Hydroxyzine induced Tardive Dyskinesia: A rare case report

Priyanka B Kolkar, Vinod Akkasali, Narayan R Mutalik, Sushmina K
Department of Psychiatry, S. N. Medical College and HSK hospital, Navanagar Bagalkote, Karnataka, India

Abstract

Tardive dyskinesia is a serious and common motor side effect of treatment with traditional neuroleptics, with an unknown pathophysiological basis. It affects 20-30% of patients on long-term neuroleptic therapy, with elderly patients being at higher risk. Tardive dyskinesia from the use of antihistamines is uncommon[1,2] and typically follows years of use. Hydroxyzine is a first generation antihistaminic of diphenylmethane and piperazine class with anticholinergic and sedative property. We report a rare case of hydroxyzine-induced TD in an elderly male with chronic abuse. This case highlights the need for vigilance even with non-dopaminergic agents.

Key words: Involuntary movements, Tardive dyskinesia, adverse drug reaction3

Introduction

Tardive dyskinesia (TD) is a delayed-onset movement disorder affecting the face, lips, tongue, trunk, and extremities, occurring in 20%-50% of antipsychotic users[1] and often persisting post-discontinuation.

TD is primarily linked to dopamine D2 receptor blockade[2], causing receptor supersensitivity in the basal ganglia. Other mechanisms include GABA depletion, cholinergic deficiency, oxidative stress, and neurotoxicity. Anticholinergics may worsen symptoms[3].

Both genetic and environmental factors[4] contribute to TD, with a 2% - 5% annual incidence[5,6] and a prevalence of 15% - 30% in long-term antipsychotic users[7] (higher in typical antipsychotic drugs (APDs): 32.4% vs. atypical: 13.1%).

Risk factors include APD use, older age, female sex, brain injury, dementia, and early extrapyramidal symptoms[8]. Elderly patients face a 3.2-fold higher risk[1] due to neurodegeneration and APD or Parkinson's medication use.

Case report

Presenting a case of an 80-year-old male who came with complaints of difficulty in initiating sleep and worry about being unable to sleep for the past eight years. He has a history of hypertension and diabetes for 30 years, for which he is on regular treatment, with no contributory family or personal history. The patient also presented with a two-month history of abnormal involuntary movements involving the lips, jaw, and oral cavity

After evaluation, it was found that a general practitioner had prescribed hydroxyzine 50 mg/day for his anxiety and sleeplessness. However, the patient had been abusing hydroxyzine at doses of 50-100 mg/day for a period of eight years. Risk factors associated with tardive dyskinesia (TD) were age and diabetes.

The neurologist's opinion indicated no other neurological abnormalities, except for orobuccolingual dyskinesia.

On examination, the patient was conscious, alert, and well-oriented. Vitals were within normal limits. There was no pallor, icterus, cyanosis, clubbing, lymphadenopathy, or edema. Systemic examination was within normal limits, and Cranial nerve examination reveals no deficits. Motor examination shows normal bulk, tone, and power in all four limbs, with normal deep tendon reflexes and no signs of rigidity or bradykinesia. Sensory examination is intact for all modalities. Cerebellar function is normal, with no dysdiadochokinesia, or intention tremors. Gait is normal, and Romberg's test is negative. No focal neurological deficits were observed. However, abnormal involuntary movements were noted in the form of puckering of lips, chewing-like motions, and jaw movements, consistent with orobuccolingual dyskinesia. Mental status examination showed that the patient walked into the OPD on his own, was well-

Address for Correspondence:

Dr. Priyanka B Kolkar
Junior Resident, Department of Psychiatry,
S. N. Medical College and HSK hospital, Navanagar Bagalkote, Karnataka, India
Email: Priyanka.b.kolkar@gmail.com

kempt and well-dressed, maintained eye contact,was cooperative with normal psychomotor activity. His mood was subjectively described as "Aram" (calm) and objectively euthymic. Thought process revealed preoccupation with sleep, with no perceptual disturbances. Memory assessment showed an immediate recall of digit forward - 5 and digit backward - 3, with intact recent and remote memory. Judgment was intact, and insight was graded as 4.

