

# A Case of *Aspergillus* Mural Endocarditis Presenting With Complete Atrioventricular Block after Liver-Kidney Transplantation



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## INTRODUCTION

Invasive aspergillosis is a rare but fatal infection in patients undergoing solid organ transplantation. Among various infectious complications caused by the *Aspergillus* species, endocarditis is a rare but fatal disease with a mortality rate of nearly 100% without surgical treatment.<sup>1</sup> The *Aspergillus* species are the most common causative organisms of fungal endocarditis within 30 days after solid organ transplantation,<sup>2</sup> but this endocarditis is usually diagnosed postmortem because *Aspergillus* rarely grow in routine blood cultures.<sup>1</sup> In particular, primary mural endocarditis is often diagnosed after the occurrence of embolization, which results in delayed treatment and poor prognosis.<sup>3</sup> Here we present a rare case of primary mural endocarditis caused by *Aspergillus* species in a patient who underwent simultaneous liver and kidney transplantation.

## CASE PRESENTATION

A 61-year-old man with diabetes mellitus and hypertension visited our outpatient clinic reporting a dry cough, which had begun 10 days earlier. Forty days earlier, he had undergone simultaneous liver and kidney transplantation because of hepatitis C–related liver cirrhosis with hepatocellular carcinoma and end-stage renal disease. Subsequently, he had been treated with tacrolimus, mycophenolate mofetil, and prednisolone for the prevention of acute rejection.

At the time of admission, the patient's blood pressure was 107/58 mm Hg, his heart rate was 99 beats/min, and his body temperature was within the reference range. Cardiac murmur was not auscultated, and breathing sound was clear. On laboratory examinations, leukocytosis was not detected, and the level of serum C-reactive protein was not elevated. However, his paranasal sinus and chest radiograph showed bilateral maxillary sinusitis and a new small consolidation in the right upper lung field. On the subsequent non-contrast chest computed tomographic scan, centrilobular nodules were observed in the right upper lobe of the lung, suggesting active

tuberculosis or a fungal infection (Figure 1). Additional laboratory sputum tests to exclude tuberculosis, such as an acid-fast bacilli test and polymerase chain reaction, showed negative results.

On the hospital day (HD) 8, the patient's heart rate suddenly dropped to 50 beats/min. Electrocardiography revealed complete atrioventricular block (CAVB). Fever had developed 3 days after the first detection of bradycardia. On echocardiography performed on HD 12, a huge mass (36 × 18 mm) firmly attached to the posterolateral wall of the left ventricle was found, which led to flow acceleration at the mid-level of the left ventricle (Figure 2, Videos 1-5). The mass was not observed on previous echocardiography, which was performed immediately after transplantation because of elevations of cardiac enzymes (Figure 3, Videos 6-9). Vegetation or thrombus was suspected, but there was no microbial growth in routine blood cultures and left ventricular systolic function was normal. Diastolic mitral and tricuspid regurgitation was accompanied by CAVB (Figure 4). A temporary pacemaker was inserted on HD 14.

On HD 14, sudden motor aphasia and left-sided weakness developed, and multiple embolic cerebral infarction were detected on subsequent magnetic resonance imaging. On HD 15, transesophageal echocardiography–guided punch biopsy of the left ventricular mass was performed via thoracotomy. Voriconazole treatment was empirically started on the day of the biopsy on the basis of clinical suspicion and gross finding in the surgical field. On that day, the result of serum *Aspergillus* galactomannan antigen assay was positive (index = 5.05), and polymerase chain reaction for *Aspergillus* species was also positive in the serum sample. In addition, *Aspergillus* species was identified in his sputum and bronchoalveolar lavage. In the left ventricular biopsy specimen, numerous septate and branched fungal hyphae were observed via hematoxylin and eosin and Gomori methenamine silver staining (Figure 5).

Despite the antifungal treatment and supportive care, status epilepticus due to repetitive septic embolic infarction and septic shock caused by central line–associated bloodstream infection developed. The patient died on HD 32 of multiorgan failure related to septic shock. The timeline of the patient's clinical course is summarized in Figure 6.

