

Tacrolimus-induced Reversible Cerebral Vasoconstriction Syndrome after Heart Transplant: Case Report

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Abstract

We describe the case of a patient with a recurrent severe headache that occurred after heart transplant surgery. She was diagnosed with reversible cerebral vasoconstriction syndrome (RCVS) since typical imaging was seen through brain contrast computed tomography. Tacrolimus, an immunosuppressant, was suspected as the cause of the RCVS. The treatment was switched to cyclosporine, after which there was rapid improvement of her symptoms. This case highlights the importance of an immediate diagnosis to switch immunosuppressants to relieve symptoms and prevent progression to severe neurological dysfunction.

Introduction

Reversible cerebral vasoconstriction syndrome (RCVS) is a rare condition characterized by an acute, recurrent and severe headache called “thunderclap headache”. This condition is seen in imaging as multifocal segmental vasoconstriction of cerebral arteries. Although the pathogenesis of the RCVS remains unclear, it has been reported that the disease can occur in certain situations such as exposure to vasoactive or immunosuppressive drugs, and prevail throughout the postpartum period.^{1,2} The diagnosis of RCVS needs a high level of clinical suspicion. Herein, we describe a successfully treated case of tacrolimus-induced RCVS after heart transplant.

Case Presentation

A 44-year-old woman with a history of dilated cardiomyopathy, who had been supported with a left ventricular assist device for four years, underwent heart transplant. A triple-drug regimen consisting of prednisolone, mycophenolate mofetil, and tacrolimus was initiated. Since she had mild renal dysfunction, basiliximab was injected in advance. Tacrolimus was initiated on the fifth day after surgery.

She suddenly presented with a thunderclap headache and vomiting six days after the operation. Although brain computed tomography (CT) demonstrated, no signs of hemorrhage or infarction were detected. She also had hypertension; thus, a calcium channel blocker was promptly administered, which achieved well-controlled blood pressure. However, recurring symptoms required her to take analgesics (Fig. 1). Therefore, brain CT angiography was performed, which revealed the typical “strings and beads” appearance due to segmental vasoconstriction of bilateral posterior cerebral arteries (Fig. 2A, white arrow-heads). Based on these findings, she was diagnosed with RCVS.

Tacrolimus, a drug suspected to cause the RCVS, was discontinued although its blood concentration was within the target range, and cyclosporine was given instead. The symptoms immediately improved and never recurred. Signs of allograft rejection were not observed and she was discharged without any neurological complications. Release of cerebrovascular constrictions was observed on subsequent brain magnetic resonance angiography (MRA) three months after discharge (Fig. 2B, white arrow-heads).

Discussion And Conclusions

RCVS is characterized by acute and repetitive thunderclap headache and the multi-segmental vasoconstriction of cerebral arteries on imaging. Prompt diagnosis and treatment are vitally important because RCVS may progress to encephalopathy, cerebral infarction and hemorrhage.^{1,2} Although brain MRA is a useful diagnostic modality³, CT angiography was initially performed in this case since temporary epicardial pacing leads were placed after surgery, which led to the diagnosis of the RCVS. Moreover, a high level of clinical suspicion is necessary for the diagnosis since it is an underappreciated disease among clinicians.

Management of the RCVS usually consists of resting, treating symptoms (e.g. analgesics), and controlling the blood pressure. Calcium channel blockers have been reported to be effective in relieving the symptoms^{1,2}, but their impact on cerebral vasoconstriction or stroke severity remains unclear. In addition, like our case, some patients have refractory symptoms despite achieving a well-controlled blood pressure. This case emphasizes withdrawal of the causative drug as the most effective treatment for improving the symptoms, and for relieving cerebrovascular constrictions seen on subsequent imaging.

RCVS should be considered as a possible cause of headache in heart transplant recipients because an immunosuppressive agent may be the trigger. Immediately changing immunosuppressants is effective for cases with these conditions.

Declarations

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None to declare.

Declarations

Funding

None to declare.

Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethics approval and consent to participate and for publication

The Institutional Review Board of Osaka University Hospital (no. 16105; date, 2016/2/11) approved this paper, and written informed consent was given by the patient for the use of records and publication. The procedures followed were in accordance with the Declaration of Helsinki.

