



Acute psychotic disorder associated with immunosuppressive agent use after renal transplantation: a case report

Fulya Gok & Meliha Zengin Eroglu

To cite this article: Fulya Gok & Meliha Zengin Eroglu (2017) Acute psychotic disorder associated with immunosuppressive agent use after renal transplantation: a case report, Psychiatry and Clinical Psychopharmacology, 27:3, 314-316, DOI: [10.1080/24750573.2017.1356062](https://doi.org/10.1080/24750573.2017.1356062)

To link to this article: <https://doi.org/10.1080/24750573.2017.1356062>



© 2017 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group



Published online: 07 Aug 2017.



Submit your article to this journal [↗](#)



Article views: 5811



View related articles [↗](#)



View Crossmark data [↗](#)



Citing articles: 3 View citing articles [↗](#)

CASE REPORT



Acute psychotic disorder associated with immunosuppressive agent use after renal transplantation: a case report

Fulya Gok and Meliha Zengin Eroglu

Department of Mental Health and Disease, Health Science University, Haydarpasa Numune Training and Research Hospital, Istanbul, Turkey

ABSTRACT

Kidney transplantation is the best treatment option for end-stage renal disease in appropriate patients. Immunosuppressant agents given in this duration can cause many psychiatric disorders. In this paper, we present a young kidney transplant patient with psychosis constituted delusions about his transplanted kidney after 4 years later from transplantation. He had refused to take his immunosuppressant pills because of psychotic process. In this paper, we wanted to discuss the psychiatric risks of immunosuppressant agents and importance of the psychiatric treatment in this aspect.

ARTICLE HISTORY

Received 18 April 2017
Accepted 13 July 2017

KEYWORDS

Renal transplantation;
immunosuppressive agents;
psychosis; aripiprazole

Introduction

Prevalence of end-stage renal disease has been increasing in Turkey as well as all over the world. End-stage renal disease is a general health problem because of its high prevalence, changing pattern of aetiology, complex, and expensive treatment modalities required [1]. Kidney transplantation is the best treatment option for end-stage renal disease as it gives patients the chance to return to a satisfactory quality of life [2]. Today, compared with dialysis, kidney transplantation in patients with end-stage renal disease is widely accepted as a treatment method due to its advanced short- and long-term survival benefits. However, transplantation and life-long immunosuppressant treatment have their own problems [3]. Many psychiatric disorders such as major depressive disorder, mania, anxiety disorder, adjustment disorder and psychotic disorder, cognitive and memory impairment can be seen in any postoperative period in renal transplantation patients [4,5]. In this paper, we present an acute psychotic disorder case where psychosis occurred 4 years after the kidney transplantation.

Case presentation

A 26-year-old, single male patient had kidney transplantation surgery after being treated with dialysis for four years. Recently, the patient was taken to the emergency department by his family because of vomiting and weakness symptoms. He was transferred to the nephrology service. While he was being treated, his doctors consulted to the psychiatry department as he refused to take his drugs. As a result, the patient with

no other significant history of any mood, anxiety, or substance use disorder was admitted to our clinic with suspected acute psychotic episode four years after renal transplantation surgery while he was getting immunosuppressive agents. It was learned that the patient had not received their medication, cyclosporine 150 mg/day, mycophenolate mofetil 1500 mg/day, prednisolone 5 mg/day, for the last 1 month after starting the psychotic complaints.

His family history was also negative in terms of psychiatric disorders. The patient's mental status examination revealed mutism and negativism. He had a clear conscious state but not responding to verbal commands and making eye contact. According to information received from family members the patient had strange behaviours, religious preoccupation that may be caused by his delusions of persecution and reference. His communication with people decreased and he was socially isolated. The most important thing was that the patient had not taken his immunosuppressive drugs for the last month.

His hematologic and biochemical panels including renal function tests and urine examination were all within the normal ranges. Serum electrolytes were within the normal limits as well. The patient's cyclosporine level was 39.7 ng/ml. The magnetic resonance imaging (MRI) of the brain and electroencephalography showed no abnormalities. After the examinations, treatment regimen of parenteral haloperidol 20 mg/day and biperiden 10 mg/day was started in his inpatient admission because the patient refused to take oral medication. His mutism resolved in first week but his rising sinful thoughts and delusions about the transplanted kidney belongs to someone else caused to

CONTACT Fulya Gok  fufubo@hotmail.com

© 2017 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group
This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

agitation. He said that he wanted his transplanted kidney to be removed by a surgical operation from his body. His total Positive and Negative Syndrome Scale (PANSS) score was 122. Within two weeks, the patient showed marked improvement. His negativism disappeared and he agreed to take the oral medications (psychiatric and immunosuppressive). Haloperidol dosage was reduced and aripiprazol was started 5 mg/day and altered to 20 mg/day.

