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MINI-FOCUS ISSUE: VALVULAR HEART DISEASE

INTERMEDIATE

CASE REPORT: CLINICAL CASE

Don't Stop Beleafing

A Unique Case of Fungal Infective Endocarditis

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ABSTRACT

We present the case of a 60-year-old man who was successfully treated for obstructive fungal infective endocarditis of the ascending aorta caused by *Geotrichum capitatum*. This extremely rare cause of fungal infective endocarditis required surgical and prolonged medical management, facilitated by effective multidisciplinary cooperation. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:672–7) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 60-year-old man was transferred to Royal Brompton Hospital, London, United Kingdom, with a 1-week history of night sweats and myalgia. On examination, his chest was clear on auscultation, with heart sounds S1, S2, and click. He had no focal signs of infection and no peripheral signs of infective endocarditis (IE). He was clinically stable on arrival; normopneic, normotensive, and mildly tachycardic at 92 beats/min.

LEARNING OBJECTIVES

- For high-risk patients, such as those with congenital cardiac disease, early consideration of fungal infection is essential in the diagnosis and management of IE.
- Treatment with an extended course isavuconazole was effective for a severe deep fungal infection caused by *Geotrichum capitatum*.
- The use of multidisciplinary decision making should be advocated alongside multimodality imaging in complex cases of endocarditis, in the absence of clear guidelines.

PAST MEDICAL HISTORY

This patient was born with a Sievers type 0 (anteroposterior) bicuspid aortic valve. He underwent homograft aortic valve replacement for mixed aortic valve disease and aortic root replacement for a dilated ascending aorta in 1995. Subsequently, in 2016, he underwent a redo aortic valve and root replacement for severe aortic regurgitation. Recovery was complicated by ventricular fibrillation cardiac arrest secondary to severe left main stem stenosis, requiring emergency percutaneous coronary intervention. He had good functional cardiovascular capacity and spent the previous summer working in his garden, weeding and clearing dead leaves.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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TABLE 1 Admission Blood Tests and Values

Blood Tests	Result	Normal Value
White blood cell count, $\times 10^9$/l	14.1	4.4–10.1
Neutrophil count, $\times 10^9$/l	12.7	2.1–6.7
Eosinophil count, $\times 10^9$/l	0.0	0.1–0.5
C-reactive protein, mg/l	79	0–10
Hemoglobin, g/l	104.0	134–166
Platelet count, $\times 10^9$/l	180	136–343
Creatinine, μmol/l	92	60–120
Estimated glomerular filtration rate, ml/min/1.73 m^2	73	>60

DIFFERENTIAL DIAGNOSIS

IE was strongly suspected, considering his congenital heart condition and the presence of a prosthetic valve. Another differential diagnosis was *Mycobacterium chimaera* infection following potential inadvertent exposure during cardiopulmonary bypass for his surgery in 2016. Sepsis secondary to community-acquired pneumonia or urinary tract infection was ruled out by the referring hospital.

INVESTIGATIONS

On admission, his blood values showed raised inflammatory markers (Table 1). Three sets of peripheral blood cultures from the referring hospital returned positive results for *Geotrichum capitatum*. Two further sets isolated the same organism. The microbiology department advised testing for 1,3-β-D-glucan (BDG), and the result was positive; the initial concentration was >500 pg/ml (normal <80 pg/ml).

An electrocardiogram showed normal sinus rhythm, a normal PR interval, a narrow QRS complex, and a nonprolonged QTc. Chest radiography revealed bilateral pleural effusions, but no focal consolidation (Figure 1). Sputum and urine cultures were negative for bacteria.

The transthoracic echocardiogram (TTE) showed a severely dilated left ventricle with a moderately reduced ejection fraction of 35% to 40%. The aortic root and ascending aorta appeared normal, with a well-seated and unobstructed aortic valve replacement. However, the flow velocity and gradients in the ascending aorta had significantly increased compared with previous echocardiograms (Figures 2A and 2B, Table 2). Doppler study demonstrated turbulent flow in the ascending aorta. No obvious vegetation was seen on native or prosthetic valves.