Biochemical investigations were within normal limits. The patient was advised neuroimaging but declined. Hamilton Anxiety Rating Scale (HAM-A) score of 6 (minimal or no anxiety) was applied to rule out anxiety symptoms. Further assessments were conducted to rule out extrapyramidal disorder using clinical scales, which showed Abnormal Involuntary Movement Scale (AIMS) score of 10 (mild to moderate tardive dyskinesia), Mini-Mental Status Examination (MMSE) score of 24/30 (mild cognitive impairment), Barnes Akathisia Rating Scale score of 0 (no akathisia), Simpson-Angus Extrapyramidal Side Effects Scale score of 0 (no drug-induced parkinsonism or extrapyramidal symptoms).

He was advised to discontinue hydroxyzine and was started on clonazepam 1 mg twice daily, which was gradually tapered and stopped over next 3 to 6 month. Patient was also advised to practice sleep hygiene techniques, psychoeducation was done to patient regarding age related reduction of sleep and advised for regular followups. After stopping hydroxyzine, patient symptoms reduced, and the patient showed complete improvement within one month.

Discussion

Long-term exposure to dopamine receptor-blocking drugs is a well-known cause of persistent movement disorders, but whether non-dopamine-blocking drugs can induce a similar syndrome remains unclear[9]. TD prevalence ranges from 20-50% in neuroleptic-treated patients, increasing with age[10]. The incidence is lower in younger individuals (3-5% per year) and higher in older adults[5]. SSRIs like fluoxetine increase serotonin in the raphe nucleus, which inhibits dopamine neurons in the nigrostriatal pathway. This serotonergic inhibition reduces dopamine activity in the basal ganglia. The resulting dopamine deficiency may contribute to the development of tardive dyskinesia (TD)[11]. Our 80-year-old patient presented with perioral movements suggestive of TD.

According to the Diagnostic and Statistical Manual of Mental Disorders, 5th ed. (DSM-5-TR), TD develops during exposure to a Dopamine receptor blocking agent for at least 3 months (or 1 month in patients age 60 years or older) or within 4 weeks of withdrawal from an oral medication (or within 8 weeks of withdrawal from a depot medication)[10]. Our patient was found to be abusing hydroxyzine for a period of 8 years[4]. Reports on TD in non-dopamine receptor blocking drugs are primarily isolated case reports and small series, (mostly one case, and none larger than five)[9].

Prevention of TD is paramount; therefore, strict selection of patients to be treated with DRBAs is prudent medical practice. Long-term treatment with DRBAs (**Dopamine Receptor-Blocking Agents**) should be avoided, but, if absolutely necessary, it should be accompanied by frequent re-assessments of the need to continue treatment and high vigilance and monitoring for early symptoms and signs of TD.The main aspect of TD treatment is removal of a causative drug whenever possible, but slow taper is recommended as sudden withdrawal is more likely to precipitate TD or withdrawal emergent syndrome. High doses of clozapine and quetiapine have been reported to alleviate TD symptoms[1]. Tetrabenazine is currently considered a first line agent and the most effective medication to treat persistent and disabling TD.

