

## Aorta: Case Report

# Fungal Ball in Ascending Aorta: Disseminated Histoplasmosis 20 Years After Aneurysm Repair



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*Histoplasma capsulatum*, an Ascomycetes fungus, is the responsible pathogen for histoplasmosis. Although often asymptomatic, around 1% of cases progress to disseminated infection. Endovascular graft infections with this fungus have been reported, particularly on abdominal aortic or aortofemoral bypass grafts. Timely antifungal therapy followed by appropriate surgical intervention is vital for a favorable outcome to be achieved. We describe a case involving a 73-year-old man in whom disseminated histoplasmosis developed 2 decades after his ascending aortic aneurysm repair. He presented with a fungal ball in the proximal ascending portion of the aorta. The patient was successfully treated with an aortic root replacement and hemiarch reconstruction.

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**H**istoplasma capsulatum, classified as an Ascomycetes member, exhibits a dimorphic nature and is the causal agent behind histoplasmosis. Although many patients remain asymptomatic, it can be manifested as an influenza-like pulmonary infection.<sup>1</sup> The pathogen can spread to other body systems, causing disseminated histoplasmosis, particularly in immunocompromised hosts. Rarely, individuals with implanted prosthetics, such as vascular grafts, cardiac valves, and prosthetic joints,

can also provide a conducive environment for the fungus to thrive.<sup>2</sup>

A 73-year-old man who underwent ascending aorta aneurysm repair with a polyester graft 20 years ago presented with weight loss, fatigue, and intermittent fever during the past year. Medical history included prostate cancer, hyperparathyroidism, and stage 3 chronic kidney disease. A positron emission tomography (PET) scan was done to rule out cancer recurrence; it showed an intraluminal linear high density at the superior margin of the ascending aorta graft with partially circumferential fluorodeoxyglucose uptake extending into the root (Figure 1A). A subsequent computed tomography scan showed a calcified irregular mass in the mid ascending aorta (Figure 1B), a dilated aortic root (sinus of Valsalva diameter of 45 mm), and a bicuspid aortic valve. Transesophageal echocardiography confirmed a stenotic and calcified bicuspid aortic valve, with left ventricular ejection fraction of 60%. Infectious workup revealed negative blood cultures but a positive *Histoplasma* urine antigen level (<0.2 ng/mL) and a *Histoplasma* M band in the cerebrospinal fluid, which affected various parts of the body, including the bone marrow and aortic graft. Treatment initially involved liposomal amphotericin B but was transitioned to the lipid complex formulation because of tolerance issues and, later, to itraconazole. The patient experienced embolic events affecting the brain, kidneys, and leg. Despite therapy, his condition worsened, and a repeated PET scan suggested interval progression of fluorodeoxyglucose-avid mycotic infection involving the root of the aorta. Surgical intervention was planned, amphotericin B (AmBisome) was restarted, and itraconazole was temporarily suspended to avoid drug interactions.

The repeated sternotomy and reentry were uneventful. After heparin administration, cannulation was done in the mid arch, well beyond the graft-aorta suture line. Standard cannulation of the right atrium and placement of a left ventricular vent were done. Cardiopulmonary bypass (CPB) was initiated with systemic cooling, and the patient was cooled to 21 °C. The aortic cross-clamp was positioned above the distal suture line of the aortic graft near the origin of the innominate artery. The aorta was transected just beyond the distal suture line.

