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CASE REPORT

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AngioVac-assisted management of histoplasma capsulatum endocarditis in a bioprosthetic aortic valve: challenges and outcomes

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Abstract

Background Histoplasma capsulatum infective endocarditis (IE) is rare and often fatal, especially in prosthetic valve patients, due to delayed diagnosis and limited therapeutic options. This case demonstrates the utility of AngioVac for managing large fungal vegetations, underscores the importance of considering fungal IE in culture-negative cases, and highlights the role of a multidisciplinary approach in high-risk patients.

Case summary We report a 76-year-old female with a bioprosthetic aortic valve who presented with persistent culture-negative fever, splenic infarcts, and large vegetations on her prosthetic valve. Extensive diagnostic workup confirmed fungal endocarditis after AngioVac-assisted debulking revealed H. capsulatum on tissue cultures. Despite prompt initiation of antifungal therapy and multidisciplinary management, her course was complicated by recurrent embolic events, septic shock, and eventual death.

Conclusion This case underscores the importance of considering fungal IE in culture-negative cases, especially in high-risk patients such as those with prosthetic valves. It also highlights the role of advanced diagnostic techniques and minimally invasive interventions like AngioVac in managing complex cases, despite their limitations.

Keywords Histoplasma endocarditis, Fungemia, AngioVac, Aortic valve endocarditis, Vegetation, Case report

Introduction

Infective endocarditis is a serious condition involving infection of the endocardium or heart valves, which can lead to significant morbidity and mortality if untreated [1]. Causes vary and include bacterial, fungal, and other etiologies. One of the fungal causes is Histoplasma capsulatum, an endemic fungus primarily found in the Ohio and Mississippi River valleys [2]. While histoplasmosis often manifests as a mild respiratory illness, it can disseminate in immunocompromised individuals or those with prosthetic heart valves, causing severe complications such as fungal endocarditis [3].

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Case presentation

A 76-year-old female with a history of aortic valve replacement (AVR) with a bioprosthetic valve in 2015 and rheumatoid arthritis (RA), previously managed with methotrexate (MTX), had been experiencing recurrent fevers and malaise for three months, leading to three prior hospitalizations. An extensive infectious workup was performed during these admissions, including blood cultures, urine cultures, and serological testing. She tested positive for Epstein-Barr virus (EBV) IgG and IgM and West Nile virus (WNV) IgG a month before this admission, though all blood and urine cultures remained sterile. Her fevers persisted despite the discontinuation of MTX. Transthoracic echocardiography (TTE) was performed twice but showed no vegetations. A previous computed tomography angiography (CTA) of the chest was unremarkable.

The patient was admitted again a month after her previous hospitalization. Laboratory results on presentation revealed significant hyponatremia (sodium 123–125 mmol/L), mild normocytic anemia (hemoglobin 10.5 g/dL), hypoalbuminemia (albumin 2.7 g/dL), and elevated inflammatory markers, including C-reactive protein (CRP, 11.5 mg/dL) and erythrocyte sedimentation rate (ESR, 55 mm/hr). Despite multiple blood cultures, no bacterial growth was identified. An autoimmune panel, including anticardiolipin antibodies and lupus anticoagulant testing, was negative. Renal and liver function tests were within normal limits except for hypoalbuminemia. Urine antigen testing for *Histoplasma* was negative.

Initial abdominal CT revealed splenomegaly and a wedge-shaped area of lower attenuation in the spleen, consistent with a splenic infarct (Fig. 1). Chest CTA was unremarkable. Given her history of valve disease, a repeat TTE was performed, which did not show any vegetations. However, a transesophageal echocardiogram (TEE) demonstrated thickened valve leaflets with restricted motion and large vegetations involving all three leaflets of the bioprosthetic aortic valve (Fig. 2A and B), raising concerns for infective endocarditis.

The patient was initially started on broad-spectrum antibiotics (Vancomycin, cefepime and metronidazole), and cardiothoracic surgery was consulted for a possible redo aortic valve replacement. However, surgical intervention was deferred due to her worsening neurological status. She developed aphasia and altered mental status, raising concerns for a stroke. Initial imaging, including MRI and head CT, was unremarkable, while EEG showed moderate diffuse encephalopathy. Her condition continued to deteriorate, with new-onset hemibody weakness and hyperreflexia, raising concerns for partially treated meningitis or an embolic stroke. Given the high risk of embolic events from the large vegetations on her bioprosthetic aortic valve, a multidisciplinary discussion involving structural cardiology and cardiothoracic surgery resulted in the decision to proceed with AngioVac debulking to reduce the embolic burden before considering surgical intervention. A repeat TEE on day 12 of admission revealed worsening vegetations and a severely elevated mean gradient of 45 mmHg across the aortic valve (Fig. 3A and B).

