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Case report

Acute myocardial infarction secondary to mucormycosis after lung transplantation

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ABSTRACT

We present a case of a 57-year-old man who underwent bilateral lung transplantation for idiopathic pulmonary fibrosis. His immediately post-operative course was complicated by fever and cardiac arrest. Despite supportive care and broad-spectrum antibiotics, he experienced continued clinical decline. Autopsy results indicated angioinvasive mucormycosis and coronary arteritis resulting in acute myocardial infarction as the cause of death.

Case presentation

A 57-year-old man with idiopathic pulmonary fibrosis was evaluated for lung transplantation. His past medical history was significant for hypertension, dyslipidemia and chronic total occlusion of the right coronary artery with good collateral blood flow from the circumflex artery. After a negative stress test, he was listed for bilateral lung transplantation. The donor was a healthy, 30-year-old man who succumbed to injuries from motorcycle accident. Donor lung imaging revealed metallic debris in the left-sided airways indicating dirt contamination (Fig. 1a). Bronchoscopic examination revealed debris in the airway consistent with gravel, and it was therapeutically cleared. The donor was treated with intravenous vancomycin and cefepime, and after resolution of airway sections, improvement on chest imaging and demonstration of excellent graft function, the lungs were accepted for transplantation. The patient underwent an uneventful bilateral lung transplantation. Induction therapy consisted of basiliximab, methylprednisolone, and mycophenolate mofetil and the patient received intravenous (IV) vancomycin, levofloxacin, cefepime and inhaled amphotericin prophylactically. Donor cultures grew multiple organisms, including *Enterobacter cloacae, Escherichia vulneris, Bacillus, Coagulase-negative staphylococcus, Mycobacterium species, Candida keyfre, Aspergillus ochraceus* and *Fusarium spp,* for which IV voriconazole was added to the patient's antibiotic regimen.

On the fifth postoperative day, the patient developed a fever of 101.9 °F along with tachycardia and tachypnea. Blood cultures and bronchoscopic cultures were obtained, and IV cefepime was switched to IV meropenem. The following day, he suffered a cardiac arrest with pulseless electrical activity (PEA) requiring cardiopulmonary resuscitation for 14 min; return of spontaneous circulation was achieved. Arterial blood gas and routine chemistries did not reveal an obvious cause for PEA arrest. He was intubated and veno-arterial extracorporeal membrane oxygenation (VA-ECMO) support was initiated, and a transesophageal echocardiogram revealed akinesis of inferior and lateral walls and newly reduced left ventricular ejection fraction of 35 %. EKG revealed ST-segment elevation in the infero-lateral wall leads (aVF, V5 and V6), and troponin I levels rose to > 200 ng/mL raising concerns for an acute myocardial infarction. Coronary angiogram revealed 100 % occlusion of left circumflex artery without coronary atherosclerosis. Balloon angioplasty was performed with recanalization of circumflex artery up to first obtuse marginal artery, and an intra-aortic balloon pump was inserted. The patient was initiated on IV heparin. Despite these measures, the patient continued to require escalating doses of vasopressors and

