

Successful Deceased Donor Kidney Transplantation after survived isolated Aspergillus fumigatus Pericarditis using Isavuconazole Prophylaxis: A Case Report

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Abstract

Background: Invasive fungal infections represent a major challenge in solid organ transplantation due to the risk of reactivation under immunosuppression. Aspergillus pericarditis is an uncommon manifestation associated with high mortality, and data guiding transplant decisions after such infections are limited.

Case Presentation: A 48-year-old female with end-stage renal disease on hemodialysis presented with constrictive pericarditis and severe hypotension. Aspergillus fumigatus isolated by tissue culture after subtotal pericardiectomy. She was treated with voriconazole for four months with complete clinical resolution and underwent deceased donor kidney transplantation two months after treatment. The patient required temporary hemodialysis due to immediate postoperative delayed graft function and tacrolimus was started four days later. Secondary prophylaxis from transplantation onwards was with isavuconazole, due to its mild, highly predictable CYP3A4 inhibition that allowed safe titration of calcineurin inhibitors without volatile toxic spikes. Kidney transplantation was successful with no rejection or major infection. Over a 2-year follow-up, the patient had stable allograft function without fungal recurrence.

Conclusion: Kidney transplantation may be feasible in selected patients with previously treated invasive aspergillosis when careful risk stratification, pre-transplant mycological eradication with the strategic deployment of newer-generation triazoles like isavuconazole to safely manage complex post—transplant pharmacokinetic interactions and tailored immunosuppression.

Keywords: Kidney Transplantation, Invasive Aspergillosis, Pericarditis, Isavuconazole, Delayed Graft Function, ESRD.

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Introduction

Invasive aspergillosis is a serious opportunistic infection associated with significant morbidity and mortality, particularly among immunocompromised individuals. Cardiac involvement, especially pericardial disease, is rare and often difficult to diagnose due to nonspecific clinical features [2].

Traditionally, recent invasive fungal infection has been considered a relative contraindication to organ transplantation because of the risk of recurrence following immunosuppressive therapy [3]. However, evolving evidence and recommendations from organizations such as the Infectious Diseases Society of America suggest that transplantation may be considered after adequate treatment and

resolution of infection, provided that individualized risk assessment is performed [1].

We describe a rare and clinically significant case of successful deceased donor kidney transplantation following treated Aspergillus pericarditis.

Case Presentation: A 48-year-old female, a known case of End stage renal disease (ESRD) with unknown native kidney disease (possible Chronic Glomerulonephritis) presented to Manipal hospital Whitefield, Bangalore and she was enlisted for cadaver kidney transplant.

She was found to have constrictive pericarditis (Thickened pericardium with conical ventricles, dilated atrial chambers, IVC and hepatic veins-

concerning constrictive pericarditis). She had severe peripheral edema and severe hypotension. Her blood pressure was 80mm Hg systolic and diastolic of 60mm Hg. Maintenance hemodialysis was severely compromised by profound systemic hypotension, leading to sub-optimal clearance and progressive uremic symptoms. There were no features suggestive of infections such as fever, chills or any other symptoms. There was no evidence of myocarditis or endocarditis. Cardiologists suggested pericardiectomy. Due to socioeconomic constraints, the patient underwent urgent subtotal pericardiectomy at an external facility. In tissue culture, she was found to have *Aspergillus fumigatus* in the pericardium tissue.

Pre-Transplant Management: Following diagnosis, the patient was initiated on systemic antifungal therapy with Voriconazole, a triazole antifungal drug of choice against invasive aspergillosis⁴. Over the course of treatment, her hemodynamic status improved, with blood pressure stabilizing to 110/80 mmHg. She showed clinical improvement, and there was no evidence of ongoing or disseminated infection.

Despite stabilization, her overall quality of life remained significantly impaired due to ESRD.

Transplant Procedure and Immunosuppression: Following multidisciplinary evaluation and confirmation of infection control, the patient underwent deceased donor kidney transplantation upon availability of a suitable organ. She underwent transplantation within 2 months of

completion of the antifungal therapy. Induction immunosuppression was administered using anti-thymocyte globulin at a total dose of 1.5 mg/kg, divided over five doses, along with intravenous methylprednisolone totalling 1500 mg over three days. Maintenance immunosuppression was initiated with mycophenolate mofetil on the day of surgery. Tacrolimus introduction was delayed as part of protocol. Perioperative antifungal therapy with Isavuconazole was started from the day of transplantation as secondary prophylaxis against recurrence. Isavuconazole was selected because it exhibits a significant more predictable and milder drug-drug interaction profile with calcineurin inhibitors compared to voriconazole, allowing for safer stabilization of tacrolimus troughs. [4]

Postoperative Course: The immediate postoperative period was complicated by delayed graft function, necessitating two sessions of hemodialysis. However, there was progressive improvement in graft function, and dialysis was discontinued by postoperative day four. The patient started on tacrolimus on day 4.