On day 14 of admission, the patient underwent percutaneous debulking using the AngioVac system under TEE and fluoroscopic guidance, with extracorporeal membrane oxygenation (ECMO) suction/flow support. Approximately 4 cm of vegetative material was

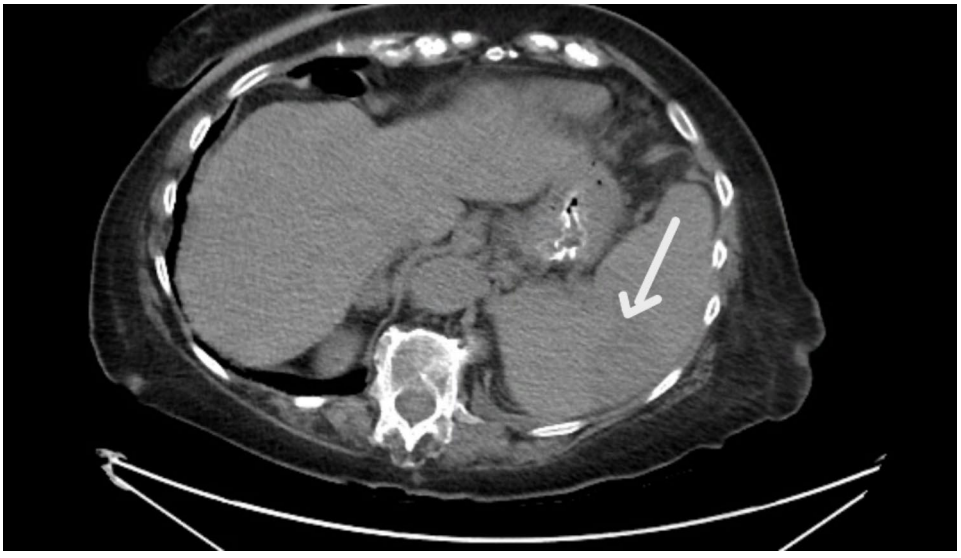

Fig. 1 CT of the abdomen demonstrating splenomegaly with a wedge-shaped area of lower attenuation within the spleen, consistent with a splenic infarct. The region of low attenuation is highlighted, indicating an area at risk for infarction

