Case report

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A Case Report of Lithium-Induced Tardive Dyskinesia

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Abstract:

Our case involves an elderly patient with bipolar disorder with a history of long-term low-dose lithium monotherapy (600 mg/day) who subsequently developed tardive dyskinesia as an adverse drug reaction. Generally, tardive dyskinesia is an iatrogenic movement disorder resulting from the long-term use of dopamine-blocking agents. However, lithium, a mood stabilizer with a mechanism of action that is not completely understood, has also been identified in some studies for its potential impact on dopamine synthesis and transmission. While common adverse effects of lithium include nausea, vomiting, and fine tremors, it rarely causes movement disorders. Limited reports exist regarding tardive dyskinesia associated with lithium usage. Following normal laboratory investigations, lithium was discontinued and diazepam was prescribed instead. Subsequent follow-up visits showed an improvement in symptoms.

Keywords: adverse effects, bipolar disorder, lithium, tardive dyskinesia

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Introduction

Tardive dyskinesia is a delayed side effect associated with antipsychotic medication, characterized by abnormal, irregular, involuntary choreoathetosis affecting the head, body, and limbs. Common manifestations include perioral movements, tongue darting, twisting, and protrusion, as well as chewing and lateral jaw movement, facial grimacing, and lip-puckering. Tardive dyskinesia, however, rarely manifests within the first 6 months of treatment[1]. The most common pathogenesis of tardive dyskinesia is prolonged exposure to neuroleptic drugs, leading to the upregulation of D2 receptors and postsynaptic dopamine receptor supersensitivity[2]. While antipsychotic medications are well-known triggers of tardive dyskinesia, cases associated with lithium monotherapy are rarely reported.

Case report

Our case involved a male patient in his mid-60s who was diagnosed with bipolar disorder 40 years ago. Initially, he experienced a depressive episode lasting around 3 months, followed by subsequent manic episodes with psychotic features. Lithium was selected as the treatment because it is the first-line treatment for bipolar disorder. He had undergone long-term lithium carbonate monotherapy at a dosage of 600mg/day since being diagnosed in his 20s, resulting in symptom improvement and remission for 20-30 years. He experienced only one depressive episode and one manic episode before going into remission. No other neuroleptic medications were used. Lithium was the only medication used throughout the entire 40-year period. The patient had no concurrent chronic diseases, took no other medications or substances, and was never prescribed any antipsychotic medication. There was no family history of abnormal movements, and he had not experienced any prior movement disorder. However, over the past 3 years, the patient began to experience mild teeth grinding. Upon evaluation, his blood lithium level was measured at 0.184 mEq/L. Another laboratory test found the following results: FT3 2.1 pg/ml, FT4 1.56 ng/dl, TSH 0.82 uIU/mL, BUN 5.7 mg/dl, Cr 0.79mg/dl. Electrolytes, liver function tests, and complete blood count all fell within normal limits.

Over the past 2 years, the patient's abnormal movements got worse, manifesting as frequent jaw movements, tight and forceful biting, and difficulty in fully opening his mouth. These symptoms were experienced throughout the day, impeding his ability to speak and eat. The accidental biting of a spoon led to less food intake and fatigue. Pronunciation difficulties added to his distress. Interestingly, there was temporary alleviation of his symptoms during distractions such as exercise, cutting grass, or writing. No other family members had ever experienced similar symptoms before, and the patient also denied drinking alcohol or smoking for at least the past 15 years. These symptoms persisted day and night and caused toothaches. Physical examinations revealed evidence of tooth decay and orobuccal dyskinesia, but no tremors, cogwheel rigidity, ataxia, or motor deficits were observed. Motor power was graded as V in all extremities, with bradykinesia but no speech changes. Systemic physical examinations also fell within normal limits. A neurological examination conducted by a consulting neurologist identified orobuccal dyskinesia but revealed no focal neurological deficits or other abnormalities that could explain the patient's symptoms.

As the patient's symptoms continued to deteriorate, the lithium dosage was reduced to 300mg/day, and 2mg/day of diazepam was added. Within 2 weeks, there was a slight improvement in orobuccal dyskinesia, and bipolar disorder did not relapse. Consequently, lithium was discontinued due to concerns about abnormal movements. The patient was then treated with 4mg/day of diazepam and advised to monitor both orobuccal dyskinesia and mood changes.

After an 11-month follow-up period, the patient remained in remission and was solely taking only 4 mg/day of diazepam. His tardive dyskinesia showed continued improvement and eventually ceased altogether.

Discussion

Tardive dyskinesia is associated with various factors, including neurological problems and medication use. In this particular case, the patient did not display any neurological deficit symptoms and his laboratory results fell within normal limits, making it unlikely that his condition was caused by neurological diseases.

Another possibility was the medication he was taking, which in this case was only lithium carbonate. Patients with lithium toxicity may experience muscle trembling, jerking, or joint stiffness, all of which mimic the symptoms observed in tardive dyskinesia. However, this scenario was also less likely as the patient exhibited no other signs of lithium toxicity, and his blood lithium level was within the normal range at 0.184 mEq/L. Given that the patient was taking lithium solely, any adverse effects stemming from other drugs were also unlikely.

