Case Reports

Tardive Dyskinesia and COVID-19 Vaccination. Is there A Relation?

Mohamed Eltohamy[1] and Tabitha Pollard[2]

[1]*Department of Psychiatry, AFCM*

[2]*Saint Josef Health System, Indiana. USA*

ABSTRACT

Tardive dyskinesia (TD) is a condition that presents as involuntary uncontrollable and repetitive movements of the face, tongue, limbs, and trunk that can occur after prolonged use of dopamine receptor blocking agents such as antipsychotics. This case report describes a 63-year-old male patient who developed severe TD in June of 2021. His highest recorded abnormal involuntary movement scale (AIMS) score was 34 in September of 2022. In addition to escitalopram, aripiprazole was added as adjunct treatment for his depression in 2018. Dosing of aripiprazole ranged from 5-10mg for three years. Aripiprazole was weaned over a three-week in December of 2021.

Also the patient has family history of Parkinson's disease which is known for increasing risk of developing TD in patients treated with antipsychotic medications. But, just one month prior (May 4, 2021) to the onset of TD, this patient received Janssen COVID-19 vaccination. After being quickly tapered off aripiprazole the patient continued escitalopram and clonazepam.

In February of 2022 he was started on Valbenazine 40mg daily. He showed a dramatic improvement in TD with a 75% reduction of AIMS score despite some remaining truncal movements. This case discusses the importance of routine monitoring and early identification of tardive dyskinesia in patients with depression who are being treated with low dose antipsychotic not remarkable inducing TD in small doses. There is discussion about the importance of pharmacogenomic testing and gene variations that should be considered when prescribing psychotropics. Furthermore COVID-19 vaccination(s) may also play a role in TD susceptibility and severity.

Key Words: Aripiprazole, COVID-19 vaccination, tardive dyskinesia.

Received: 08 February 2024, **Accepted:** 02 March 2024

Corresponding Author: Mohamed Eltohamy, MD, Department of Psychiatry, AFCM,. **Tel.:** +2 010 0090 8194, **E-mail**: mumdotohamy@yahoo.com

ISSN: 2812-5509, 2024, Vol. 2, No. 1

INTRODUCTION

Tardive dyskinesia (TD) is a condition that occurs after prolonged exposure to dopamine receptor blocking agents. It is characterized by uncontrollable repetitive involuntary movements of the face, tongue, limbs and/or other locations of the body. Interestingly, for example, this patient's movements presented initially in his abdomen and feet. TD can be both distressing and debilitating for those affected[1]. Aripiprazole is an atypical antipsychotic (second-generation antipsychotic) with a novel mechanism of action involving a mixture of agonistic, partial agonistic and antagonistic activity at dopamine and serotonin receptors. Aripiprazole is approved by the Federal Drug Administration for treatment of schizophrenia, bipolar I disorder, and as an adjunct for major depressive disorder[2].

Aripiprazole has been associated with the development of TD, particularly in patients with a family history of Parkinson's disease. With the recent COVID-19 pandemic, there was an urgency to vaccinate patients at substantial risk for severe COVID-19 illness. In addition to the well-known risk factors, severe mental illness is another indicator for contracting COVID-19 infection severe enough to require hospitalization[10]. Special consideration should be considered when administrating covid-19 vaccination(s) to patients taking psychotropic medications due to its potential impact on movement disorders that has been recorded in some patients[4]. The potential interaction of COVID-19 vaccines with antipsychotic medications, particularly the risk of developing tardive dyskinesia, is a concern that needs further investigation[3].

Furthermore, we must now acknowledge the immense importance of pharmacogenomic testing to evaluate patients being treated with dopamine receptor blocking agents. Having the ability to test drug metabolizing enzymes in mental health patients can allow the prescriber to better predict how psychotropic medications will be metabolized by a particular patient. Variations in individual pharmacokinetics can impact levels of drug concentrations at its site of action. Inadvertently increasing effectiveness of an antipsychotic medication by not knowing pharmacokinetic variability could lead to

DOI: 10.21608/ARCMED.2024.268744.1043

undesired adverse drug reactions including increased risk of tardive dyskinesia. As discussed in the scenario below with our case presentation poor 2D6 metabolizers can have potentially sizeable adverse effects to 2D6 substrate medications[11].