Availability of data and material

Not applicable.

Code availability

Not applicable.

Author's contributions

Conception and design of study: KI, SK and DY.

Drafting the manuscript: KI.

Revising the manuscript critically for important intellectual content: KT and SM.

All authors read and approved the final manuscript.

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Figures

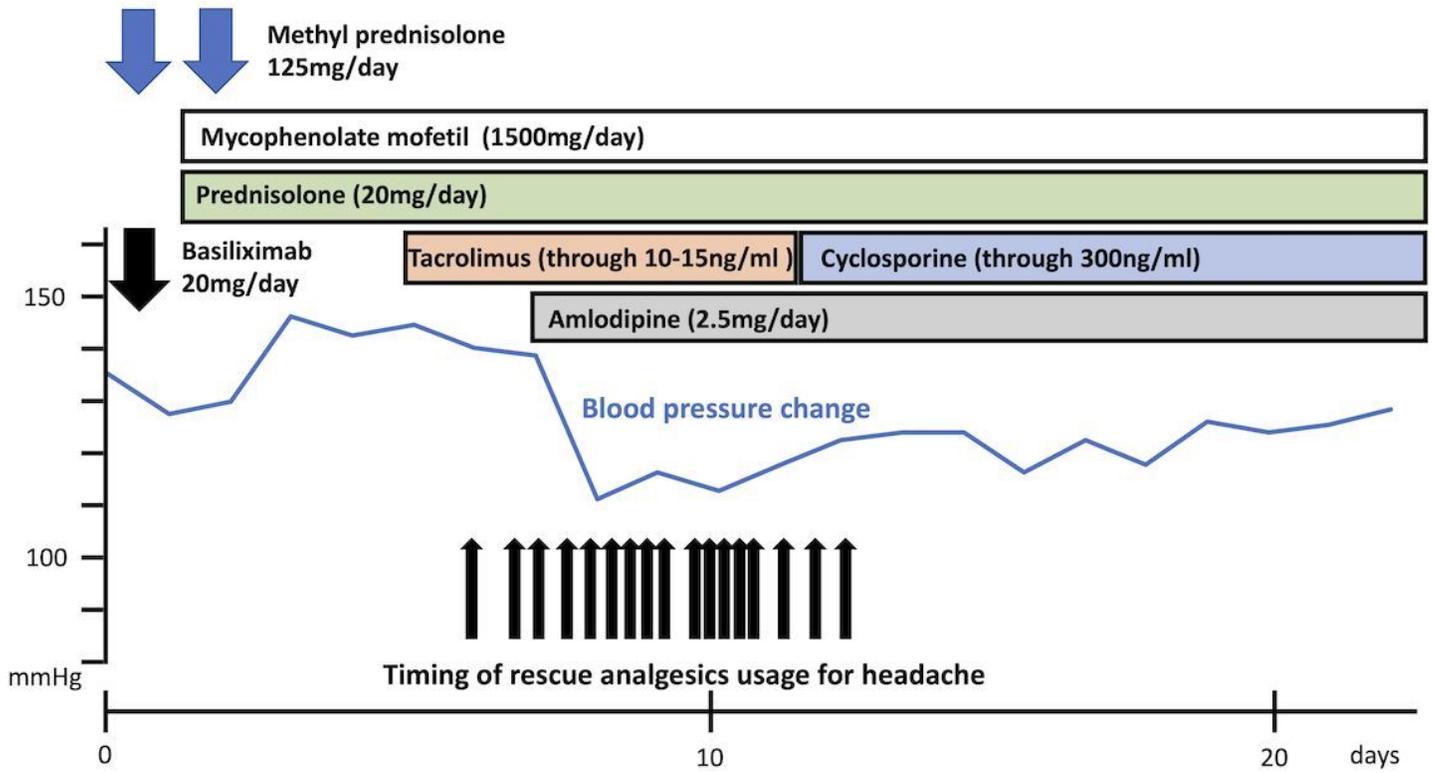


Figure 1

Clinical timeline after heart transplant. Black arrows mean using of analgesics for headache. Headache did not improve despite decreased blood pressure, but it promptly improved after cyclosporine replaced tacrolimus.

