

# Tacrolimus-Associated Posterior Reversible Encephalopathy Syndrome after Heart Transplantation

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The posterior reversible encephalopathy syndrome (PRES) is an uncommon neurotoxicity known to occur following solid organ transplantation, potentially associated with cyclosporine and tacrolimus.<sup>1,2</sup> It was originally described by Hinchey et al. in 1996 as a reversible syndrome characterized by headache, altered mental function, seizures, and visual disturbances,<sup>3</sup> and represents a clinical and neuroradiological entity with typical neurological deficits, distinctive magnetic resonance imaging (MRI) features, and a benign clinical course. Herein, we present the case of a 39-year-old man with a medical history of idiopathic cardiomyopathy who developed severe headache, visual disturbances, and altered mentation 20 days after orthotopic heart transplantation while awaiting predischARGE routine surveillance endomyocardial biopsy (EMB) in the hospital. His immunosuppressive therapy included 7 mg of tacrolimus, 720 mg of sodium mycophenolate, 20 mg of prednisone, and valganciclovir. Upon neurological examination, he exhibited no focal deficits, with a blood pressure of 120/80 mmHg and a pulse of 100 beats/min. Laboratory findings were unremarkable, with tacrolimus levels of 9.2 ng/mL, consistent with his stable previous levels. Initially managed with diazepam and intravenous phenytoin, a brain MRI revealed findings suggestive of PRES, including vasogenic edema evident in the occipital and temporo-occipital junction. Tacrolimus was discontinued, and cyclosporine was initiated, leading to resolution of symptoms without recurrence of symptoms. The patient was discharged from the hospital in stable condition. Subsequent EMB results, two weeks later, showed no signs of rejection. Available data indicate that the incidence of PRES following heart transplantation was estimated to range between 0.49% and 1.6%. By the end of 2023, our group had performed 500 heart transplants,<sup>4</sup> with a cumulative incidence of 0.4 cases per 100 transplants since the program's

inception in 1997. Calcineurin inhibitors (CNIs) tacrolimus and cyclosporine have revolutionized the care of heart transplant patients by reducing episodes of acute and chronic rejection. PRES can be associated with CNIs due to their vasoconstrictive effects and direct injury to the vascular endothelium, resulting in vasogenic edema. Although data on drug-induced PRES are limited, the risk of tacrolimus-induced PRES appears to be higher than that of cyclosporine-induced PRES, leaving the definitive cause of PRES still unexplained. The literature suggests that MRI is superior to computed tomography for PRES diagnosis and that early diagnosis is crucial for preventing sequelae, including cerebral ischemia, cerebral hemorrhage, cerebral herniation, and status epilepticus.<sup>5,6</sup> Switching from tacrolimus to cyclosporine, or vice versa, is a treatment option. The resolution of our patient's neurological symptoms occurred upon discontinuation of the offending CNI.

## Author Contributions

Conception and design of the research, Acquisition of data and Critical revision of the manuscript for content: Sousa GG, Barreto Júnior JEF, Pimentel RBNL, Carneiro TAP, Vieira JL; Analysis and interpretation of the data and Writing of the manuscript: Vieira JL.

## Potential conflict of interest

No potential conflict of interest relevant to this article was reported.

## Sources of funding

There were no external funding sources for this study.

## Study association

This study is not associated with any thesis or dissertation work.

## Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Hospital de Messejana Dr. Carlos Alberto Studart under the protocol number 73509423.2.0000.5039. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

## Keywords

Tacrolimus; Magnetic Resonance Spectroscopy; Posterior Leukoencephalopathy Syndrome

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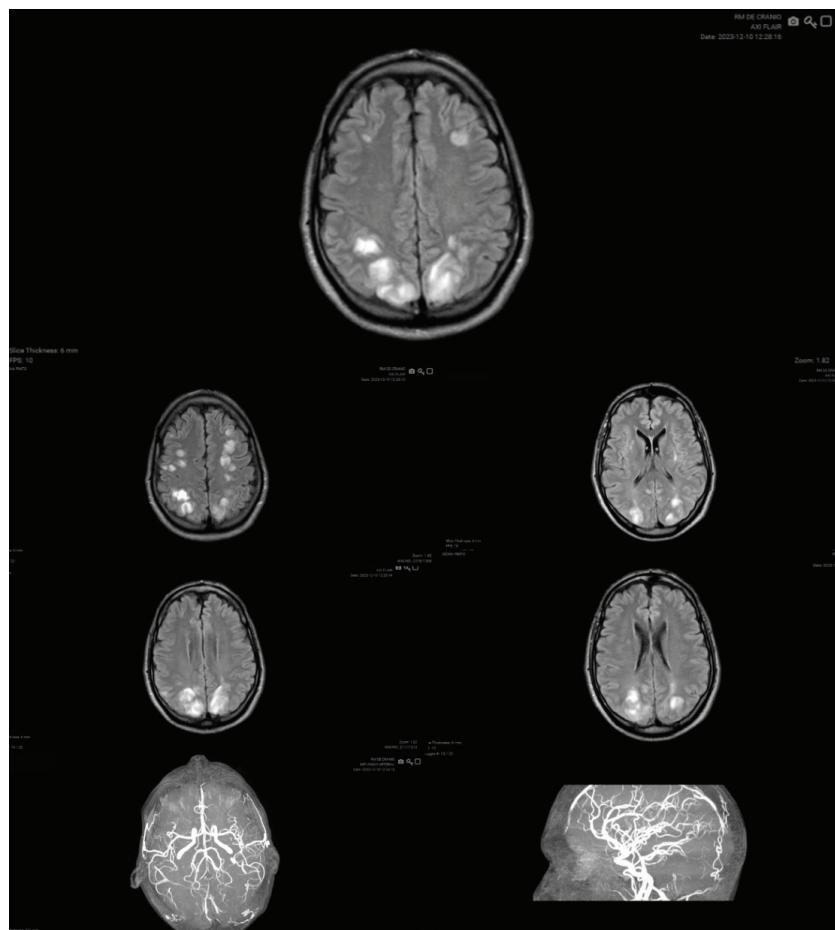
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Manuscript received February 06, 2024, revised manuscript February 11, 2024, accepted February 11, 2024

Editor responsible for the review: Lídia Zytynski Moura

DOI: <https://doi.org/10.36660/abchf.20240005>



**Figure 1** – Brain magnetic resonance imaging findings of posterior reversible encephalopathy syndrome (PRES), including vasogenic edema evident in the occipital and temporo-occipital junction.

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