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Descent into Mania: A Case of Tacrolimus-Induced Psychosis

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Abstract

Background: Tacrolimus has historically been used as an effective immunosuppressant in solid organ transplants. Although it is standard care in most organ transplants, it is accompanied by a vast number of side effects, including headache, fatigue, and even psychosis. The neurotoxic side effects that accompany tacrolimus are usually apparent at supratherapeutic doses and resolve after dose adjustment or discontinuation.

Case Presentation: We present a case of a 68-year-old male who sustained tacrolimus-induced mania post- transplant, refractory to both medication tapering and removal. He ultimately required the use of prolonged antipsychotic therapy.

Conclusion: This study highlights the necessity for thorough psychiatric evaluations in patients undergoing organ transplantation as well as the continued need for further research and interventions in patients undergoing prolonged immunosuppressive therapy. This report may signify a novel mechanism of dose-independent neurotoxicity secondary to tacrolimus.

Keywords: psychosis; tacrolimus; neurotoxic; neuropsychiatric side effects

Introduction

For decades, tacrolimus has been used as an effective immunosuppressant in hepatic and other solid organ transplantation. Studies have outlined the vast number of side effects caused by this medication- including headaches, seizures, paresthesia's, fatigue, and hypertension [1]. Further studies have shown brief psychosis, delirium, and agitation as side effects of this drug, often occurring when the medication is taken in supratherapeutic doses [1]. Reversible neurotoxic side effects have been demonstrated to resolve shortly after dose adjustments of prescribed tacrolimus, or a switch to cyclosporine [2,3]. We present a case of sustained tacrolimus-induced mania, unresponsive to both medication tapering and removal, necessitating the use of prolonged antipsychotics for mania and psychosis.

Case Presentation

A 68-year-old male, with a past medical history of end-stage liver disease secondary to Hepatitis C infection, underwent orthotopic liver transplantation. Post-operatively, he was started on 80mg of prednisone, 3mg of tacrolimus, and 1000mg of mycophenolate. The prednisone was tapered down until being completely discontinued on postoperative day (POD) 3. The tacrolimus dose was increased to 5mg on POD 6, but the patient experienced some episodes of confusion, leading to a decrease to his original dose of 3mg. Additionally, his mycophenolate dose was progressively tapered down, until being completely discontinued on POD 14. On POD 20, he experienced an acute episode of encephalopathy that resolved after a perihepatic fluid collection was noted and drained. His symptoms resolved and he was discharged on POD 23 on 3mg of tacrolimus. Two-month post-transplant, his family began to notice a change in his baseline behavior and personality. They described him as having excessive amounts of energy, a euphoric mood, distracted thoughts, rapid speech, and no longer requiring sleep. The patient mentioned having ideas popping into his head on ways to make large amounts of money and went on to spend exorbitant amounts of money on peanut brittle. The patient denied any auditory or visual hallucinations, as well as any suicidal or homicidal thoughts. He had no history of alcohol or drug use. His family history is notable for a brother who committed suicide secondary to manic depression. Both the family, and the patient, confirmed that he had never experienced any prior symptoms like this.

The patient's hospital workup included an MRI showing no acute intracranial abnormalities. Toxic and metabolic panels were also negative for any derangements. His tacrolimus dose was tapered down to 1mg per day from 3mg, with no resolution in his manic symptoms. It was completely discontinued on

admission day 3 and switched to 250mg of cyclosporine, with no improvement in manic symptoms. Eventually, the patient was diagnosed with medication-induced mania and started on 10mg of olanzapine. After one week of treatment, and significant resolution in manic symptoms, the patient was discharged on 20mg of olanzapine and 250mg of cyclosporine.

