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Aspergillus Spondylodiscitis in an Immunocompetent Patient With Recurrent *Aspergillus* Endocarditis; A Clinical Case Report

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Introduction. Fungal endocarditis is a very uncommon and deadly illness that causes inflammation in the heart's lining, including the valves. *Aspergillus* endocarditis is the second most common cause of prosthetic endocarditis, especially the aortic valve, after *Candida* spp. *Aspergillus* endocarditis can occur on native and prosthetic valves, even in immunocompetent hosts.

Case Report. In this article, we describe a case of recurrent aortic valve *Aspergillus* endocarditis occurring in a Caucasian man without previously known immunocompromised status with multiple brain septic emboli and spondylodiscitis. The patient was successfully responsive to liposomal amphotericin B.

Discussion. Early recognition in patients with underlying immunosuppressive conditions and immunocompetent hosts is critical to decreasing the mortality rate. Aspergillosis must be considered in every patient with a prior valve replacement history and culture negative endocarditis. Surgical debridement and appropriate antifungal agents are required to resolve the problem.

Keywords. *Aspergillus* endocarditis; immunocompetency; spondylodiscitis; recurrent aspergillus endocarditis.

Fungal endocarditis is a very uncommon and deadly illness that causes inflammation in the heart's lining, including the heart valves. *Aspergillus* endocarditis (AE) is the second most common cause of prosthetic endocarditis, especially the aortic valve, after *Candida* spp [1, 2].

The number of AE cases has gone up and is expected to increase even more because there are more invasive procedures, cardiac devices, prosthetic valves, and immune system suppressors being used. AE does not have many of the signs clinicians use to diagnose infective endocarditis, where the blood culture is usually negative and there may not be a fever. These complications lead to late diagnosis and proper treatment and a higher mortality rate [3].

In this article, we describe a case of recurrent aortic valve *Aspergillus* endocarditis occurring in a Caucasian man without previously known immunocompromised status with multiple brain septic emboli and spondylodiscitis.

CASE PRESENTATION

In September 2023, an intubated 35-year-old Caucasian man with a history of previous multiple valve replacements was transferred from the cardiac surgery ward to the intensive care unit of Imam Khomeini Hospital, Tehran, Iran, presenting with a blood pressure drop and possible septic shock. A huge aortic valve vegetation was discovered in early evaluation upon cardiac ultrasonographic findings. Fungal polymerase chain reaction was positive for aspergillosis. At first, amikacin 1 g daily intravenously (IV), meropenem 2 g 3 times a day IV, Linezolid 600 2 times per day IV, voriconazole 200 mg twice per day, and amphotericin B liposomal (5 mg/kg) 400 mg IV daily, were ordered.

Regarding the patient's medical history of the bicuspid aortic valve, he had had aortic valve replacement 4 times, with the last replacement on current admission based on echocardiographic findings. The echocardiograph revealed a shaggy semimobile mass of approximately (18 mm × 15 mm × 14 mm) attached to the aortic valve (suggestive of vegetation and an echo-free space of about 18 mm × 30 mm) in the posterior part of the aorta with extension to intervalvular fibrosa and to and fro flow suggestive of a pseudoaneurysm. Also, there was severe paravalvular leakage from the dehiscence part of the aortic

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Table 1. Patient's Aortic Valve Replacement Surgeries

Date	Symptoms	Echocardiographic Findings	Outcome
August 2022	No symptom during follow-up with echocardiogram	Bicuspid aortic valve	Aortic valve replacement
November 2022	Loss of appetite, weight loss, petechial lesions on arm and eyes	Aortic vegetation	Gram-negative pulmonal endocarditis (suspected fungal infection because of large vegetation but did not receive antifungal treatment)
May 2023	Dyspnea, petechial lesions	Aortic vegetation	Culture of vegetation positive for *Aspergillus flavus*; voriconazole was started
September 2023	No symptoms during follow-up with echocardiogram	Bioprosthetic aortic valve leakage, aortic large pseudoaneurysm, aortic vegetation	Positive polymerase chain reaction of vegetation for *Aspergillus* spp

Table 2. Laboratory Results

Laboratory Test		Result
Blood, urine, and endotracheal cultures		Negative
Brucella Widal, Coombs Widal, 2ME-T		Negative
Galactomannan		0.69 (reference range, <0.5 index)
Immunologic panel	IgG	1240 (normal range)
	IgG1	522 (normal range)
	IgG2	268 (normal range)
	IgG3	80 (normal range)
	IgG4	72.5 mg/dL (02–126 mg/dL)
	IgM	136 (37–286 mg/dL)
	IgA	383 (82–400 mg/dL)
	C3	150 (75–175 mg/dL)
	C4	37 (16–48 mg/dL)
	CH50	120 (42–236 U/mL)
	NBT-DHR	Normal (55–82 %)

Abbreviations: C, complement; CH50, complement total activity; Ig, immunoglobulin; NBT-DHR, nitroblue tetrazolium–dihydrorhodamine assay

valve leaflet and a large echo-free space of approximately 50 mm × 41 mm at the level of ascending aorta suggestive of abscess formation with compression effect on the superior vena cava (Supplementary Data). In the patient's medical history, a diagnosis of *Aspergillus* endocarditis was definite with the culture of *Aspergillus flavus* in vegetation in a previous episode of endocarditis, treatment with voriconazole 200 mg twice daily was started for the patient about 6 months before this episode. His past surgical procedures are summarized in Table 1.

