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Case Report
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Posterior Reversible Encephalopathy Syndrome: A Reversible Tacrolimus Induced Neurotoxicity in a Heart Transplant Recipient- A Case Report

Anantharaman R, Vivek M, Madhusankar N, Arulkumar A and Cherian KM*

Department of Cardiology, Frontier Lifeline Hospital, India

Abstract

Tacrolimus is widely used immunosuppressive drug following heart transplantation. Mild to severe form of neurological symptoms are known to occur with use of Tacrolimus. Posterior Reversible Encephalopathy Syndrome (PRES) is one such manifestation, which can present with multitude of neurological symptoms. We report a case of PRES in a heart transplant recipient receiving Tacrolimus.

Keywords: Tacrolimus; Heart transplant; Posterior reversible encephalopathy syndrome

Introduction

Tacrolimus is one of the commonly used immunosuppressive drugs in patients undergoing heart transplantation. Side effects include renal and nervous system also. Posterior Reversible Encephalopathy Syndrome (PRES) is one of the rare neurotoxic manifestations featured with, headache, generalized seizures, nausea, visual disturbances, altered mental status and focal neurological deficits, coma. The incidence varies up to 32% in solid organ transplants. This article describes a case of PRES in a heart transplant recipient receiving Tacrolimus.

Case Report

Our patient is an 18-year-old boy with a history of idiopathic dilated cardiomyopathy, who underwent orthotopic heart transplant 5 months prior to the onset of his neurologic symptoms. His past medical history included hypothyroidism, megaloblastic anemia, CKD. During the transplant surgery he had induction therapy with Basiliximab. He was started on triple immunosuppressant therapy with steroids, Mycophenolate Mofetil (MMF) and Tacrolimus following transplant. His Tacrolimus levels were closely monitored and dose adjusted. His post-transplant course was complicated by reactivation of pulmonary tuberculosis for which he received Anti Tuberculosis Therapy (ATT). He was commenced on usual prophylactic medications including Valganciclovir for CMV and Trimethoprim/Sulfamethoxazole for *Pneumocystis jiroveci* pneumonia-PCP. In the fifth month, he presented with headache of sudden onset, staring in to space with right gaze preference, and altered mental followed by tonic-clonic seizure. His blood pressure was 200/100 mm Hg due to the PRES. He was intubated and put on mechanical ventilator in view of LOC. He was started on anti-epileptic treatment, once stable he was weaned off from ventilator and extubated on the same day.

MRI Brain (Figure 1A) done showed multiple ill-defined areas of non-diffusion restricting, T1 iso-hypo, T2/T2 FLAIR hyper intense signal in the bilateral cerebral hemispheres, thalami, external capsules/perisylvain regions, entire brainstem and cervical spinal cord consistent with PRES (Posterior Reversible Encephalopathy Syndrome) also known as Reversible Posterior Leukoencephalopathy Syndrome (RPLS). He was diagnosed with Leukoencephalopathy (possibly Tacrolimus induced). His Tacrolimus was discontinued and commenced on anti-epileptics. Viral IgM serology for CMV/EBV/HTLV was negative. He received supportive treatment and did not have further seizure episodes. He improved with no residual neurological deficits. Repeat MRI images (Figure 1B) had revealed resolution of PRES once the offending Tacrolimus had been discontinued.

Alternative immunosuppressant like Rapamycin or Sirolimus was discussed with the nephrologists and on consensus; he was continued with Sirolimus, MMF along with low dose long term oral steroids (Prednisolone 5 mg per day).

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Correspondence:

Anantharaman R, Department of Cardiology, Senior Consultant Cardiologist and Lead for TAVR, Heart Transplant and Stem Cell Therapy, Frontier Lifeline Hospital, KM Cherian Heart Foundation, Chennai, 600101, India, Tel: 0091979160913; E-mail: anantharamancardio@gmail.com

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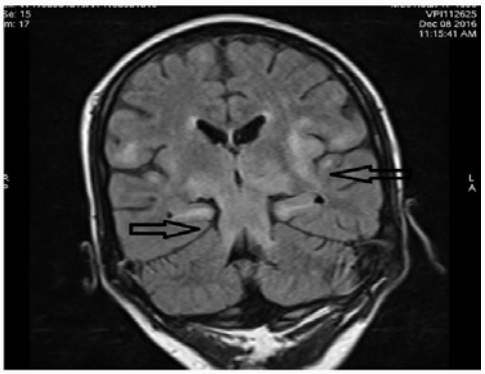

Figure 1A: Multiple ill defined areas of hypert intense signals involving thalami, external capsules/perisylvian regions, entire brainstem and cervical spinal cord.

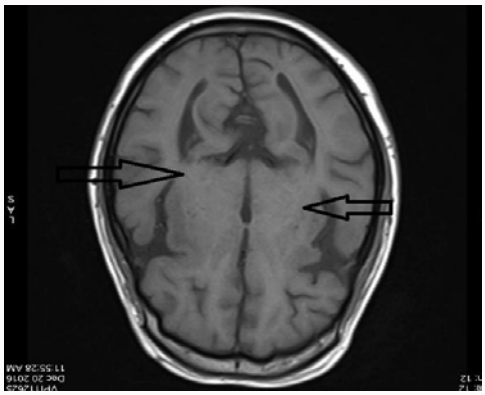

Figure 1B: Repeat MRI after 2 weeks of discontinuing Tacrolimus showing all the lesions have cleared.

Discussion

Tacrolimus related neurotoxicity ranges from mild neurologic adverse effects like (40% to 60%) to major side effects like (5% to 8%) [1]. PRES is characterized by vasogenic edema of the posterior cerebral territory. Apart from the parieto-occipital region it may also affect the posterior portion of frontal lobe and temporal lobe [2-8]. The white and gray matter is affected commonly. MRI (diffusion weighted MR imaging) is very sensitive in distinguishing between vasogenic edema and cytotoxic edema in the setting of cerebral ischemia [3,5-7].

PRES has been reported with Cyclosporine [4], and with other organ transplant like liver [3] and allogenic hematopoietic stem cell transplantation [9].

If recognized early and treated, PRES is typically a reversible phenomenon, but permanent brain injury may occur if left undetected. The neurotoxicity or PRES has not been shown to correlate with the blood levels of Tacrolimus but are thought to be related to the total amount of drug in the body [8].

Significant levels of Tacrolimus have been demonstrated in the CSF showing that this drug can cross the blood brain barrier. First step in the management is discontinuation or change in the offending immunosuppressant. This usually leads to clinical improvement. Control of hypertension and seizures will be required. To avoid recurrence, Tacrolimus may be able to be replaced with other agents like Rapamycin or Sirolimus.

Our patient improved clinically with resolving PRES once the drug was discontinued. He was switched over to cyclosporine later.

Conclusion

Tacrolimus-associated PRES though uncommon, is a dangerous complication in the post-transplant setting where higher levels of immunosuppressant are used to prevent rejection. Prompt recognition and early treatment is the key in this condition, as it potentially reversible complication. Alternative immunosuppressant agents should be considered to reduce the recurrence.

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