Tardive dyskinesia typically arises as an iatrogenic movement disorder, primarily resulting from the prolonged use of dopamine antagonist drugs. Common risk factors include D2 receptor occupancy levels, the usage of anticholinergic and antiparkinsonian drugs, advanced age, female gender, the presence of organic brain damage, schizophrenia with negative symptoms, and the development of early extrapyramidal symptoms during antipsychotic medication use[3]. According to Witter et al., the underlying pathological mechanisms of tardive dyskinesia encompass post-synaptic dopamine receptor supersensitivity, diminished activity of GABAergic striatal neurons, maladaptive synaptic plasticity, and neurodegeneration within the neurotransmitter systems of the motor pathway[4].

In contrast, lithium, a widely used drug for treating bipolar disorder in both acute treatment and prophylaxis, has a mechanism of action that is still not fully understood. It is known to modulate serotonin release at presynaptic sites, as well as regulate arachidonic acid and the protein kinase C signaling cascades[5]. Some preclinical studies have explored the impact of lithium on dopamine synthesis and transmission[6]. Although long-term lithium administration does not affect normal arousal-related increases in cortical acetylcholine release, it does reduce dopamine-mediated increases in acetylcholine, which may affect the efficacy of bipolar disorder prophylaxis[5]. Some theories suggest that lithium may prevent dopamine receptor supersensitivity, particularly as it relates to the development of manic episodes[7]. However, hypotheses regarding dopamine receptor binding remain inconclusive[6].

Previous studies have reported cases of lithium-induced tardive dystonia and lingual dystonia[8,9]. Additionally, tardive dyskinesia has been observed following lithium intoxication[10]. Dinan et al. reported that the prevalence of tardive dyskinesia in bipolar disorders increased with age and in patients who were treated with lithium for a long time[11]. Fountoulakis et al. noted that tardive dyskinesia can even occur at low doses of lithium (600 mg/day)[12]. In our case, long-term use of low-dose lithium monotherapy (600 mg/day) in an older patient resulted in tardive dyskinesia, an uncommon adverse effect. The symptoms improved upon the discontinuation of lithium and the addition of benzodiazepines. Therefore, patients who undergo lithium therapy should be assessed for tardive dyskinesia at each visit in order to ensure early detection and timely management.

Recently, the United States Food and Drug Administration (FDA) approved medications for the treatment of tardive dyskinesia, namely Valbenazine and Deutetrabenazine. These medications work by inhibiting vesicular monoamine transporter type 2 (VMAT-2), which

is responsible for transporting and storing serotonin, norepinephrine, and dopamine. By reducing synaptic dopamine release and the stimulation of post-synaptic receptors, they effectively ease the symptoms of dyskinesia. If lithium discontinuation does not alleviate the symptoms, either of these drugs may be considered a treatment option for patients with tardive dyskinesia[13].

In our case, these drugs were not yet available. Consequently, the primary approach was the discontinuation of lithium. If this is not feasible, an alternative strategy involves transitioning to other treatments with lower D2 receptor affinity, such as quetiapine, which can also serve as a medication for managing bipolar disorder[14].

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Conflict of interest

There are no conflicts of interest to declare.

References

1. Boland R, Verduin M, Ruiz P. Kaplan & Sadock's synopsis of psychiatry. 12th edition. Philadelphia: Wolters Kluwer; 2022.
2. Waln O, Jankovic J. An update on tardive dyskinesia: from phenomenology to treatment. Tremor Other Hyperkinet Mov 2013;3.
3. Cloud LJ, Zutshi D, Factor SA. Tardive dyskinesia: therapeutic options for an increasingly common disorder. Neurotherapeutics 2014;11:166-76.
4. Witter DP, Holbert RC, Suryadevara U. Pharmacotherapy for the treatment of tardive dyskinesia in schizophrenia patients. Expert Opin Pharmacother 2017. doi: 10.1080/14656566.2017.1323874.
5. Corbella, B, Vieta E. Molecular targets of lithium action. Acta Neuropsychiatr 2003;15:316-40. doi: 10.1046/j.1601-5215.2003.00049.x.
6. Lennox R, Mangi XX. Lithium. In: Schatzberg A, Nemeroff C, Psychopharmacology. Washington: The American Psychiatry Press; 1998:379–427.
7. Swerdlow NR, Lee D, Koob GF, Vaccarino FJ. Effects of chronic dietary lithium on behavioral indices of dopamine denervation supersensitivity in the rat. J Pharmacol Exp Ther 1985;235:324–9.
8. Chakrabarti S, Chand PK. Lithium-induced tardive dystonia. Neurol India 2002;50:473.
9. Aggarwal R, Garg D, Dhamija RK. Lithium-Induced Lingual Dystonia. Ann Indian Acad Neurol 2020;23:383-34. doi: 10.4103/aian.AIAN_369_19.
10. Meyer-Lindenberg A, Krausnick B. Tardive dyskinesia in a neuroleptic-naive patient with bipolar-I disorder: persistent exacerbation after lithium intoxication. Mov Disord 1997;12:1108–1109.
11. Dinan T, Kohen D. Tardive dyskinesia in bipolar affective disorder: relationship to lithium therapy. Br J Psychiatry 1989;155:55-7. doi: 10.1192/bjp.155.1.55.
12. Fountoulakis KN, Tegos T, Kimiskidis V. Lithium monotherapy-induced tardive dyskinesia. J Affect Disord 2019;244:78–9.
13. Touma KTB, Scarff JR. Valbenazine and Deutetrabenazine for Tardive Dyskinesia. Innov Clin Neurosci 2018;15:13-6.
14. Ricciardi L, Pringsheim T, Barnes TRE, Martino D, Gardner D, Remington G, et al. Treatment Recommendations for Tardive Dyskinesia. Can J Psychiatry 2019;64:388-99. doi: 10.1177/0706743719828968.