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UNEXPECTED EXTRAPYRAMIDAL REACTION: ACUTE TARDIVE DYSKINESIA FOLLOWING SHORT-TERM METOCLOPRAMIDE USE IN A PATIENT WITH DIABETES AND CHRONIC KIDNEY DISEASE

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Abstract
Tardive dyskinesia (TD) is a potentially irreversible extrapyramidal movement disorder characterized by involuntary, repetitive movements, predominantly affecting the orofacial region. Although most commonly associated with prolonged exposure to dopamine receptor–blocking agents, TD may also arise following the use of gastrointestinal prokinetics such as metoclopramide. Female sex, diabetes mellitus, advanced age, and renal impairment are recognized risk factors that increase susceptibility, yet TD remains underrecognized outside psychiatric settings. A 49-year-old woman with poorly controlled type 2 diabetes mellitus presented with nausea, vomiting, and generalized weakness. Laboratory findings demonstrated normocytic anemia, uncontrolled hyperglycemia (HbA1c 9.2%), and acute-on-chronic kidney disease (eGFR 22 mL/min/1.73 m²). She received standard supportive therapy, including intravenous metoclopramide. Within 24 hours, she developed repetitive tongue protrusion and orofacial dyskinesia. Neuroimaging and electrolyte evaluation were unremarkable, and there was no history of prior neuroleptic exposure. Metoclopramide was promptly discontinued, leading to gradual improvement and complete resolution of symptoms within two weeks. Antiemetic therapy was switched to ondansetron. This case underscores that acute TD may occur after short-term metoclopramide use, particularly in patients with diabetes and renal dysfunction. Heightened clinical awareness and cautious prescribing are essential to prevent this potentially disabling adverse effect.
Keywords: *Tardive dyskinesia; Metoclopramide; Extrapyramidal symptoms; Drug-induced movement disorder*

INTRODUCTION

Tardive dyskinesia (TD) is a chronic, often disabling hyperkinetic movement disorder characterized by involuntary, repetitive, and stereotyped movements, predominantly affecting the orofacial musculature. Although classically associated with long-term antipsychotic therapy, TD is now recognized as a potential adverse effect of various non-antipsychotic dopamine receptor blocking agents (DRBAs), including gastrointestinal prokinetics such as metoclopramide.[1,2]

Metoclopramide is widely prescribed for nausea, vomiting, gastroparesis, and functional gastrointestinal disorders due to its dopamine D2 receptor antagonism in the chemoreceptor trigger zone and gastrointestinal tract. However, central dopamine blockade also predisposes patients to extrapyramidal side effects (EPS), ranging from acute dystonia and akathisia to parkinsonism and tardive syndromes. Despite regulatory warnings limiting duration of use, metoclopramide remains one of the most commonly implicated non-antipsychotic drugs associated with TD.[3,4]

Several studies have identified patient-specific risk factors that substantially increase susceptibility to TD, including female sex, advanced age, diabetes mellitus,

Nusantara Hasana Journal
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E-ISSN: 2798-1428

and renal impairment. Diabetes mellitus is thought to contribute through oxidative stress, microvascular damage, and altered dopaminergic neurotransmission, while chronic kidney disease (CKD) leads to reduced drug clearance and prolonged central nervous system exposure. [2,5,6]

Importantly, TD has traditionally been viewed as a late-onset complication of prolonged DRBA exposure. However, recent clinical observations and pharmacovigilance data suggest that acute or early-onset TD can occur in vulnerable individuals even after short-term exposure. This phenomenon is particularly underrecognized in non-psychiatric settings, where abnormal movements may be misattributed to metabolic derangements or functional disorders.

This case report aims to highlight an unusual presentation of acute tardive dyskinesia following short-term metoclopramide administration in a patient with multiple established risk factors, underscoring the need for heightened vigilance in routine clinical practice.

CASE PRESENTATION

A 49-year-old woman presented to the emergency department with a three-day history of persistent nausea, recurrent vomiting, and generalized weakness. She denied abdominal pain, hematemesis, altered bowel habits, or neurological symptoms at initial presentation. Her medical history was significant for type 2 diabetes mellitus for more than 10 years, with documented poor glycemic control. She had no known history of psychiatric illness, cerebrovascular disease, or prior exposure to antipsychotic or other neuroleptic medications.