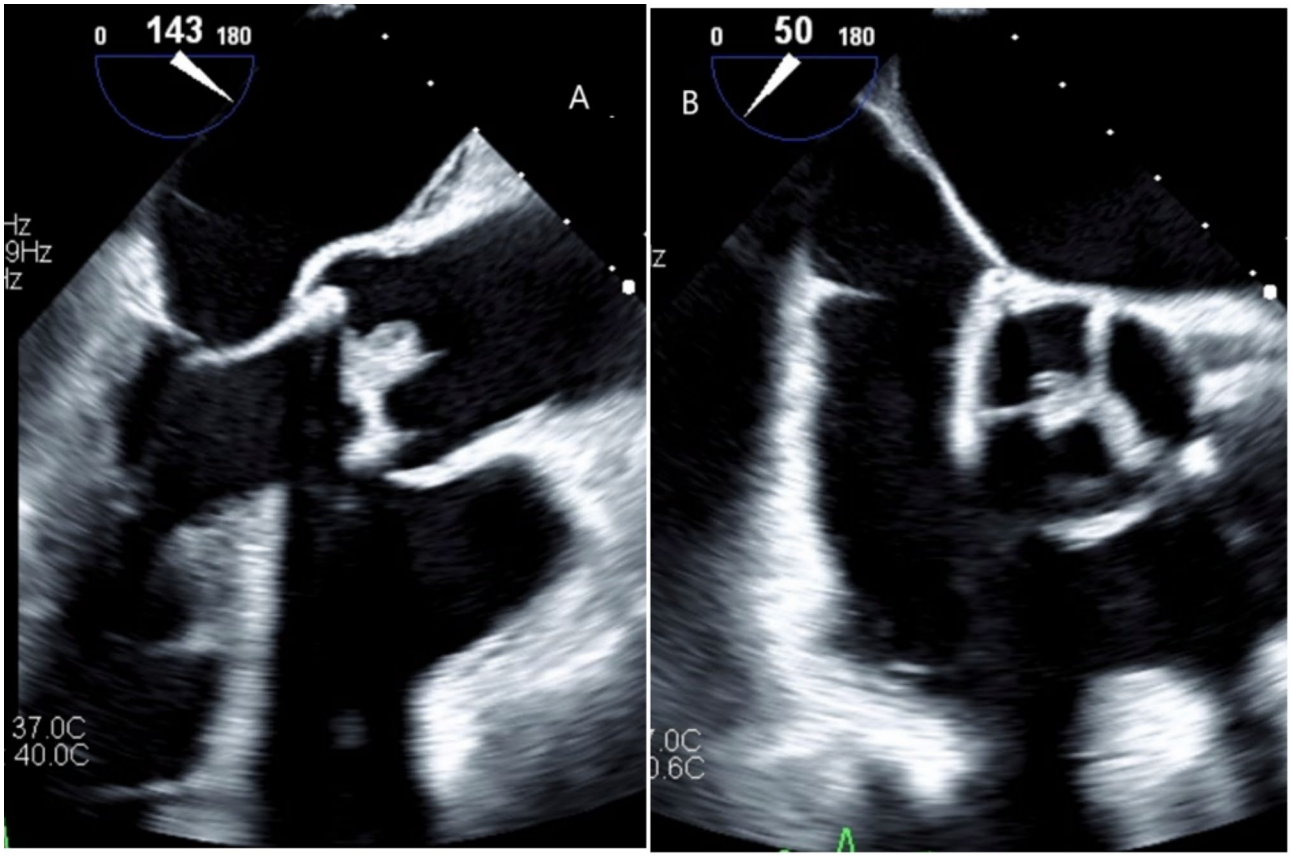

Fig. 2 **A** and **B**: Initial TEE demonstrating thickened bioprosthetic aortic valve leaflets with restricted motion. A large vegetation is visible involving all three leaflets

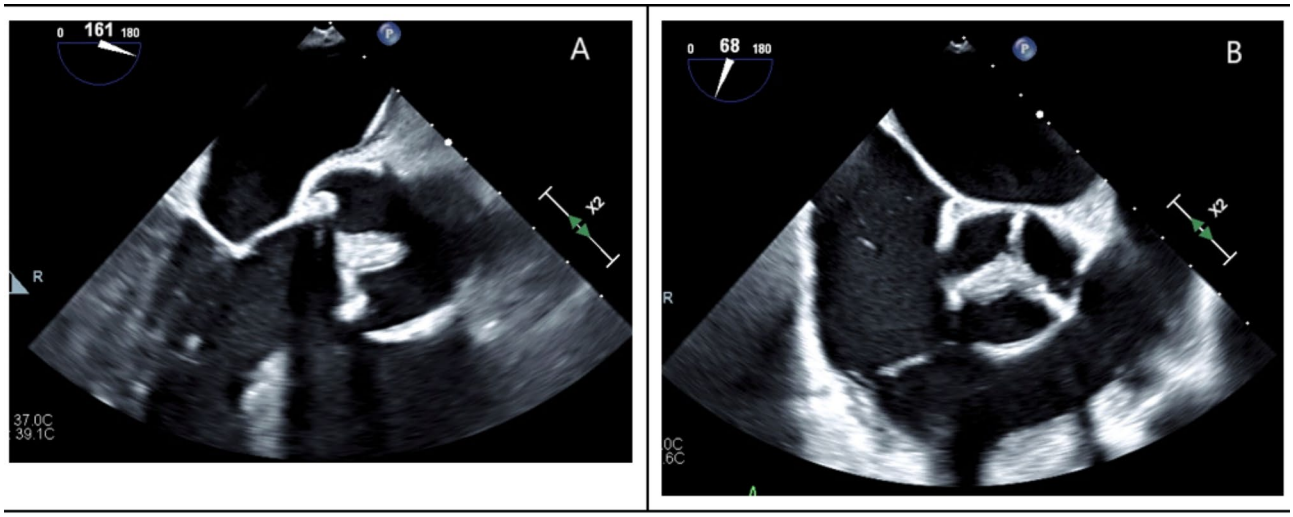

Fig. 3 **A** and **B**: Repeat TEE demonstrating worsening vegetations on the bioprosthetic aortic valve with further restricted leaflet motion

successfully extracted from the bioprosthetic valve (Fig. 4). A TTE performed after the AngioVac procedure showed no remaining vegetations. However, no follow-up TEE was performed due to the patient's condition. Tissue cultures obtained during the procedure grew Histoplasma capsulatum, confirming a diagnosis of fungal endocarditis. The patient was started on antifungal therapy with amphotericin B, with plans for long-term itraconazole.