## DISCUSSION

Herein, we report a case of primary nonvalvular, mural endocarditis in a patient without an underlying cardiac structural disease who was receiving immunosuppressive treatment. *Aspergillus* endocarditis usually presents as valvular endocarditis the aortic or mitral valve.<sup>4</sup> Mural endocarditis is extremely rare; only one case of primary mural endocarditis caused by *Aspergillus* species exists in the literature, and it was reported in 1986.<sup>1,3,5</sup> Common clinical manifestations of endocarditis, such as cardiac murmur and hemodynamic instability, are usually absent in mural endocarditis, which led to delayed diagnosis after

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## VIDEO HIGHLIGHTS

**Video 1:** Parasternal long-axis view of the vegetation.

**Video 2:** Apical four-chamber view of the vegetation.

**Video 3:** Parasternal short-axis view of the vegetation at the basal left ventricle.

**Video 4:** Parasternal long-axis view of the vegetation with color Doppler echocardiography.

**Video 5:** Apical four-chamber view of the vegetation with color Doppler echocardiography. Large mass ( $3.6 \times 1.8$  cm) is firmly attached to the posterolateral surface of the basal left ventricle. Acceleration of flow velocity is observed between the mass and the basal anteroseptal wall of the left ventricle. Diastolic mitral regurgitation suggests advanced atrioventricular block.

**Video 6:** Parasternal long-axis view of the transthoracic echocardiogram immediately after transplantation.

**Video 7:** Apical four-chamber view of the transthoracic echocardiogram immediately after transplantation.

**Video 8:** Parasternal long-axis view of the transthoracic echocardiogram immediately after transplantation with color Doppler echocardiography.

**Video 9:** Apical four-chamber view of the transthoracic echocardiogram immediately after transplantation with color Doppler echocardiography.

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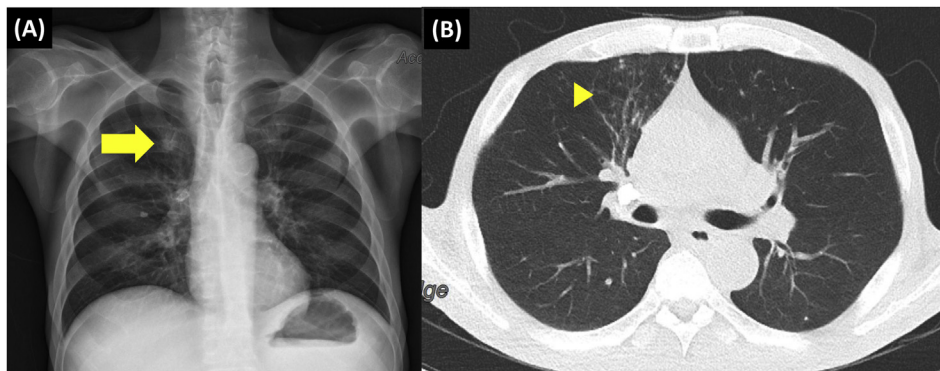
the occurrence of embolic complications in a previous case.<sup>3</sup> Furthermore, because *Aspergillus* endocarditis usually occurs in immunocompromised patients, constitutional symptoms could be absent at the initial presentation. Therefore, clinical suspicion is essential for early diagnosis. In addition, early examination of transthoracic echocardiography is crucial in the absence of signs of infective endocarditis. Because of the rapidly growing nature and the atypical location of the left ventricular mass, we initially suspected mural thrombus rather than infective endocarditis. However, the patient showed normal

left ventricular function, in which thrombus formation is difficult. The patient's immunocompromised state led us to suspect fungal endocarditis.