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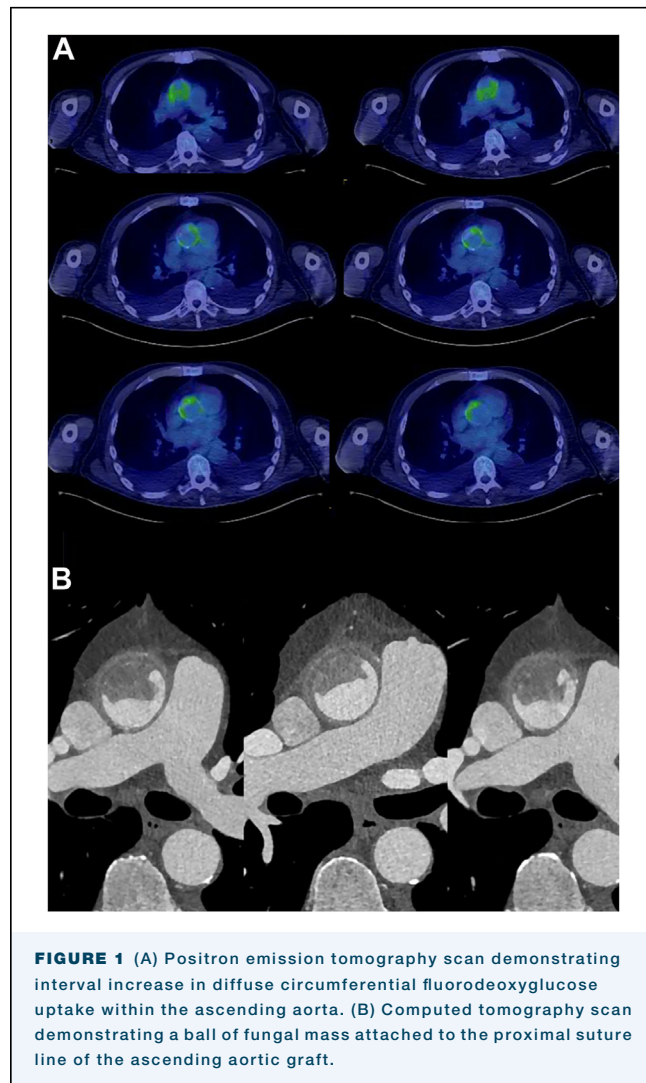
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The rest of the ascending aorta graft was mobilized and completely excised by going below the proximal suture line. Further antegrade ostial cardioplegia was given. Examination of the excised graft revealed a large fungal ball attached to the proximal suture line, almost circumferentially obstructing the orifice (Figure 2). The aortic valve on inspection showed fusion of left and right cusps, and it was heavily calcified, involving the annulus and aortomitral curtain. The valve was excised, the annulus was débrided, and the coronary buttons were appropriately fashioned in preparation of an aortic root replacement. Intraoperative culture specimens were taken from surgical explants of the infected aortic valve and graft. After excision of the graft, sutures, and pledgets from the previous surgical procedure, there remained too small a distal ascending aortic rim; therefore, we elected to do a hemiarch reconstruction to obtain better margins and also to remove the pledgets and suture material from the previous cannulation site. After sufficient cooling, circulatory arrest with retrograde cerebral perfusion was commenced. The distal ascending aorta and inferior half of the arch were excised. The surgical field was irrigated with povidone-iodine (Betadine) and saline. A 28-mm Dacron polyester graft was used to complete the hemiarch reconstruction. CPB was resumed along with systemic rewarming. For the aortic root replacement portion of the procedure, a 29-mm Konect Resilia aortic valved conduit (Edwards Lifesciences) was used, and coronary buttons were reimplemented. The graft-to-graft anastomosis was completed. The cross-clamp was released, and the patient was weaned off CPB without any issues. The total cross-clamp time was 240 minutes, and the total CPB time was 300 minutes. Postoperative transesophageal echocardiography indicated a residual mean aortic prosthetic valve gradient of 3 mm Hg and no aortic periprosthetic regurgitation, and the left ventricular ejection fraction was 45%.

The postoperative period was marked by renal failure requiring temporary dialysis. He was extubated on postoperative day 1, transitioned out of the intensive care unit on day 10, and discharged from the hospital on day 38 with a plan for long-term itraconazole. At 12-month and 18-month follow-up visits, he remained *Histoplasma* antigen negative and had regained much of his health. A computed tomography scan showed stable aortic reconstruction. Because of a prolonged QTc interval, itraconazole has been switched to isavuconazolum sulfate (Cresemba).

