Tacrolimus-induced Catatonia after Organ Transplantation: Two Case Reports

Jamie Lee, MD; Paulina Khodak, DO; Keira Chism, MD
Thomas Jefferson University Hospital, Philadelphia, PA

Introduction

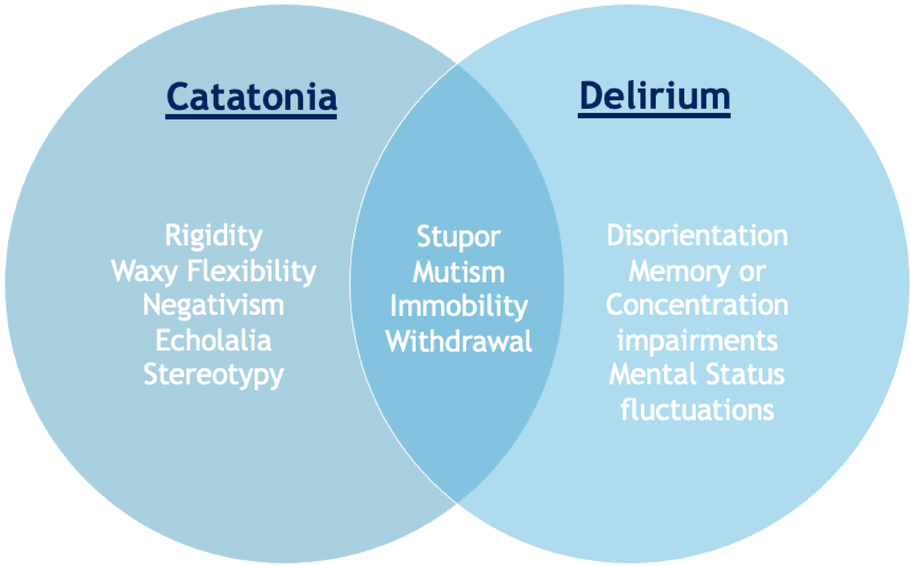
Tacrolimus is the most common immunosuppressant used after transplant to prevent organ rejection but has been reported to cause severe neurotoxicity even at therapeutic levels (Chopra, 2011). We present two cases of tacrolimus-induced catatonia in different organs (heart, liver) during the immediate post-transplant period.