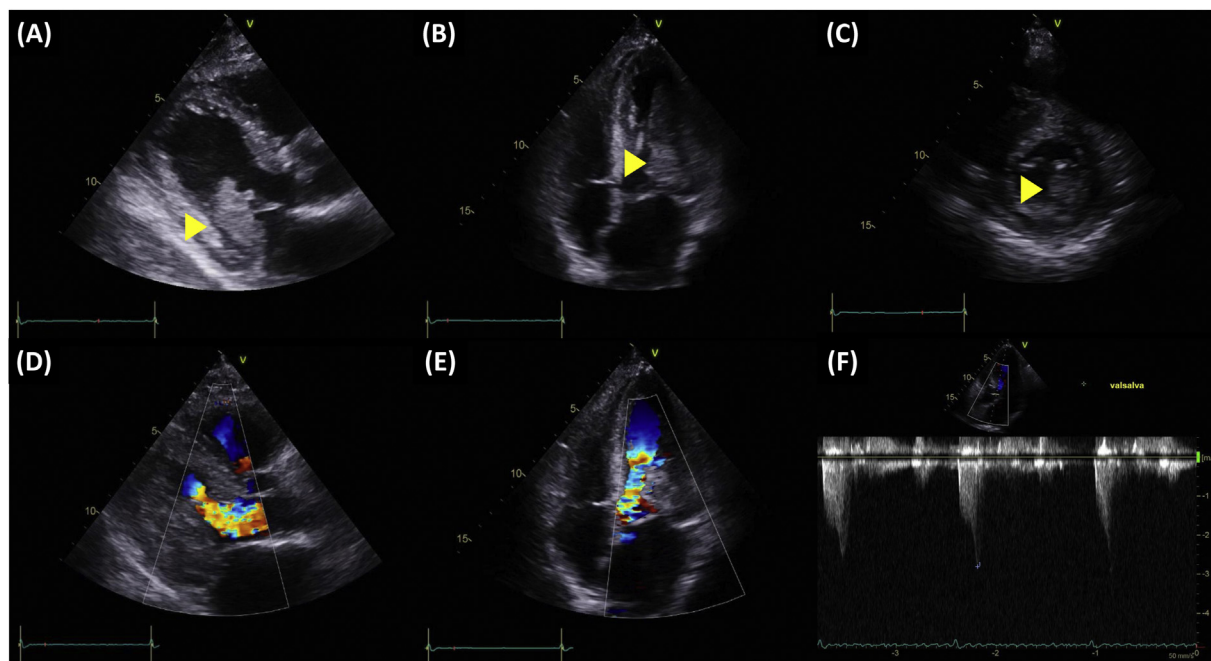
Early diagnosis of *Aspergillus* endocarditis is difficult, but the rate of its progression is very rapid. According to a review by McCormack and Pollard,<sup>4</sup> premortem diagnosis was achieved in fewer than half of patients, and the mean survival period for *Aspergillus* endocarditis was 11 days.<sup>4</sup> In addition, the vegetation in *Aspergillus* infection is large and/or pedunculated, so embolic complications frequently occur. For these reasons, a high degree of suspicion and rapid pathologic confirmation are essential for the diagnosis in patients who are predisposed to immunosuppressive conditions. In the era of organ transplantation, its clinical significance should be more emphasized. If pathologic confirmation is impossible, serum galactomannan assay and polymerase chain reaction for *Aspergillus* are helpful because the results of blood culture are rarely positive.<sup>6,7</sup> However, because the mortality of acute *Aspergillus* endocarditis was nearly 100% without surgical treatment,<sup>1</sup> early surgery for diagnosis and treatment combined with an empirical antifungal agent (voriconazole) is the best strategy for improving outcomes.<sup>4</sup>

In this case, CAVB was the first cardiac manifestation, which developed 1 month after we confirmed the absence of structural heart disease immediately after transplantation. The link between CAVB and the left ventricular mass was uncertain at the time of diagnosis, because the mass seemed attached to the posterolateral wall of the left ventricle, which was far from the atrioventricular node. However, in a previous report of infective endocarditis caused by *Aspergillus udagawae*, pathologic examination showed fungal invasion of the myocardium distal to the mass.<sup>8</sup> Considering the invasive nature of *Aspergillus* species, it might cause CAVB, although the conduction system seems not to be involved on transthoracic echocardiography. In our case, the mass rapidly grew to 3.6 cm in 35 days but was nearly immobile, even in the normally contracting left ventricle. We can assume that the deeply rooted left ventricular mass might have caused CAVB.