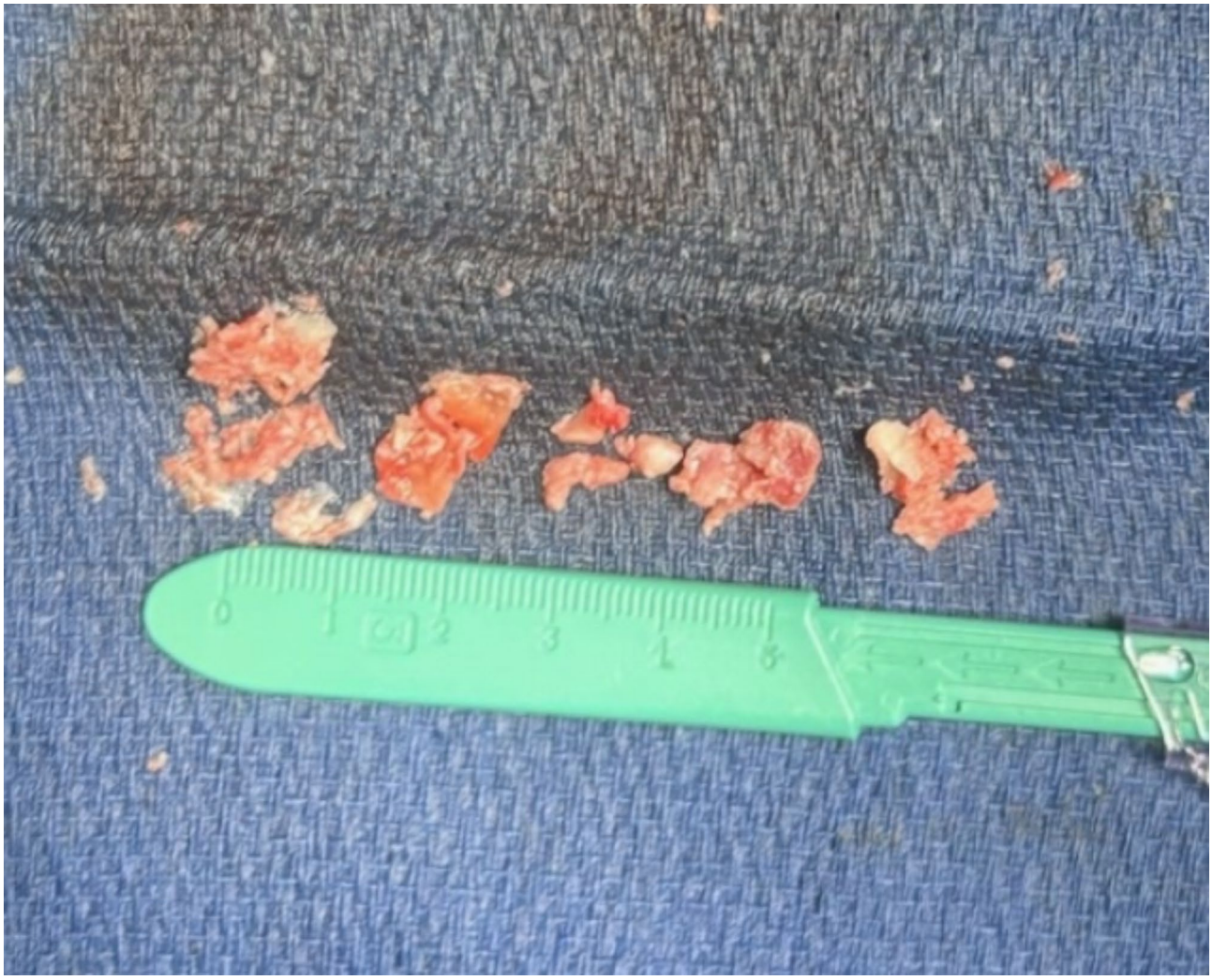

Fig. 4 Vegetative material measuring approximately 4 cm, successfully extracted during the AngioVac procedure performed under TEE and fluoroscopic guidance. A summary of the timeline of events is provided in Fig. 5

Post-procedure, her course was complicated by recurrent embolic events, including a pulmonary embolism and multiple embolic strokes, resulting in a right parietal lacunar infarct. Her neurological status progressively declined, and she became dependent on BiPAP for respiratory support. Later in her hospital course, she developed hypotension and was transferred to the ICU for the management of septic shock. Despite aggressive interventions, she experienced worsening hemodynamic instability, culminating in asystole and death.