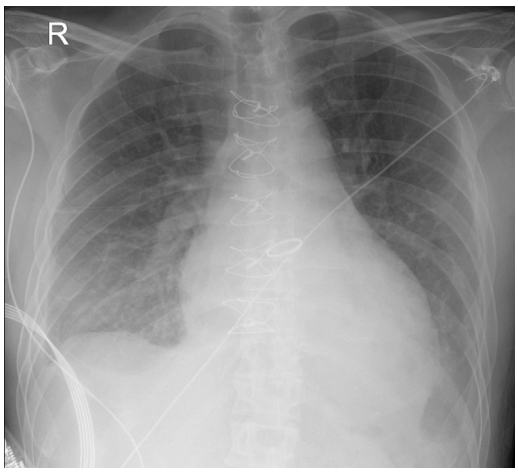
A transesophageal echocardiogram performed preoperatively confirmed a normally functioning prosthetic valve with shadowing in ascending aorta, previously unseen on TTE (Figure 3, Videos 1 and 2). These images correlated with computed tomography findings, which identified a large, irregular filling defect in the aortic root (Figures 4A to 4D).

MANAGEMENT

The patient was started on intravenous high-dose amphotericin B liposomal and flucytosine, in line with culture sensitivities. Multidisciplinary team discussions recommended urgent high-risk but life-saving surgical intervention. During surgery, an incision through the Dacron (polyethylene terephthalate) component of the previous composite graft revealed a large mass obstructing the mechanical prosthesis in the aortic position (Figures 5A and 5B). The mass was completely removed, followed by hydrogen peroxide washout. The operation was high risk, with extensive adhesions and prolonged bypass time. Because the mechanical prosthesis was well functioning and macroscopically free of vegetations, an intraoperative decision was made to leave it in place. Microbiology samples from the excised mass confirmed growth of *G. capitatum*, consistent with peripheral blood cultures (Figure 6).

His post-operative management was complicated by transient atrial fibrillation, a period of renal replacement therapy, and the development of new lateralizing neurological signs, diagnosed as subacute infarction on computed tomography, complicating immediate anticoagulation decisions. He completed a

FIGURE 1 Admission Chest Radiograph



Small bilateral pleural effusions, sternotomy wires and metallic aortic valve replacement. R = right.