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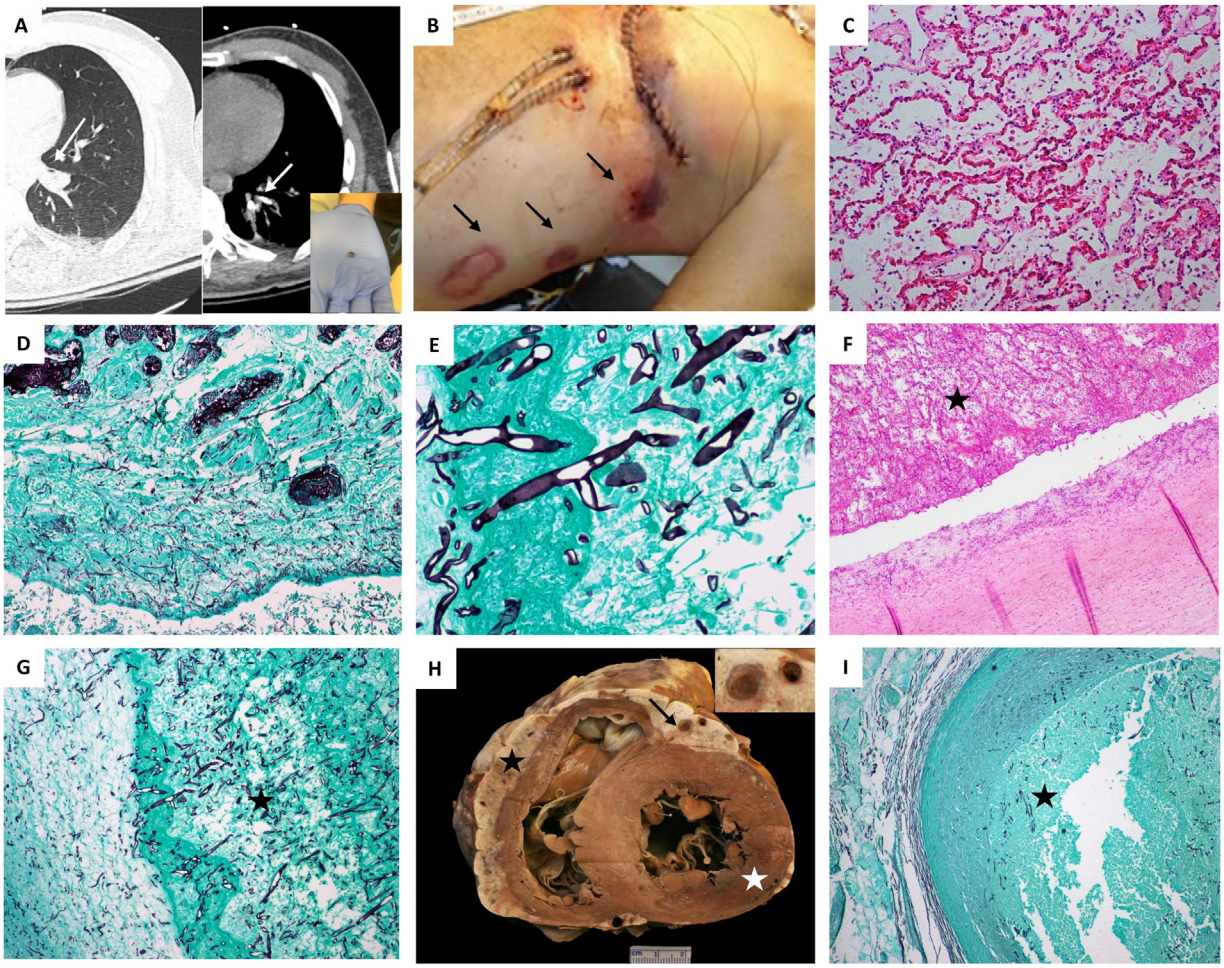

Fig. 1. Autopsy findings. Fig. 1A shows chest CT scan of the donor with evidence of debris in left main bronchus (left) and metallic debris extending into left lower lobe bronchi (right) concerning for foreign body aspiration. Fig. 1B shows necrotic skin lesions on the left chest wall extending on to the flank, indicative of invasive fungal infection. Fig. 1C shows hematoxylin & eosin (H&E) staining of lung allograft demonstrating delicate alveolar septae and intense capillary vascular congestion but no obvious fungal infection. Fig. 1D shows Grocott-Gomori's methenamine silver (GMS) stain of right mainstem bronchus with evidence of invasive fungal infection. Fig. 1E shows high power magnification of the bronchus reveals broad, sparsely septate thin walled hyphae consistent with *Apophysomyces elegans*. Fig. 1F shows H&E stain of aorta reveals aortitis with intramural thrombus (asterisk). Fig. 1G shows GMS stain of the aorta with evidence of angioinvasive fungal aortitis with near total thrombotic occlusion (asterisk). Fig. 1H shows gross cardiac autopsy reveals epicardial necrosis (black asterisk), left ventricular posterior-lateral wall necrosis (white asterisk) and Left anterior descending coronary artery occlusion (arrow). Thrombosis of LAD without plaque is consistent with septic embolization (insert). Fig. 1I shows GMS stain of epicardial coronary artery revealing angioinvasive coronary arteritis with thrombotic occlusion (asterisk).

developed acute kidney injury requiring continuous renal replacement therapy. Serial echocardiograms revealed globally akinetic ventricles progressing to complete cardiac standstill. Care was withdrawn at that time, and an autopsy was performed.