## COMMENT

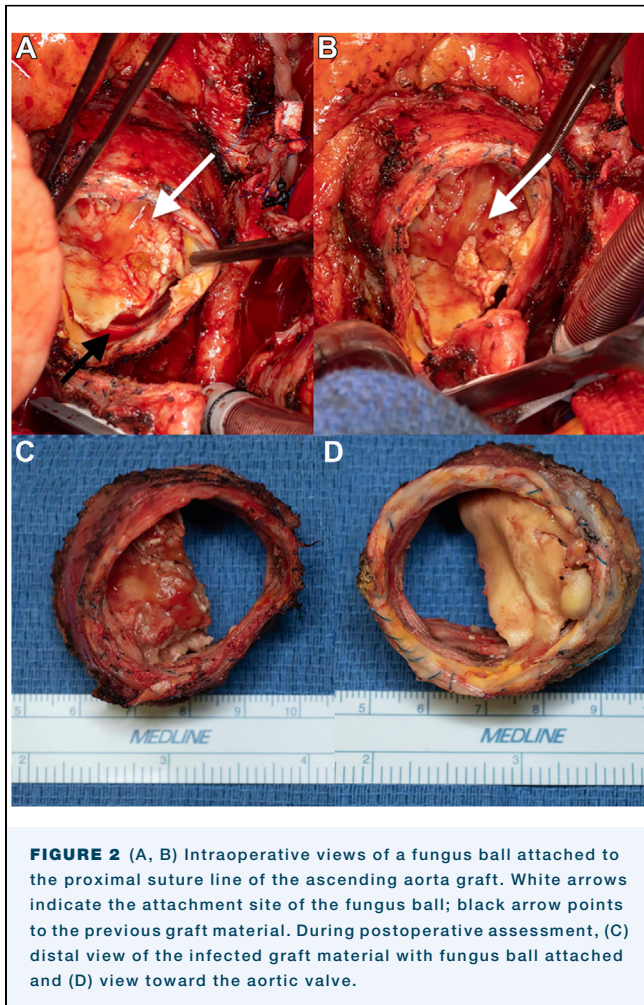
In this report, we describe a 73-year-old man in whom histoplasmosis developed 20 years after his initial ascending aortic aneurysm repair. He was found to have



**FIGURE 1** (A) Positron emission tomography scan demonstrating interval increase in diffuse circumferential fluorodeoxyglucose uptake within the ascending aorta. (B) Computed tomography scan demonstrating a ball of fungal mass attached to the proximal suture line of the ascending aortic graft.

a fungal ball in the ascending aorta graft. An initial conservative management with antifungal therapy failed; source control with a repeated sternotomy, excision of the aortic graft, aortic root replacement with a biologic valve conduit, and hemiarch reconstruction were required. There are rare reports of localized *Histoplasma capsulatum* infections linked to endovascular grafts in distal parts of the aorta, abdominal aortic grafts, and aorta-femoral bypass grafts.<sup>2,3</sup> To the best of our knowledge, *Histoplasma* fungal ball in the ascending aorta leading to disseminated histoplasmosis has not been previously reported.

The response against histoplasmosis involves cooperation between macrophages and T cells. T-cell immunity is crucial for recovery, and deficiencies in this make individuals susceptible to extensive histoplasmosis.<sup>4,5</sup> Ionizing radiation, as from radiation therapy, impairs lymphocyte function, leading to immunosuppression.<sup>6</sup> The patient in this case had a history of prostate



cancer and proton beam therapy, suggesting a possible reactivation of a latent infection instead of direct microorganism exposure.

Constitutional complaints, such as fever and reduced appetite, are common, and usual blood culture methods often fail to demonstrate growth of this organism.<sup>7</sup> In this instance, the patient's diagnosis was aided by a PET scan conducted for cancer recurrence assessment. Whereas initial test results were negative, the *Histoplasma* serology displayed a positive reaction, notably in H and M bands. The immunodiffusion assay, which assesses M and H precipitin bands, exhibits notable specificity but slightly reduced sensitivity compared with the complement fixation assay.<sup>6</sup>

*Histoplasma capsulatum* is highly sensitive to amphotericin B; however, this case highlights the need for an aggressive source control for the antifungal therapy to work. This case also suggests that patients may have safe recovery despite a complex and a high-risk operation in a setting of disseminated histoplasmosis. A long-term antifungal treatment with close surveillance is beneficial to prevent recurrence.

Ascending aorta graft infection with *Histoplasma capsulatum* is rare and may lead to disseminated histoplasmosis with multiorgan impairment. The long insidious onset, nonspecific symptoms, and limited contribution of blood cultures present diagnostic difficulties. A combination of imaging modalities and specific diagnostic tests may be needed for diagnosis. Successful treatment depends on aggressive source control with antifungal therapy and will lead to long-term recovery.

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#### DISCLOSURES

The authors have no conflicts of interest to disclose.

#### PATIENT CONSENT

Obtained.

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