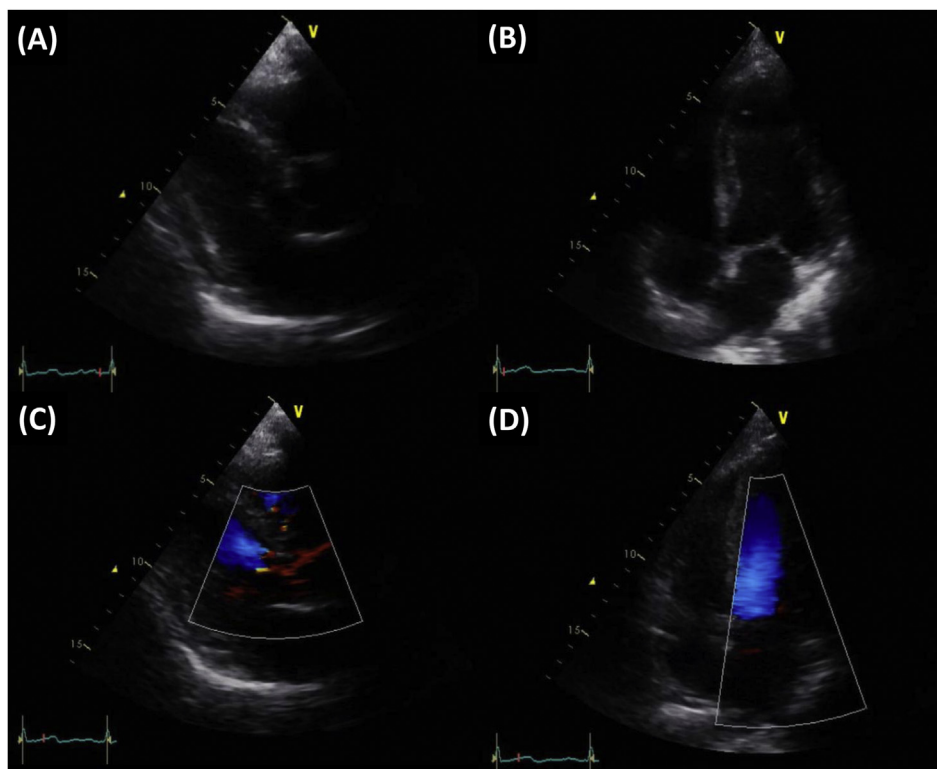
In this case, we failed to specify the species of *Aspergillus* we isolated in the patient's serum. Moreover, we could not confirm the depth of fungal invasion and the possible relationship between CAVB and mural endocarditis, because we could not perform surgery or autopsy. However, our case is an extremely rare case of primary mural endocarditis caused by *Aspergillus* species, confirmed by pathologic examination.



**Figure 1** Chest radiography and computed tomography of the patient. **(A)** Chest radiograph indicating a small consolidation in the right upper lung field (arrow). **(B)** Computed tomography showing centrilobular nodules in the right upper lobe (arrowhead).

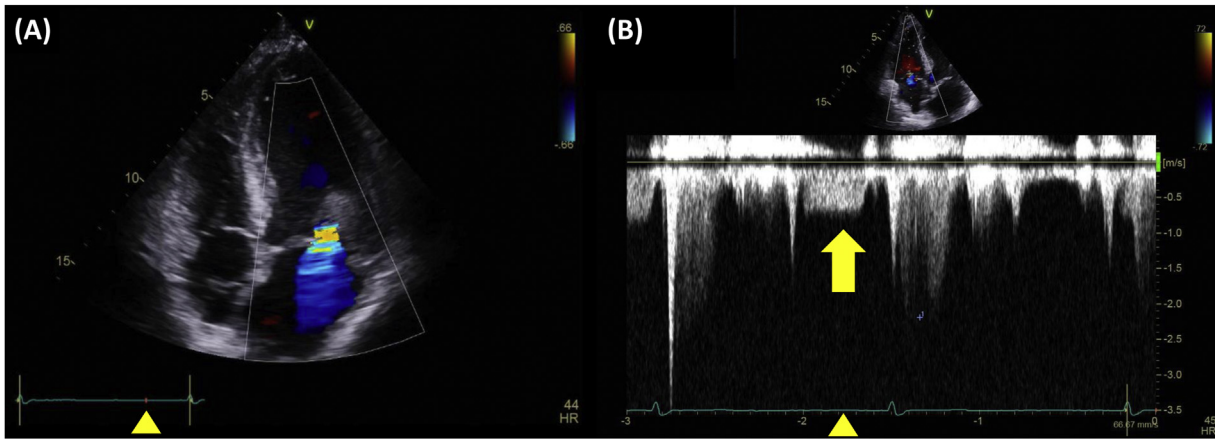


**Figure 2** Echocardiographic findings of a left ventricular mass. In the parasternal long-axis (**A**, **D**), apical four-chamber (**B**, **E**), and parasternal short-axis (**C**) views, a large mass is observed to be firmly attached to the posterolateral surface of the basal left ventricle (*arrowhead*). The size of the mass was  $3.6 \times 1.8$  cm, and it caused flow acceleration in the left ventricular outflow tract on color Doppler echocardiography (**D–F**).