To complete the patient evaluation, blood, urine, endotracheal cultures, brucella, serum galactomannan test, immunologic panel for primary immune deficiency, and abdominopelvic ultrasound were ordered. On abdominopelvic ultrasound, bilateral pleural effusion was seen; spleen and liver were intact without abscess formation. Rheumatologic tests including antinuclear antibody (ANA), and rheumatoid factor (RF) and HIV antibodies were negative. Other laboratory test results are summarized in Table 2.

The patient was extubated after proper antibiotic therapy and blood pressure rose. Forty eight hours after extubation, the patient developed a fever again and became tachycardic. The physical examination was normal. A sepsis workup was done and because of the possibility of a low voriconazole level and failure of treatment, therapeutic drug monitoring (TDM) was requested and caspofungin 50 mg IV daily was added to the patient's treatment regimen. The dose of voriconazole raised to 400 mg twice per day. Results of blood and urine culture were negative, CXR and abdominal sonography were normal, and follow-up Echocardiographic did not reveal any vegetation or abscess formation. The TDM of voriconazole was reported 0.7 mcg/mL (normal range: 1–5.5 mcg/mL). Amikacin, meropenem, and linezolid were discontinued. Three days later, lower back pain and left paraesthesia were reported. Whole lumbosacral spine, and brain magnetic resonance imaging (MRI) scans were done, respectively.

The brain MRI scan revealed subacute hemorrhagic infarction in the right inferior frontal lobe, right temporal lobe, and right centrum semiovale. These findings favor brain septic emboli after the patient's previous septic shock (Figure 1).

The lumbosacral MRI showed spondylodiscitis evidence, including low T1 and high T2 signal intensity in the vertebral bodies and the intervertebral disk between them; gadolinium enhancement on T1 weighted imaging in the affected tissues also were seen (Figure 2).

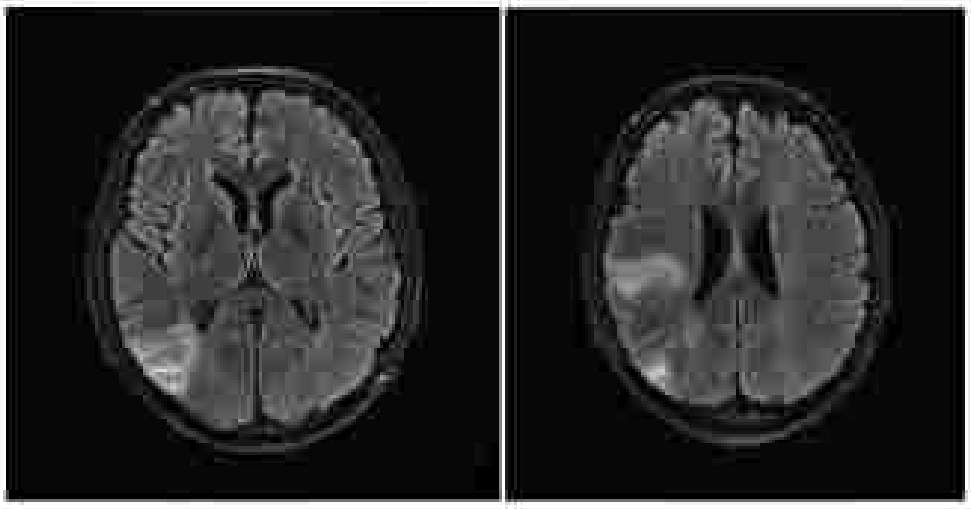

Figure 1. Patient's brain magnetic resonance imaging scan.

