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# Reversible cerebral vasoconstriction syndrome combined with posterior reversible encephalopathy syndrome after heart transplantation

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### ABSTRACT

Reversible cerebral vasoconstriction syndrome (RCVS) combined with posterior reversible encephalopathy syndrome (PRES) is a rare complication in patients treated with immunosuppressants. A 52-year-old male patient presented with seizures after heart transplantation. The patient was suspected of having PRES on brain images. Despite the strict blood pressure control, the patient presented with altered mentality and the brain images showed a newly developed large acute infarction. Digital subtraction angiography (DSA) revealed the classic "sausage on a string" appearance of the cerebral arteries – potential feature of RCVS. To our knowledge, this is the first case report to describe RCVS combined with PRES after heart transplantation.

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## 1. Introduction

Reversible cerebral vasoconstriction syndrome (RCVS) is a clinical and radiological condition, characterized by hyperacute onset of thunderclap headache, evidence of vasoconstriction in angiography and reversibility of these symptoms within weeks to months after their onset [1–3]. Posterior reversible encephalopathy syndrome (PRES) is another clinical syndrome with similar clinical features that occur mainly in the setting of hypertensive encephalopathy. RCVS and PRES seem to share clinical features and can occur together; PRES was reported to occur in 10–38% of RCVS cases [2,4–6].

In this report, we describe a patient who presented with RCVS combined with PRES after heart transplantation that resulted in severe cerebral infarction.

### 2. Case report

A 52-year-old male patient who had end-stage heart failure due to dilated cardiomyopathy underwent heart transplantation. At postoperative day (POD) 8, the patient presented with generalized

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http://dx.doi.org/10.1016/j.jocn.2017.03.042 0967-5868/© 2017 Elsevier Ltd. All rights reserved. tonic-clonic seizures. There was no abnormality on electroencephalogram (EEG) and laboratory examinations. Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) of the brain were obtained. The images showed multiple T2 hyperintense lesions in the posterior part of both cerebral hemispheres. There was no evidence of acute cerebral infarction or abnormalities of intracranial vessels (Fig. 1). The patient was suspected of having PRES as a consequence of Tacrolimus (TAC). Considering the risk of PRES worsening, the TAC dose was reduced to maintain the serum concentrations in the low-normal range. Additionally, blood pressure was strictly controlled to avoid accelerating brain edema. The patient was fully recovered a few hours later. At POD 18, the patient presented with altered mentality and bilateral motor weakness (strength of 2/5). The brain images showed a newly developed acute infarction in the fronto-parieto-occipital regions bilaterally and diffuse stenosis at multiple cerebral arteries (Fig. 2). Digital subtraction angiography (DSA) was performed and revealed the classic "sausage on a string" appearance of the cerebral arteries; this sign is a potential feature of RCVS (Fig. 3A). Laboratory examinations showed no evidence of vasculitis. To reduce stenosis and to prevent further infarction, TAC was stopped and the patient was treated with intra-arterial (IA) infusion of a calcium channel blocker (nimodipine). The vessel spasm and flow to the distal cerebral arteries improved (Fig. 3B). With treatment, the left upper extremity strength improved to 3/5. At the 3-month follow-up, brain images showed no new infarctions and

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# **ARTICLE IN PRESS**

Case report/Journal of Clinical Neuroscience xxx (2017) xxx-xxx



**Fig. 1.** (A) Axial T2 image showing multiple hyperintense signals in the cortical-subcortical regions. (B) Matched T2 hyperintense regions were observed on the corresponding apparent diffusion coefficient image. (C) The corresponding diffusion-weighted images were normal. (D) There was no definite abnormality on magnetic resonance angiography.



Fig. 2. (A–C) Diffusion-weighted images showing newly developed acute infarctions in both fronto-parieto-occipital regions. (D) Magnetic resonance angiography showed diffuse stenosis of the anterior cerebral artery, middle cerebral artery, and posterior cerebral artery.