Subsequently, the patient demonstrated stable renal function without further need for dialysis. There was no clinical, biochemical, or radiological evidence of recurrence of fungal infection during follow-up. Overall recovery was satisfactory, and the patient maintained good graft function. The Chronological clinical timeline of constrictive pericarditis and renal transplantation as been presented in the table 1 and Figure 1.

Table 1: Demonstrating the Chronological clinical timeline of constrictive pericarditis and renal transplantation.

Timeline of milestones	Clinical status and interventions	Relevant diagnostic/ laborator markers
Month 0	Presentation with sever hypotension and fluid overload, diagnosed with constrictive pericarditis	BP- 80/60mmHg ECHO- conical ventricles, thickened pericardium
Month 0+2weeks	Subtotal pericardiectomy at external facility	Pericardial tissue culture- <i>Aspergillus fumigatus</i>
Month 1-3	Induction and maintaenance of systemic antifungal therapy	Intravenous Voriconazole BP- stabilized to 110/80mmHg
Month 4	Completion of therapeutic Voriconazole course	Complete clinical resolution of cardiac symptoms
Month 6 [2 months post-fungal treatment]	Deceased donar renal transplantation performed	Induction: anti thymocyte globulin [1.5mg/kg in 5 didvide doses] + Methylprednisolone
Post operative Day 1-3	Delayed graft function [DGF]	Requires 2 sessions of hemodialysis. Isavuconazole initiated
Post operative Day 4	Resolution of DGF	Dialysis discontinued Tacrolimus started
2 years follow-up	Sustained graft survival; no fungal recurrence	Stable serum creatinine; follow-up imaging shows no pathologicall findings.

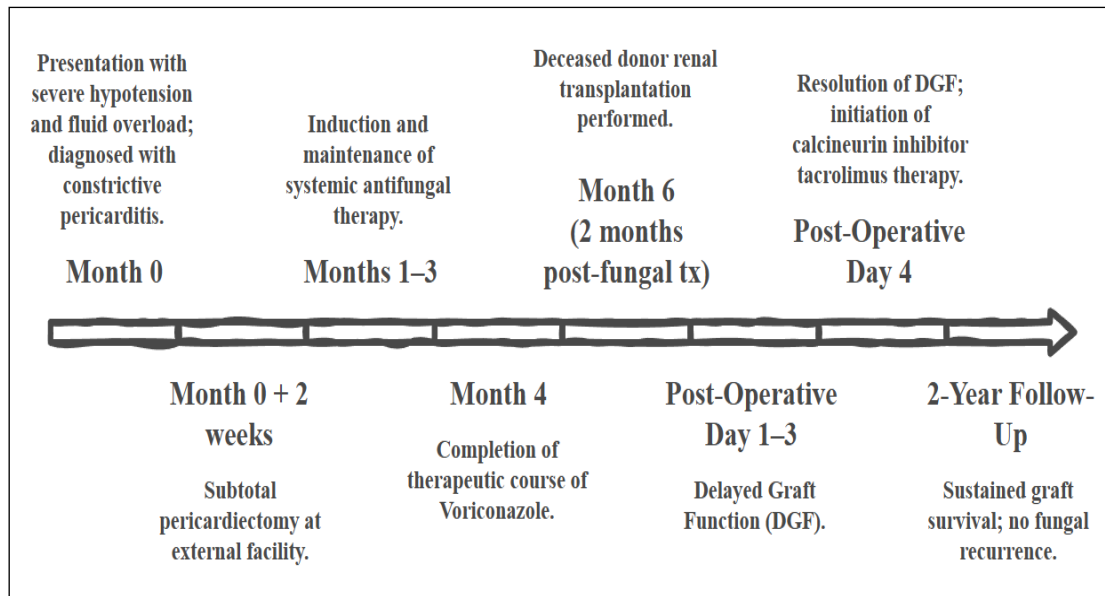


Figure 1: Chronological clinical timeline of constrictive pericarditis and renal transplantation.

Discussion

Aspergillus can cause myocarditis, endocarditis, pericarditis, a combination of these and pancarditis. Incidence of myocarditis, endocarditis and pericarditis is 83%, 17% and 17% respectively. Isolated pericarditis is rare and usually secondary to *Aspergillus pneumonia*. It commonly presents with chest pain, hypotension, cardiac tamponade or pericardial friction. According to a comprehensive literature review by Yuan Xie et al, only 27 cases are identified. 85% of these cases occurred in immunocompromised hosts with a striking overall mortality rate of 40% and notably, 6 out of 27 cases were identified only post-mortem during autopsy. While solid organ transplant recipient have been represented in historical cohorts, end stage renal disease (ESRD) on maintenance hemodialysis was not a previously characterized baseline feature among them. [5] Furthermore, isolated *Aspergillus pericarditis* typically originates from the direct extension of a contiguous pulmonary fungal infection. In contrast, our patient exhibited isolated pericardial involvement with absolute no clinical or radiological evidence of concurrent *Aspergillus pneumonia*, making her clinical presentation exceedingly atypical. The patient had constrictive pericarditis and severe hemodynamic instability necessitated a pericardiectomy and subsequent confirmation of *Aspergillus fumigatus* in tissue culture.