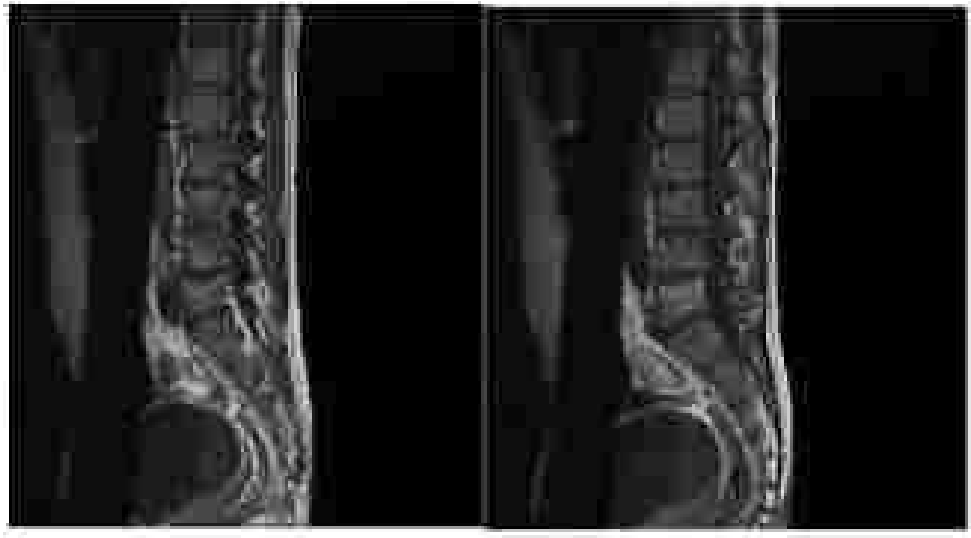

Figure 2. The patient's lumbosacral magnetic resonance imaging scan.

The TDM was in normal range after 2 weeks and signs and symptoms of back pain had significant improving. He did not need surgery. Amphotericin B liposomal and caspofungin were discontinued at the time of discharge after 2 weeks.

The patient was discharged from the hospital after 8 weeks of amphotericin therapy with an acceptable general condition, the following medication orders (voriconazole 400 mg twice per day with careful TDM), and a recommendation for regular follow up by his cardiologist.

DISCUSSION

Aspergillus endocarditis is not common and usually occurs after previous heart surgery such as valve replacement. Approximately half of the patients with infectious endocarditis experience a complication called systemic embolization, where the infection spreads to other parts of the body, especially the brain. Multiple blood cultures and routine echocardiograms in patients with a history of cardiac surgery are the best ways to make a proper diagnosis [4].

In several studies, systemic embolization following AE has been reported. Aortic embolism, splenic infarction, and aortic stroke were reported in patients with AE [5, 6]. Our study

Table 3. Immunocompetent Patients With AE on the Aortic Valve

Year	Gender	Age, y	Previous Cardiac Surgery	Embolization	Outcome
1980 [7]	Male	28	None	Renal	Alive
2004 [8]	Male	34	Subaortic membrane excision	Femoral artery	Dead
2005 [9]	Male	49	CABG	Aortic	Dead
2016 [10]	Male	35	None	None	Dead
2019 [11]	Female	63	CABG	Femoral artery	Alive
2020 [12]	Male	45	None	None	Alive
2021 [13]	Male	69	CABG	Splenic, CNS	Dead
2023 [2]	Male	74	None	CNS	Dead
2023 (current study)	Male	36	Aortic valve replacement (4 times)	CNS	Alive

Abbreviations: CABG, coronary artery bypass grafting; CNS, central nervous system.

detected multiple brain septic emboli on the patient's MRI scan after the fourth aortic valve replacement resulting from AE.

Invasive AE usually occurs in immunocompromised or drug-using patients. Posttransplant patients receiving high doses of corticosteroids or chemotherapy are most prone to developing AE. Most AEs are challenging to diagnose because of the negative blood culture and fever absence [1]. Immunocompetent patients are rarely diagnosed with AE. There have been several studies in which patients without any prior immunosuppressive condition or IV drug use had AE in their aortic valve even without any previous cardiac surgery. These cases, along with our patient, are summarized in Table 3.

In contrast to our study, *Aspergillus* spondylodiscitis was reported in immunocompromised patients following heart transplant, acute lymphoblastic leukemia, and hairy cell leukemia. Patients were treated with itraconazole, which was given as a single drug therapy or in combination with 5-flucytosine and amphotericin B. Surgical management was required in those who did not respond to medical treatment. Our report was the first immunocompetent patient with *Aspergillus* spondylodiscitis following AE [5, 6].

CONCLUSION

Aspergillus endocarditis can occur on native and prosthetic valves, even in immunocompetent hosts. Our patient did not have secondary immunodeficiency. He was tested for primary immunodeficiency (chronic granulomatous disease [CGD]/common variable immunodeficiency [CVID]) and the results were negative. The only risk factor was the patient's prosthetic valve. It is critical to consider aspergillosis in every patient with prior valve replacement history and culture-negative endocarditis. Surgical debridement and appropriate antifungal agents are required to solve the problem. Systemic embolization and *Aspergillus* discitis were also detected afterward in our case.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Patient consent statement. Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request. Considering that this article is a case report, it is acceptable according to the ethical rules of Tehran University of Medical Sciences.

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Potential conflicts of interest. All authors declare no conflicts of interest.

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