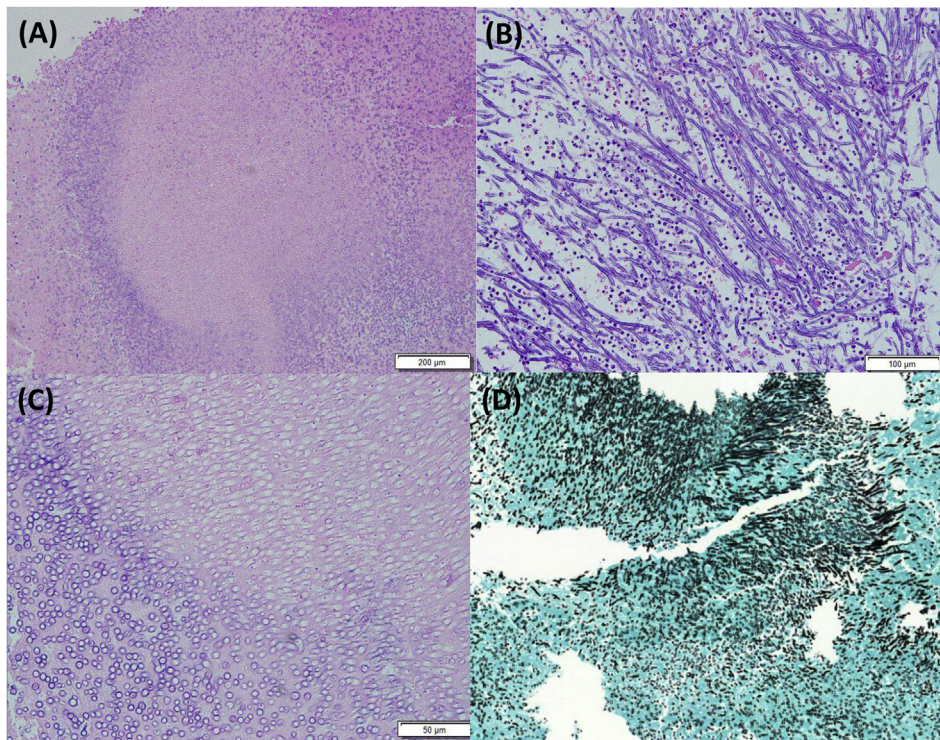


**Figure 3** Transthoracic echocardiography immediately after liver-kidney transplantation. In the parasternal long-axis (**A**, **C**) and apical four-chamber (**B**, **D**) views, no intraventricular mass was found to be obstructing the left ventricular outflow tract.

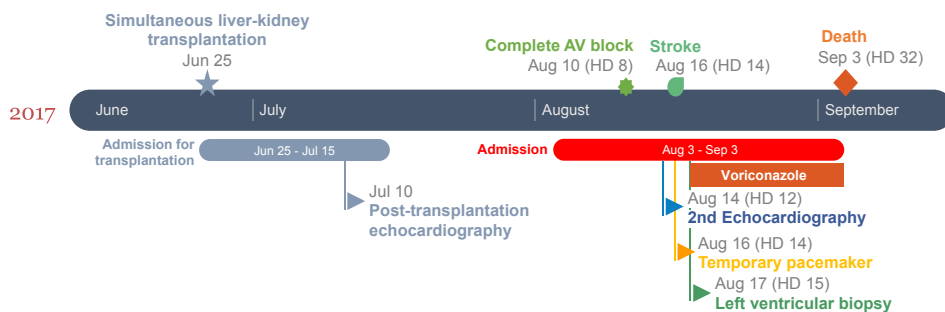




**Figure 4** Diastolic mitral and tricuspid regurgitation. **(A)** Mitral regurgitation is shown at diastole (*arrowhead* on electrocardiography) in the apical four-chamber view. **(B)** Doppler signal is seen as low velocities moving away from the transducer according to tricuspid regurgitation at diastole (*arrow*).



**Figure 5** Microscopic finding of vegetation in a left ventricular biopsy specimen. Numerous septate and branched fungal hyphae were observed via hematoxylin and eosin **(A–C)** and Gomori methenamine silver **(D)** staining.



**Figure 6** Timeline of the patient's clinical course.

## CONCLUSION

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*Aspergillus* mural endocarditis is rapidly progressive and has a fatal outcome. A high degree of clinical suspicion and early transthoracic echocardiography in patients with risk factors for fungal infection are key for early diagnosis and better outcomes.

## SUPPLEMENTARY DATA

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Supplementary data related to this article can be found at <https://doi.org/10.1016/j.case.2019.07.008>.

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