The patient was discharged after 4 weeks of hospitalization with improved functionality and the absence of previous delusions.

Discussion

Our patient is an interesting psychosis case with delusions about his transplanted kidney triggered by immunosuppressive treatment. Immunosuppressive treatment given to the patient following organ transplantation can cause many psychiatric disorders. For example a preliminary study on transplantation patients in Turkey has shown that the most common diagnosis is major depressive disorder and it was observed in 25% of all patients. The remaining diagnoses were within the affective and/or anxiety spectrum disorders [6].

Renal transplantation has been the most important treatment option for individuals who have reached end-stage renal disease, because of the developments of transplantation medicine, surgery, and pharmacology in the last years. But increased risk factors for developed psychotic features after transplantation include the use of high doses of corticosteroids, a known risk factor for psychosis, the presence of a mood disorder associated with chronic disease, the presence of metabolic disorders associated with the medical condition, use of other immunosuppressive medications in transplantation, such as calcineurin inhibitors (cyclosporine A and tacrolimus), which have known neurobehavioural adverse effects [5,7]. Our patient was using low-dose corticosteroids and cyclosporin. Therefore, it may have triggered the psychotic symptoms of long-term use of immunosuppressant.

Corticosteroids such as budesonide, dexamethasone, and prednisolone are medications widely used in many diseases such as inflammatory and autoimmune disorders. Corticosteroids used to stop the progression of the inflammatory response cause psychiatric symptoms with more complex mechanisms. Psychiatric side effects have been reported in 60% of patients using corticosteroids. While depression tends to occur with long-term use of corticosteroids, mania can occur much earlier during treatment and is associated with high-dose preparations. Psychiatric adverse effects are twice as likely to occur during the first five days of corticosteroid treatment; however, it also depends on the dosage [4]. The reported incidence of

serious psychiatric side effects of corticosteroids is low, 5–6%, and includes a wide range of cognitive (diminished memory, concentration, attention, mental speed, and distractibility), affective (depression, anxiety, irritability, emotional lability, hypomania, and mania), psychotic (visual and auditory hallucinations, delusions, thought confusion, and racing thoughts), and behavioural (restlessness, agitation, hypervigilance, and aggression) symptoms [8]. Approximately 20% of patients taking more than 40 mg prednisone or equivalent of high-dose corticosteroids are predicted to develop a psychiatric disorder such as mania, psychosis, or severe depression requiring pharmacotherapy. Additionally, previous psychiatric history, age, underlying disease, and gender were seen as risk factors in the development of corticosteroid-induced neuropsychiatric disorder [9]. Although our patient did not use high-dose corticosteroids, the use of low doses continued for a long time. We considered the long-term use of low-dose corticosteroids as a risk factor for the occurrence of psychotic symptoms.

Tacrolimus (FK506) and cyclosporine (cyclosporin A, CsA), calcineurin inhibitors, are cornerstone immunosuppressive agents given to solid organ transplant recipients to prevent and treat allograft rejection and both agents have been reported to cause psychosis. Calcineurin inhibitors have regulatory effects on both dopaminergic and the N-methyl-D-aspartate receptor (also known as the NMDA receptor or NMDAR) systems. In the case of these agents are present at high plasma levels in the patient; intravenous administration, presence of hypocholesterolemia, hypomagnesemia, previous cerebrovascular disease, hypertension, central nervous system ischemia-reperfusion injury or hepatic encephalopathy, the calcineurin inhibitors are more likely to cause neuropsychiatric findings. Correcting the metabolic abnormalities and determining the dose again to reduce the serum level of the medication can usually remove the psychotic symptoms. Tacrolimus can cause some mental disorders, including catatonia and psychosis. Psychiatric problems can be resolved with decreasing the dose or switching to another immunosuppressant for the patients who do not respond to reducing [5,10]. Our patient was also using cyclosporine, a calcineurin inhibitor. The serum level of cyclosporin was not high, but considering the fact that the patient has not been on medication for the last 1 month, the use of cyclosporin is also a risk for psychotic symptoms.

When psychotic symptoms occur under immunosuppressive treatment, medication cessation or reducing the dosage should always be the first line of treatment. But studies also support the addition of antipsychotics to treatment [9]. Low doses of typical and atypical antipsychotics may be most appropriate way to prevent side effects such as extrapyramidal (parkinsonian)

symptoms, akathisia, and neuroleptic malignant syndrome. Haloperidol, olanzapine, risperidone, and quetiapine are common choices to treat psychiatric reactions. Recent case studies reported that psychotropic drugs, such as risperidone, aripiprazole, and lamotrigine are emerging as the most effective pharmacological agents in reversing corticosteroid-related psychiatric side effects. Aripiprazole, was identified as one of the most effective psychotropic medications in managing steroid-induced mania without causing excessive sedation. It has been shown that electroconvulsive therapy (ECT) is highly effective in the treatment of steroid-induced symptoms in a small number of studies [4,8,9].