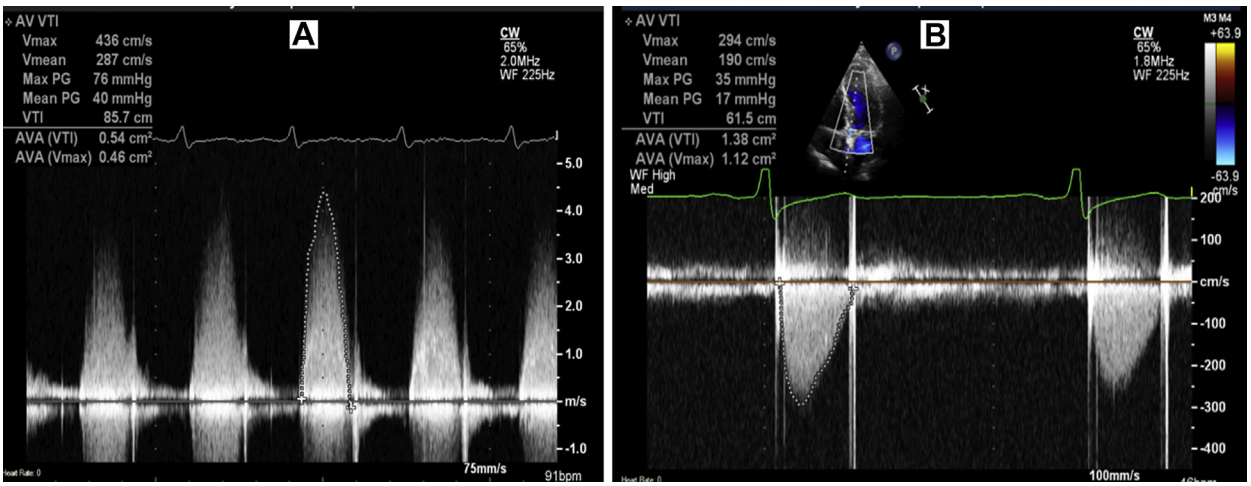
ABBREVIATIONS AND ACRONYMS

BDG = 1,3-β-D-glucan

IE = infective endocarditis

TTE = transthoracic echocardiogram

FIGURE 2 Transthoracic Echocardiogram Images



(A) Increased peak velocity and gradient in the ascending aorta detected from the suprasternal view using a nonimaging probe on admission. **(B)** Compared with 8 months earlier from the apical 5-chamber view. AV = aortic valve; AVA = aortic valve area; CW = continuous wave; max = maximum; PG = peak gradient; V = velocity; VTI = velocity time interval; WF = wall filter.

total course of combined intravenous high-dose amphotericin B liposomal and flucytosine for 8 weeks post-surgery. His response to treatment was monitored clinically, alongside inflammatory markers and BDG, which both showed a clear downtrend. He continued dual antifungal therapy, in addition to warfarin and optimal heart failure medications. He was safely discharged 4 months after his initial operation.

DISCUSSION

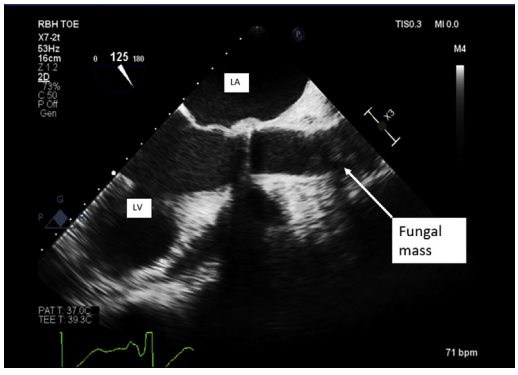
This case demonstrates the severity and long-term complications of fungal IE. Only 2% to 4% of cases of endocarditis are caused by fungi. Patients with prosthetic valves are at higher risk for fungal IE, along with intravenous drug users and immunocompromised patients (1). *Candida albicans* is the most common causative organism, representing between 50% to 80% of cases. Most patients require combined surgical intervention and prolonged antifungal therapy, but some need long-term suppressive therapy, occasionally for life (2). There are no clear guidelines

TABLE 2 Comparison of Aortic Valve and LV TTE Measurements: On Admission in December 2019, Previous TTE in April 2019, and Following Successful Therapy in October 2020

Measurement	April 2019	December 2019	October 2020
Peak gradient, mm Hg	35.0	76.0	20.5
Mean gradient, mm Hg	17.0	40.0	10.8
Area (continuity), cm^2	1.33	0.83	1.12
Mitral regurgitation	Mild	Moderate	Mild
LVEF, %	35-40	35-40	45-50
LVEDD, cm	5.83	6.03	5.23
LVESD, cm	5.20	4.54	4.82