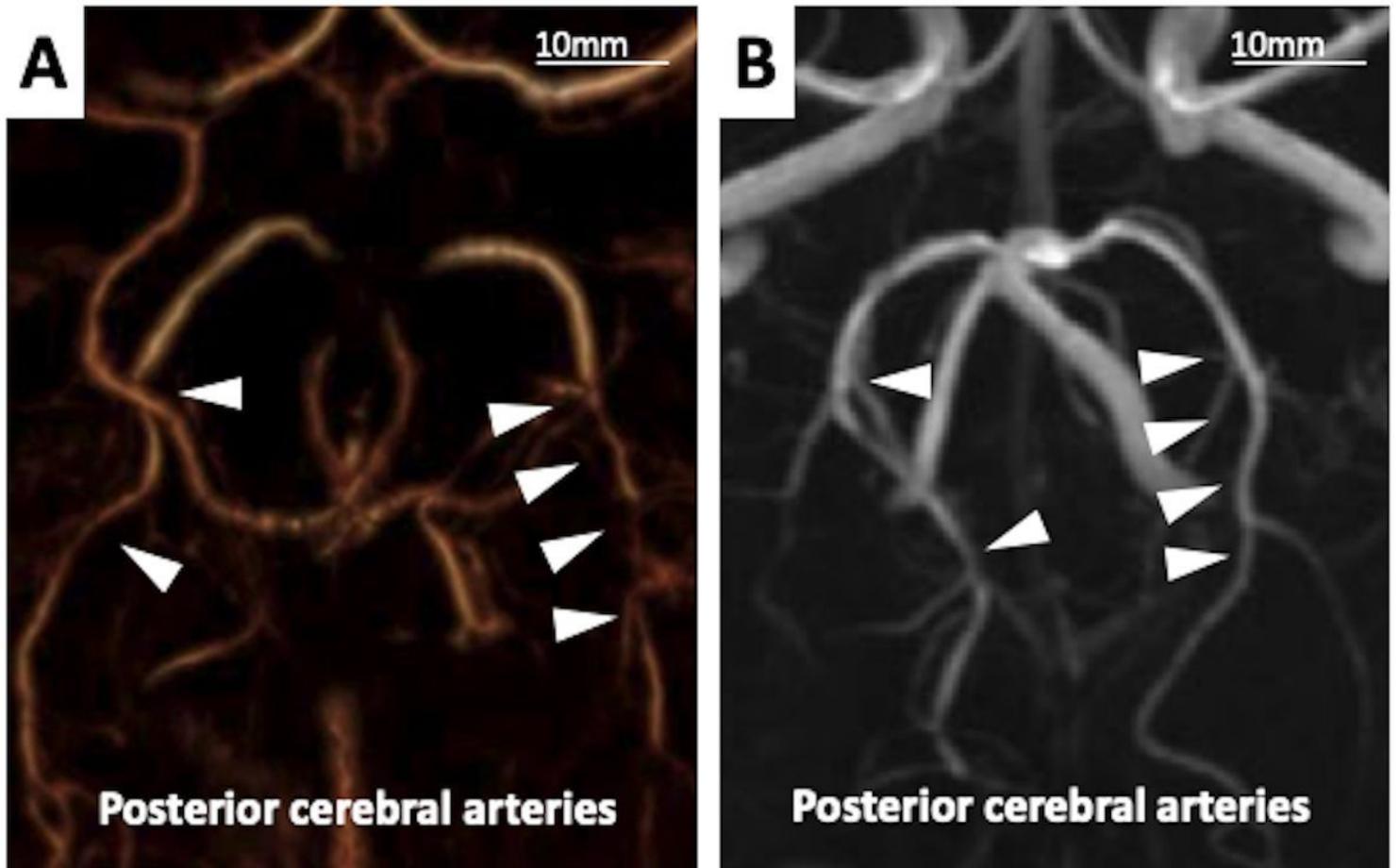


Figure 2

(A) Computed tomography angiographic imaging at the time of onset of thunderclap headache. Multifocal segmental vasoconstriction of bilateral posterior cerebral arteries was observed (white arrow-heads). (B) Magnetic resonance angiography done three months after discharge. Vasoconstriction of cerebral arteries improved (white arrow-heads).

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