CASE PRESENTATION

We present a 63-year-old married Caucasian male with four adult children and a bachelor's degree. He retired from his administrative duties due to an inability to perform computer work from his debilitating TD movements. The patient has no previous history of smoking or substance use except for occasional alcohol consumption during the holidays. Prior to 2018 he was diagnosed with major depressive disorder and started a treatment regimen consisting of hydroxyzine 20mg, propranolol 20mg, and escitalopram 20mg.

In 2018 aripiprazole 5-10mg daily was added as adjunct treatment for continued depressive symptoms. The patient's family history was significant for Parkinson's disease in his maternal great uncle and maternal cousin. A family history of Parkinson's disease may increase the chance of developing Parkinson's disease but can also increase the risk of TD developing after taking antipsychotic medication(s).

Interestingly, despite these risk factors he did remain free from involuntary movements for over three years of aripiprazole use. The patient received the Janssen COVID-19 vaccine in May of 2021. One month later, he developed involuntary repetitive movements in his abdomen and feet that progressively worsened and spread to other locations over the following months. A neurologist was consulted, and the diagnosis of TD was made. Psychiatry was eventually also consulted. Pharmacogenomic testing was obtained. He was found to be a poor CYP2D6 metabolizer. Medication adjustments were made based upon those results.

Treatment and Outcome

In February 2022, valbenazine 40mg daily was introduced, resulting in an overnight dramatic improvement of approximately 75% in TD symptoms. Some residual truncal movements remained, which gradually tapered off over a three-week period. The patient continued to receive escitalopram during this time. A neurological examination and MRI were completed by neurology. Propranolol and clonazepam were added to the treatment regimen for the treatment of TD. Due to residual movements the valbenazine dosage was increased to 80mg/day. When the valbenazine dose was increased pharmacogenomics testing was not yet completed, poor CYP2D6 metabolization of patient was not yet known.

The patient experienced a rapid onset of parkinsonism symptoms characterized by severe leg stiffness and muscle spasms. Consequently, valbenazine was gradually tapered off. A therapy combination comprising of amantadine, deutetrabenazine, and ginkgo biloba was then introduced, and clonazepam was continued. This treatment approach led to improvement in Parkinsonism symptoms but did not result in substantial improvement of TD symptoms. After review of pharmacogenomic testing escitalopram was discontinued and replaced by desvenlafaxine with a significant improvement in depressive symptoms despite ongoing severe involuntary movements. Aripiprazole was discontinued prior to the psychiatry consultation. Eventually, in 2022 Quetiapine was added to his treatment regimen for insomnia and anxiety. As an atypical antipsychotic, quetiapine has a similar profile to clozapine. Clozapine has been used in the treatment of TD. Quetiapine also offers low affinity and quick separation from post-synaptic dopamine receptors potentially offering benefits in patients suffering from TD[12].

In July 2023, the patient reported disabling severe TD movements, particularly affecting the trunk, which significantly impaired his ability to drive and perform daily activities. Due to the limited effectiveness of deutrabenazine it was discontinued. Valbenazine was reintroduced by his psychiatry team at a sustained reduced dose of 40mg/day utilizing the recommendation for lowered dosing in poor 2D6 metabolizers. This re-introduction demonstrated a dramatic improvement in TD symptoms without any recurrence of Parkinsonism symptoms. This patient had remission in depression and the most AIMS reduction with a combination of gingko biloba 240mg daily, clonazepam 0.5mg twice daily, amantadine 100mg three times daily, desvenlafaxine 75mg daily, quetiapine XR 300mg nightly and valbenazine 40mg daily.

DISCUSSION

TD is a potentially irreversible side effect of antipsychotic medications. Clinicians should consider pharmacogenomic testing in patients receiving psychotropic medications, particularly those who may be at increased risk for adverse events. Through routine screening utilizing the AIMS prompt identification and diagnosis of TD can lead to timely treatment using vesicular monoamine transporter 2 (VMAT2) inhibitors. Although aripiprazole has been previously regarded by prescribers as having less potential than other agents in causing TD, even with a few trials that reported using it as a treatment for TD[5,6].

Contrary to this previous understanding aripiprazole is slowly emerging in published data as potentially causing TD[7,8,9]. In our patient's case, the condition developed a month after the administration of the COVID-19 vaccination. While the mechanism of the vaccine's interaction with antipsychotic medications and the impact on metabolism and genetic considerations remains unclear, the potential for this interaction requires general awareness[3]. Furthermore, clinicians should weigh risks and benefits before utilizing atypical antipsychotics as adjunct treatment for depression without first considering all alternative treatment options and evaluating each patient's risk for developing TD individually.