**Fig. 3.** (A) Digital subtraction angiography (DSA) of the right internal carotid artery (ICA) showing vasoconstriction of multiple distal branches prior to treatment with intraarterial nimodipine (arrows). (B) DSA of the right ICA showing improved vasoconstriction after intra-arterial nimodipine administration (arrows).

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no vessel constriction and the patient still had residual difficulties with bilateral motor weakness with a strength of 2/5 (except for a strength of 4/5 for the left upper extremity) and decreased visual acuity.

### 3. Discussion

PRES and RCVS have been reported in neoplastic, hematologic, renal and autoimmune diseases. However, there is no report of RCVS following heart transplantation [4-8]. To our knowledge, this is the first case report to describe RCVS combined with PRES after heart transplantation.

The clinical symptoms of PRES and RCVS are similar. They are characterized by severe headache, seizures and mental changes. In most patients with PRES and RCVS, the clinical and radiological abnormalities are resolved within days or weeks [2,9]. Less than 5% of patients with RCVS develop life-threatening symptoms [1–3]. Transient or persistent focal deficits have been reported in 8–43% of RCVS cases [2]. Nevertheless, the clinical course of RCVS is generally benign with a low recurrence [10]. PRES also can become more severe, resulting in cerebral ischemia, infarction, and even death [11]. Persistent neurological deficits are reported in 10–20% of patients with PRES, and the mortality was approximately 3–6% [9]. However, the prognosis of PRES is usually favorable. Most patients recover with low recurrence rates (5–10%) [9].

The pathophysiological mechanisms of PRES and RCVS remain unknown [3,5], but they are believed to be related to dysregulated cerebral autoregulation with endothelial dysfunction [11]. The potential causes of RCVS and PRES are hypertension, eclampsia or pre-eclampsia, cancer chemotherapy, autoimmune diseases, septic shock, and immunosuppressive treatment after transplantation. which are all associated with endothelial damage or activation [2,3]. In this case, we considered the TAC as a cause of RCVS. When TAC was suspected as a cause of PRES or RCVS, discontinuation or marked reduction of TAC is essential [7]. However, abrupt discontinuation of TAC could have exposed this patient to a high risk of fatal rejection. Alternative drugs, such as Cyclosporine, were suboptimal choices for immunosuppression in the immediate time frame given the similar risks of PRES or RCVS [4]. In this case, we decreased the TAC dose first, aiming to maintain serum concentrations in the low-normal range (6-8 ng/ml). However, cerebral infarction occurred after 10 days. Then, TAC was stopped.

Regarding the management of cerebral arterial spasm, previous reports have suggested that drugs that can reverse vasoconstriction (e.g., nimodipine, verapamil, and magnesium sulfate) are helpful in symptomatic patients [1–3]. In severe cases, IA infusion of nimodipine or verapamil has been used, as well as balloon angioplasty [12–14]. Given the importance of an early detection and management of acute cerebral ischemia for reducing permanent neurological deficits, early diagnosis and treatment of RCVS and PRES can be critical, as our present case demonstrates. Although IA treatment in patients with RCVS is still debatable, we selected IA nimodipine because the patient's symptoms were seriously aggravated.

In the present case, we first diagnosed the patient's illness as PRES and treated the patient with only a dose reduction of TAC. Follow-up studies, including brain MRI and MRA, were not performed. Eventually, cerebral infarction developed due to severe RCVS and was detected 10 days after the onset of PRES. Both RCVS and PRES might be controlled if they are properly detected and managed. If RCVS had been detected earlier, the patient's prognosis might have been better.

### 4. Conclusion

This case supports that short-term follow-up with brain vascular imaging is necessary in cases of PRES to identify changes in the cerebral vascular morphology. Consulting with a neuroendovascular specialist could also be helpful. An appropriate selection of treatment, such as IA angioplasty, with appropriate timing could be critical for patients with severe cerebral vasoconstriction and ischemia.

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### **Conflict of interest**

The authors declare no conflicts of interest.

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