Discussion

Histoplasmosis is a fungal infection caused by Histoplasma capsulatum, which is primarily endemic to the Ohio and Mississippi River valleys in the United States [4]. The infection typically arises from inhaling spores present in soil contaminated with bird or bat droppings. While histoplasmosis often causes mild, self-limited disease, it can disseminate in immunocompromised patients, leading to severe manifestations, including disseminated histoplasmosis, central nervous system (CNS) histoplasmosis, and endocarditis. Fungal endocarditis, particularly due to Histoplasma capsulatum, is rare, comprising less than 5% of all infective endocarditis cases [5]. A systematic review identified only 60 cases of Histoplasma capsulatum infective endocarditis reported between 1940 and 2020. It poses a significant diagnostic and therapeutic challenge, especially in patients with prosthetic valves, where the infection tends to be more aggressive [6].

Patients with histoplasmosis endocarditis often present with non-specific symptoms, such as recurrent fever, fatigue, and weight loss, which can delay diagnosis [7]. In our case, the patient experienced persistent fevers for several months with multiple negative blood cultures, highlighting the diagnostic difficulty of culture-negative

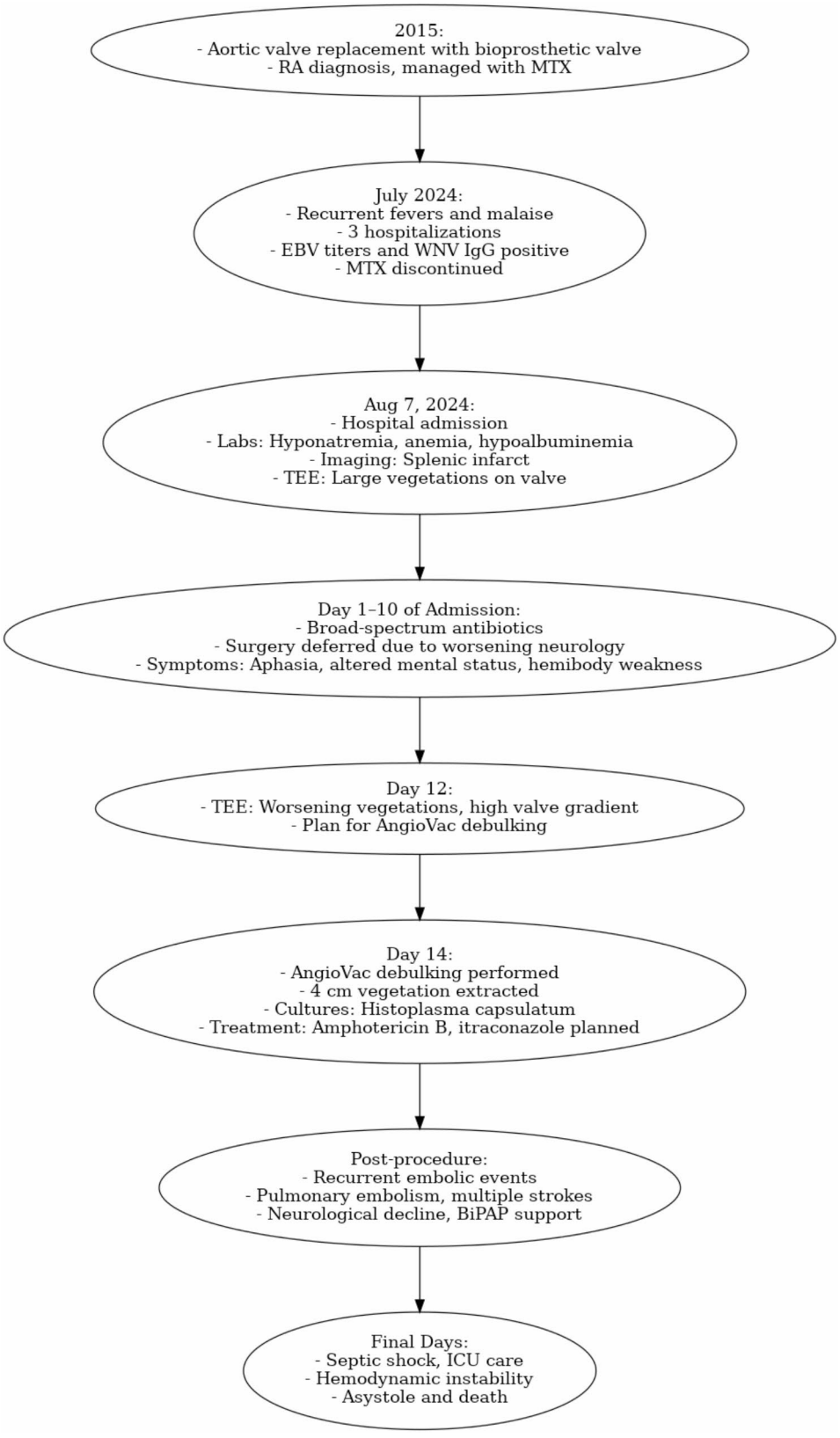

Fig. 5 Timeline of events during hospitalization and clinical decline

fungal endocarditis. Transesophageal echocardiography (TEE) was crucial, revealing large vegetations on the bioprosthetic aortic valve. TEE has a sensitivity of 87–100% for detecting vegetations, significantly outperforming transthoracic echocardiography (TTE) [8, 9].

Surgical management has traditionally been the treatment of choice for fungal endocarditis, with valve replacement often required due to the high risk of embolic events and persistent infection. However, surgical intervention carries significant risk, with reported mortality rates ranging from 57 to 62%, depending on patient comorbidities and the extent of infection [10]. AngioVac, a percutaneous device used for the aspiration of intracardiac masses, has emerged as a less invasive alternative for high-risk patients. It allows for the reduction of the embolic burden by aspirating large vegetations without the need for open-heart surgery. A scoping review encompassing 65 cases reported a success rate of 87.6% without complications, while 10.7% of cases experienced complications, such as recurrence of vegetation or persistent bacteremia [11]. In our patient, AngioVac successfully removed a 4 cm vegetation, providing temporary stabilization and enabling the initiation of targeted antifungal therapy.