We started the first-generation antipsychotic treatment in the form of injection considering the urgency due to the vital risk bearing of the drug rejection of the patient. We switched to aripiprazole, a second-generation antipsychotic, after the patient's medication refusal has passed and the psychotic symptoms have decreased. We chose aripiprazole because it is more reliable in terms of side effects, especially metabolic side effects, in young patients with chronic diseases. In addition, due to its dopamine partial-agonism, aripiprazole is also used to treat depression when symptoms cannot be controlled by an antidepressant alone. After 4 weeks, we discharged the patient with aripiprazole treatment, whose complaints were completely regressed. Our long-term plan about follow-up duration is to use aripiprazole safely because of low metabolic side effects.

Conclusion

Immunosuppressive agents are commonly used to prevent graft rejection, graft survival, and for extension of the patient's life in transplant patients. These agents, especially calcineurin inhibitors and high-dose steroids, have been associated with a range of neurobehavioural side effects, including overt psychotic symptoms [11,12]. Stopping medication, dose reduction, or antipsychotic medication may be helpful in preventing psychiatric symptoms. Most antipsychotic drugs are metabolized in the liver and their dosage is not affected by renal function and they have no significant interactions with either corticosteroids or calcineurin inhibitors [7].

The mechanisms of these psychiatric adverse effects are extremely complex, unpredictable, and usually severe. More focused attention is needed by physicians to educate patients and family caregivers to enhance. Physicians consistently alert patients about these potentially severe psychiatric side effects. Identification

of findings of immunosuppressive agents in the early stages will help in preventing occurrence of more severe psychiatric side effects and psychopathology [4].

Psychiatric treatments of these cases are important because psychotic disorders can reduce treatment compliance, which is crucial in the post-transplant period, and indirectly cause tissue rejection [5].

Disclosure statement

No potential conflict of interest was reported by the authors.

References

- [1] Suleymanlar G, Serdengeçti K, Ereğ E. Epidemiology of end-stage renal disease in Türkiye. *Türkiye Klinikleri J Int Med Sci.* 2005;1(21):1–8. (Turkish)
- [2] De Pasquale C, Veroux M, Indelicato L, et al. Psychopathological aspects of kidney transplantation: efficacy of a multidisciplinary team. *World J Transplant.* 2014;4(4):267–275.
- [3] Pawar AA, Rathod J, Chaudhury S, et al. Cognitive and emotional effects of renal transplantation. *Indian J Psychiatr.* 2006;48(1):21–26.
- [4] Kusljic S, Manias E, Gogos A. Corticosteroid-induced psychiatric disturbances: it is time for pharmacists to take notice. *Res Social Adm Pharm.* 2016;12(2):355–360.
- [5] Memetoglu ME, Yalcın O, Erbasan O. Acute psychotic disorder after cardiac transplantation possibly associated with cyclosporine and sertraline treatment: a case report. *Düşünen Adam J Psychiatry Neurol Sci.* 2013;26:111–114. (Turkish)
- [6] Arapaslan B, Soykan A, Soykan C, et al. Cross-sectional assessment of psychiatric disorders in renal transplantation patients in Turkey: a preliminary study. *Transplant Proc.* 2004;36:1419–1421.
- [7] Abbott KC, Agodoa LY, O'Malley PG. Hospitalized psychoses after renal transplantation in the United States: incidence, risk factors, and prognosis. *J Am Soc Nephrol.* 2003;14:1628–1635.
- [8] DiMartini A, Crone C, Fireman M, et al. Psychiatric aspects of organ transplantation in critical care. *Crit Care Clin.* 2008;24(4):949–981.
- [9] Gable M, Depry D. Sustained corticosteroid-induced mania and psychosis despite cessation: a case study and brief literature review. *Int J Psychiatry Med.* 2015;50(4):398–404.
- [10] Krishna N, Chiappelli J, Fischer BA, et al. Tacrolimus-induced paranoid delusions and fugue-like state. *Gen Hosp Psychiatr.* 2013;35:327.e5–327.e6.
- [11] Dave V, Mulley W, Kanellis J, et al. Managing psychosis in a renal transplant recipient with bipolar affective disorder and allograft rejection. *Nephrology (Carlton).* 2015;20(Suppl 1):2–5.
- [12] Ayna TK, Ciftci HS, Tozkir H, et al. Effect mechanism of immunosuppressive drugs. *Gaziantep Med J.* 2009;15(3):42–47. (Turkish)