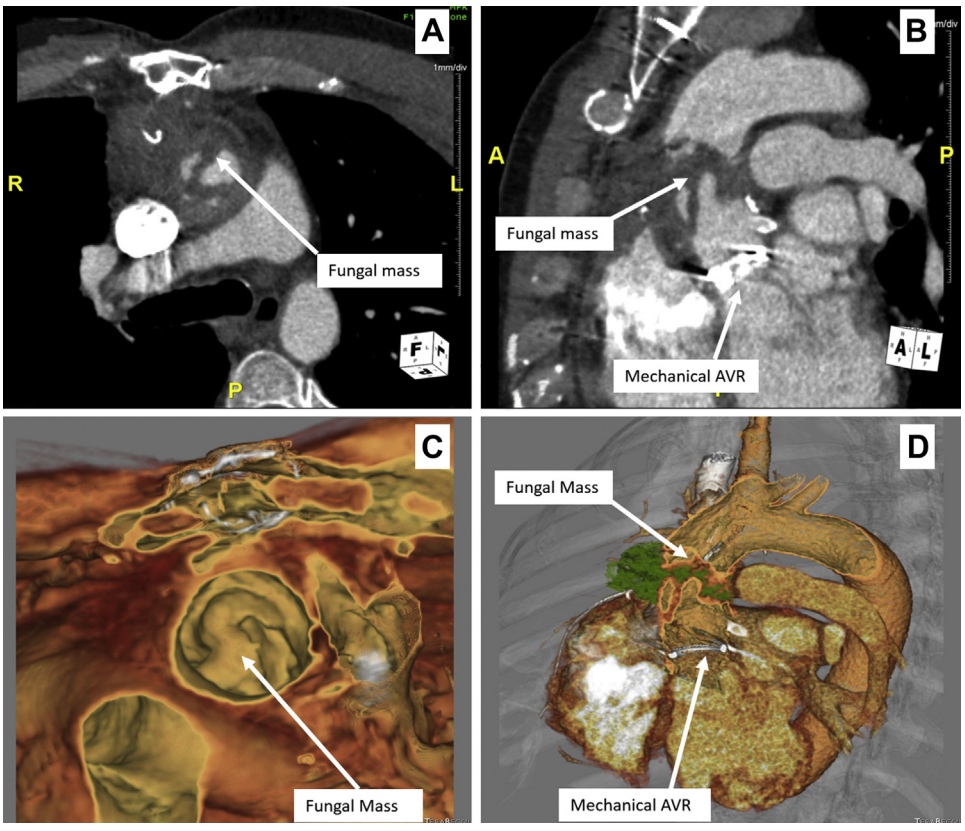
LV = left ventricular; LVEDD = left ventricular end-systolic dimension; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic dimension; TTE = transthoracic echocardiogram.

FIGURE 3 Transesophageal Echocardiogram of Left Ventricular Outflow



Echo-dense mass partially visualized in the ascending aorta, likely at the suture line from a previous operation. bpm = beats/min; LA = left atrium; LV = left ventricle; MI = mechanical index; PAT = patient; RBH = Royal Brompton Hospital; TOE = transoesophageal echocardiogram; 2D = 2-dimensional.

FIGURE 4 **Computed Tomography Scan**



Two-dimensional **(A)** axial and **(B)** sagittal images. Three-dimensional Reconstruction of a computed tomography (CT) scan of **(C)** the ascending aorta and **(D)** an obstructive mass in the ascending aorta. A, anterior; AVR = aortic valve replacement; F = feet; L = left; P = posterior; R = right.

on antifungal treatment for these types of rare fungal invasive infections (3).

G. capitatum, previously known as *Saprochaete capitata*, and now renamed *Magnusiomyces capitatus*, is a ubiquitous fungus found in soil, water, air and plants. *G. capitatum* invasive infections are very rare and are almost exclusively reported in immunocompromised patients, with a poor prognosis and a mortality rate exceeding 50% despite appropriate treatment (4). *Geotrichum* spp. IE are extremely rare. A literature review returned a single reported case of *Geotrichum candidum* IE, in a 6-year-old child with pulmonary atresia. It is posited that our patient contracted the fungus while gardening because he worked without gloves and sustained blisters on his hands.

Symptoms of fungal IE overlap heavily with those of bacterial endocarditis, thus requiring a high index of suspicion for timely diagnosis. The most common symptoms are fever, new or changing heart murmur, and major peripheral embolization, most commonly cerebral and femoral. Classic signs of endocarditis such as Osler's nodes, finger clubbing, splinter hemorrhages, and Roth spots are infrequent (5).