Pharmacogenomic testing should be considered as part of evaluating patient risk factors for adverse medication reactions. This patient's family history of Parkinson's disease is also a significant variable to consider. The use of antipsychotic medications with a strong family history of Parkinson's Disease increases the risk of developing TD. The patient took aripiprazole from 2018-2021 without abnormal involuntary movements yet developed rapid severe involuntary movements just months after receiving the COVID-19 vaccination. Questions remain as to the impact the vaccination may have had on this patient's already altered metabolic activity and development of severe TD. This case explores the complexity of TD and potential causative factors that support the need for further investigation and studies.

CONCLUSION

This case report highlights the potential interaction of COVID-19 vaccinations with antipsychotic medications. It emphasizes the importance of heightened awareness of such interactions and the need for continuous monitoring and follow-up. In patients with a family history of Parkinson's disease, particularly those taking antipsychotic medications, the risk of developing tardive dyskinesia is increased. This case shows that TD may develop even with lower doses of atypical antipsychotic agents, especially for patients with pharmacogenomic variations. Thorough evaluation and patient education are needed before initiating medication that potentially has irreversible side effects. Early diagnosis and careful management of TD can lead to significant improvement in symptoms and quality of life.

CONFLICT OF INTERESTS

There are no conflicts of interest.

REFERENCE

1. Tarsy D, Baldessarini RJ. Epidemiology of tardive dyskinesia: is risk declining with modern antipsychotics? Mov Disord. 2006; 21:589–598. doi : 10.1002/mds.20823

2. Shapiro DA, Renock S, Arrington E, Chiodo LA, Liu LX, Sibley DR, *et al*. Aripiprazole, a novel atypical antipsychotic drug with a unique and robust pharmacology. Neuropsychopharmacology. 2003; 28:1400–1411. doi : 10.1038/sj.npp.1300203

3. Meagen RS, Marisara D.Transient akathisia after the SARS-Cov-2 vaccine,Clinical parkinsonism and related disorder vol 4, 2021,100098.DOI: 10.1016/j.prdoa.2021.100098

4. Langhorne T. CDC says vaccine side-effects 'tend to be mild' in response to Indiana woman's claims in viral video. Courier & Press. Updated January 12, 2021. Accessed March 3, 2021. https://www.courierpress.com/story/news/2021/01/12/covid-vaccine-moderna-side-effects-cdc-doctor-symptoms-shawn-skelton/6646047002/

5. Kang NR, Kim MD. Tardive dyskinesia: treatment with aripiprazole. Clin Psychopharmacol Neurosci. 2011;9:1–8. doi: 10.9758/cpn.2011.9.1.1

6. Osorio RS, Agüera-Ortiz L, Hurtado de Mendoza A, Ramos I, Palomo T. Treatment of tardive dyskinesia with aripiprazole. Neurotox Res. 2010;17:432–434. doi: 10.9758/cpn.2011.9.1.1

7. Hall DA, Agarwal P, Griffith A, Segro V, Seeberger LC. Movement disorders associated with aripiprazole use: a case series. Int J Neurosci. 2009;119:2274–2279. doi: 10.3109/00207450903225553

8. Peña MS, Yaltho TC, Jankovic J. Tardive dyskinesia and other movement disorders secondary to aripiprazole. Mov Disord. 2011;26:147–152. doi : 10.1002/mds.23402

9. Wang LJ, Ree SC, Chen CK. Courses of aripiprazole-associated tardive dyskinesia: report of two cases. Prog Neuropsychopharmacol Biol Psychiatry. 2009;33:743–744. doi : 10.1016/j.pnpbp.2009.03.023

10. Gordon, Joshua. COVID-19 Risks for People with Serious Mental Illness NIMH »COVID-19 Risks for People with Serious Mental Illness (nih.gov) May 2022 NIMH » https://www.nimh.nih.gov/about/director/messages/2022/covid-19-risks-for-people-with-serious-mental-illness

11. Mrazek David A. Psychiatric pharmacogenomic testing in clinical practice. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3181940 Dialogues Clin Neurosci. 2010 Mar; 12(1): 69–76. doi: 10.31887/DCNS.2010.12.1/dmrazek

12. Mohapatra, Satyakam. Successful Management of Tardive Dyskinesia with Quetiapine and Clonazepam in a Patient of Schizophrenia with Type 2 Diabetes Mellitus Clin Psychopharmacol Neurosci. 2016 May; 14(2): 218–220. doi: 10.9758/cpn.2016.14.2.218