Discussion

A manic episode is defined by a change in baseline behavior that includes, but is not limited to, distractibility, impulsivity, thoughts of grandiosity, unsynchronized thought processes, agitation, decreased need for sleep, and rapid speech [3]. A patient can be diagnosed with experiencing a manic episode if they have at least three of the symptoms mentioned for at least one week, in addition to an elevated or irritable mood [3]. Tacrolimus, a calcineurin inhibitor, has been regarded as the gold standard immunosuppression for organ transplant since as early as 1982 [4]. Neuropsychiatric and neurotoxic side effects of tacrolimus and its other calcineurin inhibitor counterpart, cyclosporine, have been well documented in literature and have led to hypervigilant management of medication levels as many of the side effects experienced at supratherapeutic levels are often reversible and can help maintain appropriate medical stability and graft viability [1,4]. However, the presence of tacrolimus-induced mania at therapeutic levels remains a virtually unexplored topic. Previous reports have documented tacrolimus-induced psychosis when the medication is present in elevated blood concentrations. Withdrawal of the drug has reliably led to the eventual resolution of such symptoms. Some reports have also purported a switch to cyclosporine therapy to further ensure appropriate resolution of neurotoxic side effects [2,6]. A recent case report further identified a patient who experienced tacrolimus-induced psychosis at therapeutic levels suggesting that the induced psychosis may not solely depend on neurotoxic blood levels of the immunosuppressant [5]. Another similar report described a patient with nephrotic syndrome who developed tacrolimus-induced mania at therapeutic levels which only resolved after withdrawal of tacrolimus and the addition of antipsychotics [5,6]. The epigenetic influence of medications and their cross implications in familial predispositions has been noted with other psychoactive medications previously. It has been shown that the use of stimulant medications induces psychotic symptoms in children with family histories of mood disorders [7]. Similarly, a hypothesis can be formulated regarding the possibility of tacrolimus as an epigenetic influence inducing psychosis and mania, particularly in patients with familial predispositions toward mental illness, as observed in our case with a patient who had a family member with manic depression.

Conclusion

Guidelines on the use of immunosuppressant therapy and calcineurin inhibitors, such as tacrolimus and cyclosporine for renal allograft survival and the possible neurotoxic side effects of these medications, have been heavily discussed in scientific literature for many years. However, this report may signify a novel mechanism for tacrolimus's neurotoxic effects and represents further importance in the study of psychiatric comorbidities in transplant patients. This study not only emphasizes the complexity of neuropsychiatric complications in transplant patients, but also underscores the urgent need for further research on the medical management of such complications in order to ensure appropriate care and updated therapy regimens for those with predispositions to psychiatric ailments.

Abbreviations

POD: Post-operative day
MRI: Magnetic Resonance Imaging

References

1. Coe CL, Horst SN, Izzy MJ. (2020). Neurologic Toxicities Associated with Tumor Necrosis Factor Inhibitors and Calcineurin Inhibitors. *Neurol Clin.*, 38(4):937-951.
2. Emre S, Genyk Y, Schluger LK, et al. (2000). Treatment of tacrolimus-related adverse effects by conversion to cyclosporine in liver transplant recipients. *Transpl Int.*, 13(1):73-78.
3. Hu J, Mansur R, McIntyre RS. (2014). Mixed Specifier for Bipolar Mania and Depression: Highlights of DSM-5 Changes and Implications for Diagnosis and Treatment in Primary Care. *Prim Care Companion CNS Disord,* 16(2).

4. Webster A, Woodroffe RC, Taylor RS, Chapman JR, Craig JC. (2005). Tacrolimus versus cyclosporin as primary immunosuppression for kidney transplant recipients. *Cochrane Database Syst Rev*., (4):CD003961.
5. Uvais NA, Hafeeq B, Gopinathan JC, et al. (2022). Psychosis associated with tacrolimus at therapeutic serum levels. *Prim Care Companion CNS Disord*., 24(6):21cr03201.
6. Kumar A, Khrime D, Ruhela V. (2020). Tacrolimus-induced mania in a patient with nephrotic syndrome. *Indian J Pharmacol*., 52(6):531-532.
7. MacKenzie LE, Abidi S, Fisher HL, et al. (2016). Stimulant Medication and Psychotic Symptoms in Offspring of Parents with Mental Illness. *Pediatrics*, 137(1).

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