*A. fumigatus*	Liposomal amphotericin B 3 mg/kg daily Then IV voriconazole 200 mg twice daily + caspofungin 50 mg daily Then voriconazole 200 mg twice daily	Cure (18 months)

M, male; F, female; NA, not available; COPD, chronic obstructive pulmonary disease; IV, intravenous; ECMO, extracorporeal membrane oxygenation.

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