Peripheral blood cultures remain the cornerstone of diagnosis, by providing live organisms for identification and sensitivity testing. However, in the absence of positive microbiological findings, and if there is suspicion of fungal infection, a BDG level can be useful. BDG is a component of the cell wall of most fungi, yeasts, and molds. Antigen testing has a reported sensitivity of 75% and a specificity of 81% for invasive fungal infections (6). For patients with suspected IE, European Society of Cardiology guidelines recommend TTE as the first-line imaging modality, irrespective of the organism. For patients with prosthetic valves, or a high clinical suspicion despite negative TTE findings, a transesophageal echocardiogram is indicated (7).

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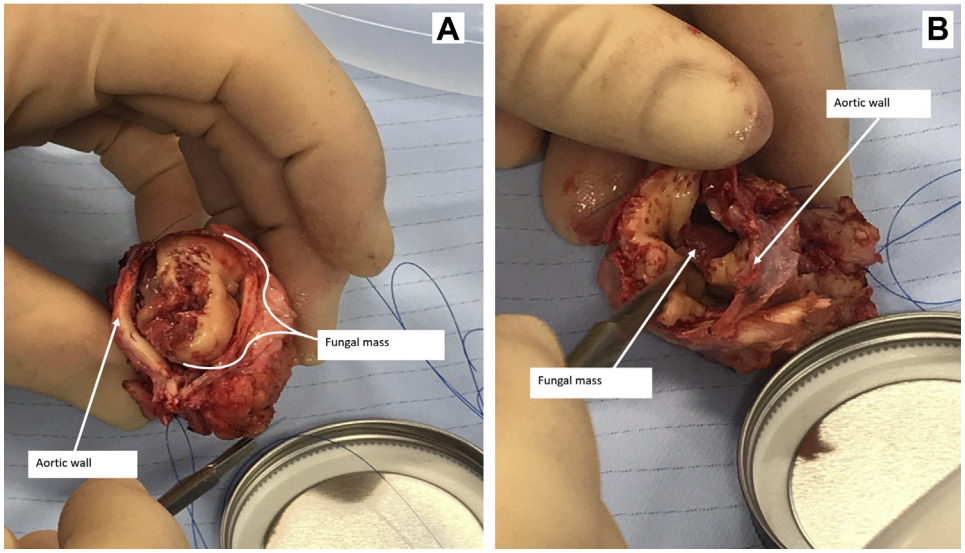
FIGURE 5 Intraoperative Images



(A and B) A large, fungating ascending aortic mass almost obstructing the aortic lumen.

FOLLOW-UP

This patient returned to the hospital shortly after discharge with nausea, fatigue, and rapidly increasing C-reactive protein (4 to 98 mg/l). He was readmitted for suspected fungal infection relapse because his antifungal therapy had recently been altered. He subsequently tested positive for COVID-19 but remained hemodynamically stable and required no supplemental respiratory support. His antifungal treatment was changed to monotherapy with oral isavuconazole, and he was discharged with fortnightly monitoring of inflammatory markers, renal function, and BDG level. Six months post-surgery, the BDG level became negative and has remained negative, with no clinical evidence of infection recurrence. Because the mechanical aortic valve replacement was left in place during surgery, there remains a risk of fungal biofilm, which is difficult to treat and fully clear. A multidisciplinary meeting recommended prolonged antifungal therapy for more than a year post-operatively.

FIGURE 6 Microbiology Samples

Geotrichum capitatum isolated from blood cultures and the explanted fungating mass.

CONCLUSIONS

This case demonstrates the clinical presentation, diagnosis, and successful management of fungal IE, caused by *G. capitatum,* obstructing the ascending aorta. Fungal IE should be considered for higher-risk patients, especially those with prosthetic valves or immunocompromise. Management often requires

surgical intervention and extensive antifungal therapy.

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KEY WORDS cardiac surgery, congenital, fungal infective endocarditis, *Geotrichum capitatum*, β-D-glucan, multidisciplinary team

APPENDIX For supplemental videos, please see the online version of this paper.