The diagnosis of hydroxyzine-induced TD was based on clinical assessment, exclusion of other movement disorders, and drug history. An 80-year-old male presented with orobuccolingual dyskinesia, characteristic of TD, with a history of hydroxyzine use for eight years at 50-100 mg/day. Advanced age and diabetes increased his susceptibility. Other movement disorders, including Parkinson's, were ruled out due to the absence of rigidity, bradykinesia, postural instability, or tremors, along with negative Barnes Akathisia and Simpson-Angus Scale scores. Normal cranial nerve, motor, sensory, and cerebellar examinations further supported this. Metabolic and nutritional causes were excluded based on normal thyroid function tests, electrolytes, vitamin B12, and inflammatory markers. An AIMS score of 10 confirmed mild to moderate TD, while an MMSE score of 24/30 indicated mild cognitive impairment, likely age-related rather than TD-linked. Biochemical tests were within normal limits, reinforcing the drug-induced nature of TD. Hydroxyzine was discontinued gradually to prevent withdrawal-related worsening. Clonazepam (1 mg twice daily) was initiated for symptom control and tapered off over 3-6 months. Psychoeducation on sleep hygiene addressed the initial insomnia concern, preventing future reliance on sedatives. Regular follow-ups ensured symptom resolution and relapse prevention. TD symptoms resolved completely within a month of stopping hydroxyzine, confirming the diagnosis. This case highlights the need to consider non-dopaminergic agents as potential TD causes,

especially in the elderly, emphasizing careful drug prescription and monitoring.

Conclusion: According to DSM-5-TR, the reflex movements must have been present for at least four weeks and antipsychotic medication should have been used for at least three months (one month in patient sixty and above). Hydroxyzine, an antihistaminic is also used as hypnotic by general practitioners and can lead to serious motor side effect like tardive dyskinesia after long term use. As per Naranjo's Adverse Drug Reaction Probability Scale score is 5[12]. There are very few case reports documented. Hence we must be aware of possible serious side effects especially in geriatric population.

References

1. *Waln O, Jankovic J. An update on tardive dyskinesia: from phenomenology to treatment. Tremor Other Hyperkinet Mov (N Y). 2013;3:tre-03-161-4138-1.*
2. *Zai CC, Tiwari AK, Basile V, De Luca V, Müller DJ, King N, et al. Association study of tardive dyskinesia and five DRD4 polymorphisms in schizophrenia patients. Pharmacogenomics J. 2009 Jun;9(3):168-73.*
3. *Jensen N, Oliveira JR. Basal ganglia vulnerability to oxidative stress. Front Neurosci. 2014 Apr 21;8:80.*
4. *Fedorenko OY, Loonen AJ, Lang F, Toshchakova VA, Boyarko EG, Semke AV, et al. Association study indicates a protective role of phosphatidylinositol-4-phosphate-5-kinase against tardive dyskinesia. Int J Neuropsychopharmacol. 2015 Apr 1;18(6):pyu117.*
5. *Correll CU, Leucht S, Kane JM. Lower risk for tardive dyskinesia associated with second-generation antipsychotics: a systematic review of 1-year studies. Am J Psychiatry. 2004 Mar 1;161(3):414-25.*
6. *Gebhardt S, Härtling F, Hanke M, Mittendorf M, Theisen FM, Wolf-Ostermann K, et al. Prevalence of movement disorders in adolescent patients with schizophrenia and in relationship to predominantly atypical antipsychotic treatment. Eur Child Adolesc Psychiatry. 2006 Oct;15(7):371-82.*
7. *Kim J, MacMaster E, Schwartz TL. Tardive dyskinesia in patients treated with atypical antipsychotics: case series and brief review of etiologic and treatment considerations. Drugs Context. 2014;3:212-267.*
8. *Cornett EM, Novitch M, Kaye AD, Kata V, Kaye AM. Medication-induced tardive dyskinesia: a review and update. Ochsner J. 2017 Jun 20;17(2):162-74.*
9. *D'Abreu A, Friedman JH. Tardive dyskinesia-like syndrome due to drugs that do not block dopamine receptors: rare or non-existent: literature review. Tremor Other Hyperkinet Mov (N Y). 2018;8:588.*
10. *American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed., Text Revision (DSM-5-TR).2022. Washington,DC. p. 807-19.*
11. *Di Giovanni G, Esposito E, Di Matteo V. Role of serotonin in central dopamine dysfunction. CNS Neurosci Ther. 2010 Jun;16(3):179-94.*
12. *Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981 Aug;30(2):239-45.*

Conflict of interest: Nil
Source of funding: Nil

Date received: Apr 12, 2025
Date accepted: Dec 15, 2025