Autopsy report

Grossly, patient's skin had patches of necrotic areas along the left chest all extending on to the flank (Fig. 1b). Lungs revealed intact, delicate alveolar septae with diffuse vascular congestion (Fig. 1c). Bronchi revealed invasive fungal infection (Fig. 1d) with broad, sparsely septated thin-walled hyphae consistent with *Apophysomyces elegans*, a fungus of the order Mucorales (Fig. 1e). There was evidence of aortitis (Fig. 1f) with near total luminal occlusion (Fig. 1g). Cardiac autopsy revealed multifocal coronary artery thrombosis without plaque, consistent with septic embolization, along with myocardial and epicardial necrosis (Fig. 1h). Examination of the coronary arteries revealed angioinvasive arteritis with thrombotic occlusion (Fig. 1i).

Discussion

Infections in the immediate post-transplant period are either donor-derived or nosocomial [1]. Incidence of donor-derived infections in solid organ transplant recipients varies from 2.1%–23.4% [2] and can be classified as expected (known infection present in the donor) or unexpected [3]. The rate of transmission is also affected by the inoculum of pathogens, the organ transplanted, the use of different immunosuppressive agents and use of perioperative antimicrobial prophylaxis [4]. In lung transplant recipients, the most common donor derived infections are bacterial pneumonias [5]. Fungal infections are less common [6] and are usually caused by *Candida* or *Aspergillus* followed by *Mucorales*, *Fusarium* and *Scedosporium* [7]. Mucormycosis is a rare invasive fungal infection caused by fungi of the order Mucorales that includes Rhizopus, Mucor, Rhizomucor, Cunninghamella, Lichtheimia, Saksenaea, and Apophysomyces. They are ubiquitous in nature, found in decaying vegetation and soil. In immunosuppressed patients, they cause vascular invasion with subsequent

infarction and necrosis of the affected organs [8]. In transplanted lungs, mucormycosis can affect bronchial anastomoses or pulmonary parenchyma and is associated with high mortality rates. As in our case, blood and respiratory cultures are usually negative, and mucormycosis is usually diagnosed by direct examination or post-mortem culture of the affected tissue [9]. Transmission of mucormycetes from the organ itself is rare, but it is associated with high mortality [3]. Treatment includes early surgical debridement in combination with IV amphotericin-B [3,10]. Azole antifungals such as posaconazole or isavuconazonium can be considered as salvage treatment or when clinical stability is achieved, but not as first-line therapy [10]. While use of prophylactic antifungal agents could prevent many of potentially transmissible fungal infections, it is unlikely that those would have been of help in our patient's case due to the heavy inoculum.

Clinical course

The patient developed angioinvasive mucormycosis with *Apophysomyces elegans*, resulting in mediastinitis, bronchitis, aortitis and coronary arteritis with *in situ* coronary arterial thrombosis and subsequent acute myocardial infarction. The clinical presentation mimicked acute myocardial infarction in that the patient had ST-elevation, elevated cardiac biomarkers, and regional wall motion abnormalities. On coronary angiogram, the presence of multi-focal coronary artery thrombosis without underlying coronary plaques suggested septic embolization. Although autopsy confirmed invasive mucormycosis, multiple cultures during the patient's hospital course did not yield *Apophysomyces elegans,* thereby delaying initiation of IV amphotericin B. We suspect that the source of angioinvasive mucormycosis in our patient was aspiration of soil and foreign debris during the motorcycle accident. It is likely that after deposition of apophysomyces in the alveoli, the use of high dose steroids and basiliximab facilitated angioinvasive disease and rapid dissemination to other vascular structures.

Conclusion

This case of an invasive mold infection leading to life-threatening illness in an immunocompromised patient presented clinically as acute myocardial infarction. Donor-derived fungal infections in lung transplant recipients can result in graft loss and high mortality, and due to the angioinvasive nature of mucormycosis, its clinical presentation can mimic organ infarction. Given the difficulty of isolating these organisms in standard culture and high mortality rates associated with these infections, consideration of broadening antifungal coverage to liposomal amphotericin B early in a patient's clinical course should be considered when fungal infection is suspected. Additionally, donor lung contamination with soil should be considered during the donor evaluation process, as it can be the source of invasive mold infection.

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