The current therapeutic standard for cardiac aspergillosis mandates a multimodal approach combining aggressive surgical debridement or pericardiectomy with prolonged systemic antifungal therapy. Infectious Disease Society of America (IDSA) guidelines recommend voriconazole and lipid-associated amphotericin B

for initial treatment. Secondary agents include caspofungin and posaconazole. [1] Recently Isavuconazole has shown significant benefit in treatment of Invasive aspergillosis. [4] Treatment duration varies from approximately 3 months to several years based on patient's immune status and response to therapy. Current patient responded very well to Voriconazole. [6] In our case, transplantation was safely executed 4 months and 26 days after the initial diagnosis and exactly 2 months of completion of antifungal therapy. To our knowledge, this represents the first reported case of successful deceased donor renal transplantation following treatment of *Aspergillus fumigatus pericarditis*. This expands upon previous landmark literature, such as the successful renal transplantation reported by Varughese et al. executed 3 months following *Aspergillus terreus peritonitis* in a continuous ambulatory peritoneal dialysis patient, demonstrating that deep-tissue fungal boundaries can be safely navigated if complete mycological eradication is achieved prior to allograft implantation. [7]

The selection of an appropriate secondary antifungal prophylaxis in the immediate post transplantation period is a critical clinical decision. Historically, invasive aspergillosis has been regarded as a major contraindication to transplantation due to high recurrence rates under immunosuppression [3]. However, current evidence indicates that transplantation may be feasible after adequate treatment and resolution of infection, particularly when careful patient selection and monitoring are employed [1].

The patient was started on the tacrolimus (calcineurin inhibitor) on day 4 of post-operative day. The use of Isavuconazole in this case was

significant. While voriconazole remains highly effective against *Aspergillus* species, its utilization in transplant recipient is profoundly complicated by its potency as a cytochrome P450 3A4 (CYP3A4) inhibitor, which causes unpredictable, marked elevation in calcineurin inhibitor (CNI) levels. To circumvent these severe drug-drug interactions, we utilized isavuconazole as secondary prophylaxis starting from the day of transplantation.

Data from the landmark SECURE trial from Maertens et al. established the non-inferiority to voriconazole in the treatment of invasive mould infections, with a more favourable safety profile and fewer drug interactions, particularly with calcineurin inhibitors [4]. These pharmacological advantages make it a suitable choice in transplant recipients.

From a strict pharmacological point of view, it is important to note that, although isavuconazole is a moderate CYP3A4 inhibitor, the inhibitory effect is far more predictable and milder than that of voriconazole or posaconazole, in contrast to the common clinical misconception of no metabolic interactions.

This predictable interaction window was particularly advantageous in our patient in whom the immediate post-operative course was complicated by delayed graft function (DGF) requiring temporary hemodialysis. Tacrolimus initiation was intentionally delayed until post-op day 4 to allow for initial graft recovery. With the introduction of co-administration of isavuconazole, our team was able to safely titrate tacrolimus to target therapeutic trough levels without the volatile and toxic spikes precipitated often with more potent triazoles. This case contributes valuable evidence to the limited literature of pre-transplant aspergillus pericarditis and supports the feasibility of transplantation in carefully selected patients with previously treated invasive fungal infections.

Conclusion

This case provides important clinical evidence that previous life-threatening *Aspergillus* pericarditis does not preclude successful deceased donor kidney transplantation. A purposeful safety window between infection resolution and transplantation, stringent pre-transplant infection control, reduced surgical morbidity, and the judicious use of newer generation triazoles such as isavuconazole can pave

the way for favourable long-term outcomes by safely traversing the intricate pharmacokinetic terrain of post-transplant immunosuppression. Individualized immunosuppression and multidisciplinary decision-making are essential to optimize outcomes in such high-risk cases.

Learning Points: Treated *Aspergillus* pericarditis is no longer an absolute kidney transplant contraindication once complete mycological resolution is achieved and is now feasible in selected patients with appropriate risk assessment. Mild and predictable inhibition of CYP3A4 by isavuconazole allows for safer and more stable tacrolimus titration when compared to older, more variable triazoles. Protection of the allograft can be achieved successfully by delayed initiation of tacrolimus in the setting of immediate DGF protects the vulnerable kidney without compromising essential secondary antifungal prophylaxis. Multidisciplinary evaluation remains crucial in managing complex transplant candidates.

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