A structured review assessed whether vegetation size in infective endocarditis indicates the need for surgery. Among 102 identified papers, 16 provided the best evidence. Vegetations were classified as small (< 5 mm), medium (5–9 mm), or large (≥ 10 mm), with ≥ 10 mm predicting embolic events and increased mortality in left-sided endocarditis. Large vegetations, especially those persisting after 4–8 weeks of antibiotics or causing complications (e.g., abscess, valvular destruction, persistent fever), necessitated surgery. A multicenter study of 384 patients confirmed that vegetations > 10 mm and high mobility predicted embolic events. Meta-analyses and cohort studies further linked ≥ 10 mm vegetations with embolic risk, while vegetation area > 1.8 cm^2 also predicted complications. In right-sided endocarditis, vegetations > 20 mm correlated with higher mortality. Strong evidence supports surgery for left-sided vegetations ≥ 10 mm [12].

While AngioVac offers a less invasive option with fewer immediate surgical risks, it is not without complications. The procedure carries risks of bleeding, vascular injury, and incomplete removal of vegetative material, which may necessitate further intervention [13]. On the other hand, valve replacement surgery provides a definitive solution by removing the infected tissue entirely but is associated with higher perioperative risk, particularly in frail patients with multiple comorbidities [14]. The decision between AngioVac and surgical valve replacement should be guided by patient factors, vegetation size, and the presence of embolic phenomena, all of which influence prognosis.

Conclusion

This case underscores the importance of considering fungal endocarditis in patients with culture-negative fever, particularly those with a history of valve replacement or residence in endemic areas for histoplasmosis. Utilizing advanced diagnostic imaging and a multidisciplinary approach can enhance patient outcomes. Early intervention with AngioVac, followed by definitive antifungal therapy, may offer a viable strategy for managing complex cases, potentially reducing the morbidity and mortality associated with fungal endocarditis.

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Author contributions

S.E and R.G. supervised and oversaw the work. The literature search was conducted by R.A. and A.S., while the analysis and interpretation of the literature were performed by O.S., Q.Q., C.G., and M.B. All authors contributed to drafting the case report. R.A., Q.Q., and A.S. reviewed and edited the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

No ethical approval is needed as this is a case report requiring only the consent of the human subjects involved in the study.

Consent for publication

Written informed consent was obtained from the patient to publish this case report.

Competing interests

The authors declare no competing interests.

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