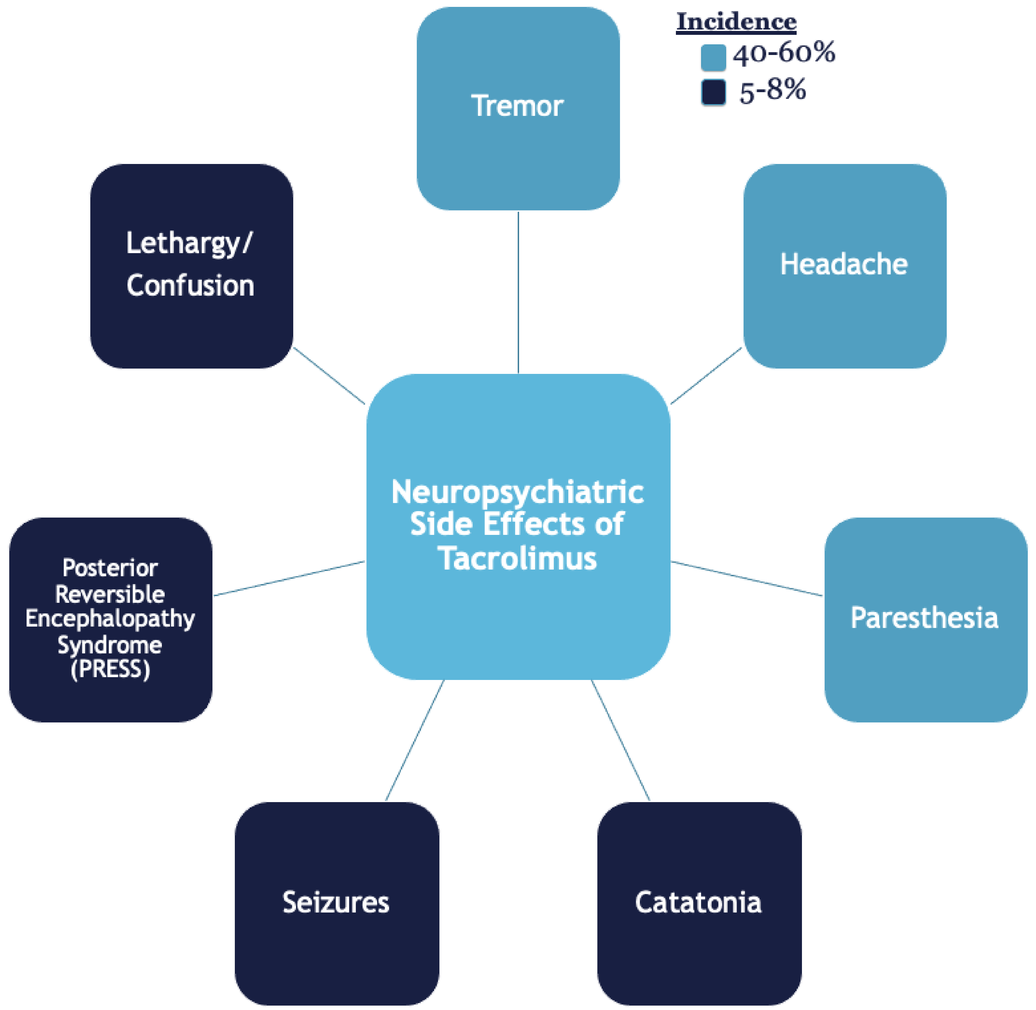
Case 1: Post Heart Transplant

A 65-year-old male with end-stage heart failure and psychiatric history of depression underwent a heart transplantation. The patient had serious complications including temporary use of ECMO. Psychiatry service was consulted several weeks after transplant due to concern for prolonged delirium. Patient was noted to be minimally interactive with Bush-Francis Catatonia Rating Scale (BFCRS) of 11. Tacrolimus level had increased significantly, although was in the therapeutic range. Ultimately, tacrolimus was switched to cyclosporine and the catatonia resolved.

Case 2: Post Liver Transplant

A 43-year-old woman with no prior medical or psychiatric history developed acute liver failure of unknown etiology after travel outside the country. She underwent a liver transplantation and her post-transplant course was complicated by septic shock and delirium. On initial psychiatric evaluation, the patient was noted to be markedly paranoid though interactive. Low dose, intravenous haloperidol was started. The following day, the patient was noted to be minimally responsive with BFCRS of 15. Tacrolimus level was in the therapeutic range. Lorazepam challenge slightly improved the catatonic symptoms but additional lorazepam was found to cause sedation. Due to concern for tacrolimus-mediated catatonia, tacrolimus was discontinued and subsequently the catatonia resolved.





Discussion

Tacrolimus is an effective immunosuppressive medication used in the post-transplantation period but has a high incidence of causing neurotoxicity, which can manifest as catatonia (Chopra, 2011). The exact mechanism is not well understood, but it is hypothesized that calcineurin is involved in GABA and glutamate activity (Davis, 2020). Tacrolimus-related catatonia can be easily missed in the midst of medical complications and concurrent delirium (Wilson, 2017).

Tacrolimus-mediated catatonia and neurotoxicity can occur even when the tacrolimus serum level is within therapeutic range (Chopra, 2011). The most definitive treatment for tacrolimus-induced catatonia is reduction or discontinuation of tacrolimus. It is thought that tacrolimus neurotoxicity can lead to permanent neurological damage, making early detection and management important (Bechstein, 2000).

In a literature case review, most cases of Tacrolimus induced catatonia were found to be post liver transplant though some case reports post heart or kidney transplant have also been published.

More methodical screening and formal study of prevalence and risk factors for tacrolimus neurotoxicity is warranted to guide immunosuppression regimens for transplant recipients.

Conclusions

- Catatonia can present as a manifestation of tacrolimus neurotoxicity.
- Tacrolimus neurotoxicity can occur during any period post-transplant, even when serum levels are within normal range.
- It is important to differentiate between catatonia and delirium which may present with overlapping features.
- Early identification can lead to rapid treatment, which can prevent further neurotoxicity and prolonged hospitalization.

Reference

Bechstein WO. Neurotoxicity of calcineurin inhibitors: impact and clinical management. Transpl Int. 2000;13(5):313-26.

Chopra A, et al.: Catatonia as a manifestation of tacrolimus-induced neurotoxicity in organ transplant patients: a case series. General Hospital Psychiatry 2012; 34(2): 209.e9–11.

Davis L, Tripathi S: Neuropsychiatric Complications of Immunosuppressants: A Case Report of Tacrolimus-Induced Catatonia in a Liver Transplant Recipient. Prim Care Companion CNS Disord 2020; 22(1):19l02481.

Wilson JE, et al.: Delirium and Catatonia in Critically Ill Patients: The Delirium and Catatonia Prospective Cohort Investigation. Crit Care Med. 2017 Nov;45(11):1837-1844.

Tatreau JR, Laughon SL, Kozlowski T. Catatonia After Liver Transplantation. Ann Transplant. 2018 Aug 28;23:608-614.