CSA-Induced PRES after Heart Transplantation—Report of Two Cases and Review

Katharina Huenges1 Philipp Kolat1 Bernd Panholzer1 Assad Haneya1

1Department of Cardiovascular Surgery, University of Schleswig-Holstein Campus Kiel, Kiel, Germany

Address for correspondence Katharina Huenges, MD, Department of Cardiovascular Surgery, University of Schleswig-Holstein Campus Kiel, Arnold-Heller-Straße 3, Hs 18, Kiel 24105, Germany (e-mail: Katharina.Huenges@uksh.de).

Introduction

In end-stage cardiomyopathy, heart transplantation is still the gold standard. Despite all improvements made in the posttransplant care, there are still severe greatly feared complications that can occur after the heart transplantation.

Case Description

Here we report about a 48-year-old female patient with end-stage heart failure due to hypertrophic nonobstructive cardiomyopathy that underwent orthotopic heart transplantation (oHTx) in our center. The patient was bridged-to-transplant with a left ventricular assist device (LVAD). Two years after LVAD implantation, the patient was listed on high-urgency status for transplantation with hemodynamically relevant aortic insufficiency. Besides her cardiac history, there were no other relevant comorbidities; in particular, no neurologic disease was known in this patient.

The initial course after oHTx was complicated by severe bleeding in VAD-associated coagulation disorders, requiring thoracic reexploration. Finally, we could extubate the patient on the sixth postoperative day. Immunosuppression therapy was started right after the transplantation, according to our institutional standard, with a triple drug therapy consisting of cyclosporine A (CSA, target level 200 ng/mL, twice daily), mycophenolate mofetil (MMF, 2 × 1000 mg daily), and corticosteroids (initial 5 mg/kg bodyweight, conservation dose 5 mg daily). Induction therapy with antithymocyte globulin or similar substances was not applied in this patient.

Six weeks after transplantation, the patient started to feel unspecific unwell and intermittent nausea with vomiting occurred. Electrolyte levels were massively deranged and during the immediate cause search a sudden, no self-limiting generalized cerebral seizure happened.

Initial cerebral computed tomography (CCT) showed occipital hypodense white matter and no bleeding or signs of cerebral infarction. Immunosuppression levels were within...
normal ranges at that time. After this event, the patient was neurologically inconspicuous again. Two days later, the patient had to be transferred to intensive care-unit due to sudden somnolence.

Repeated CCT revealed progressive symmetrical leukoencephalopathy including, besides the occipital, also the frontal region and morphological apposite to posterior reversible encephalopathy syndrome (PRES) with further increasing cerebral edema (►Fig. 1).

Reviewing literature revealed that there is only scarce data about drug-induced PRES, one known risk factor is the application of calcineurin inhibitors (CNI).1–3 Case reports describe the risk of tacrolimus-induced PRES higher than cyclosporine-induced PRES,1,2,4 leaving the actual definite cause for PRES still unexplained. After excluding the other known elicitors for PRES or known causes for cerebral seizures, we were faced with the uncertain situation how to react in our patient, just 2 months after heart transplantation.

To our opinion, CNI-free immunosuppression regimen so early after transplantation may have led to an unbearable risk of heart rejection. Since PRES is more often reported in patients with tacrolimus immunosuppression, we feared that by solely switching the medication from CSA to tacrolimus in our patient the PRES symptoms could deteriorate.

After interdisciplinary consultation and careful literature review, the immunosuppression therapy was changed to a quadruple therapy with increased cortisone (mainly to reduce the intracerebral edema), unmodified MMF dose, low-dose CSA (new target level 50–80 ng/mL), and additional mechanistic target of rapamycin inhibitor everolimus (target level 4–8 ng/mL).

Within the first days, a steady improvement in both clinical and morphological in the diagnostic imaging was detectable. First myocardial biopsy after the changed immunosuppression regimen was ISHLT OR, AMR0. Echocardiographic examination showed no signs of acute rejection. After further stabilization and with marked improvements in general condition, the patient was able to be discharged to cardiac rehabilitation center 6 weeks after the first cerebral seizure attack.

**Conclusion**

PRES occurred in this case shortly after heart transplantation. Under a quadruple therapy with cortisone, unmodified MMF, low-dose CSA, and additional everolimus, the symptoms declined. This quadruple regimen may be an alternative therapy strategy in patients with the rare disorder of PRES under standard therapy after organ transplantation.

**Conflict of Interest**

None.

**References**

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