On physical examination, the patient appeared mildly dehydrated but was hemodynamically stable. Vital signs revealed a blood pressure of 128/78 mmHg, heart rate of 86 beats per minute, respiratory rate of 18 breaths per minute, and body temperature of 36.8°C. Neurological examination was unremarkable, with intact cranial nerves, normal muscle tone, strength, and reflexes, and no involuntary movements observed at admission.

Laboratory investigations demonstrated normocytic anemia (hemoglobin 10.4 g/dL), elevated fasting plasma glucose, and poor long-term glycemic control (HbA1c 9.2%). Renal function tests revealed acute on chronic kidney disease, with an estimated glomerular filtration rate (eGFR) of 22 mL/min/1.73 m². Serum electrolytes, including sodium, potassium, calcium, and magnesium, were within normal limits.

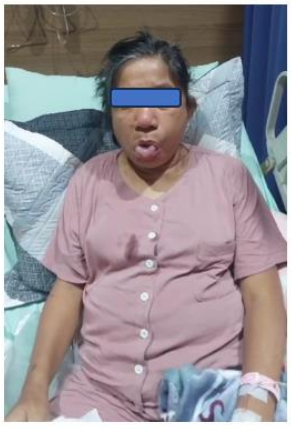

Figure 1. Orofacial Dyskinesia Characterized by Repetitive Tongue

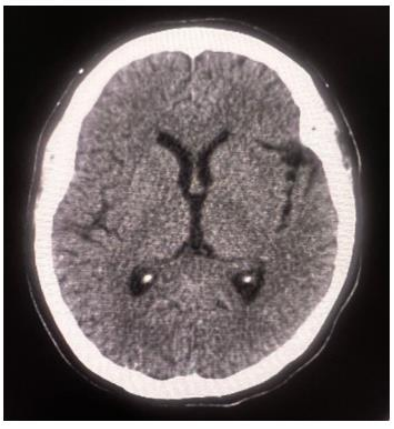

Figure 2. Neuroimaging revealed normal findings with no structural

Nusantara Hasana Journal
Volume 5 No. 7 (Desember 2025), Page: 208-212
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Initial management consisted of intravenous fluid resuscitation, correction of mild metabolic derangements, proton pump inhibitor therapy, and antiemetic treatment. Metoclopramide was administered intravenously at standard antiemetic dosing. No dose adjustment was made at that time despite underlying renal impairment. Within 24 hours of metoclopramide administration, the patient developed abnormal involuntary movements characterized by repetitive tongue protrusion, lip smacking, and orofacial dyskinesia. The movements were continuous, non-rhythmic, and exacerbated by stress, but diminished during sleep. There was no associated alteration in consciousness, focal neurological deficit, or seizure activity.

A repeat neurological examination revealed isolated orofacial dyskinesia without rigidity, tremor, or bradykinesia. Brain computed tomography (CT) scan showed no evidence of acute intracranial pathology. Repeat laboratory testing confirmed stable electrolytes and metabolic parameters. Given the temporal relationship between symptom onset and metoclopramide exposure, a diagnosis of acute metoclopramide-induced tardive dyskinesia was made.

Metoclopramide was immediately discontinued, and supportive management was initiated. The patient was switched to ondansetron for ongoing nausea control. Over the subsequent five days, the intensity and frequency of involuntary movements gradually decreased. Complete resolution of dyskinetic movements was observed by the second week of hospitalization. The patient was counseled extensively regarding avoidance of future metoclopramide use and discharged with optimized glycemic control and scheduled nephrology follow-up.

DISCUSSION

Recent literature has increasingly recognized tardive dyskinesia as an adverse effect of anti-dopaminergic medications, particularly with extended exposure.[7] This case provides a clinically relevant example of acute tardive dyskinesia occurring after short-term exposure to metoclopramide in a high-risk patient. Although TD is most commonly linked to cumulative dopamine receptor blockade, accumulating evidence indicates that duration alone does not fully account for individual vulnerability. Instead, host-related factors and pharmacokinetic alterations play a decisive role.

Blockade of dopamine D2 receptors within the basal ganglia has been implicated as the underlying mechanism responsible for tardive dyskinesia as well as other extrapyramidal manifestations, including acute dystonia.[8] Metoclopramide is an agent approved by the United States Food and Drug Administration for the management of gastroparesis.[9] In this case, metoclopramide was administered to manage acute nausea and vomiting in the emergency setting, owing to its established antiemetic and prokinetic effects.

The prevailing pathophysiological model of TD involves dopamine D2 receptor supersensitivity within the basal ganglia following sustained antagonism, leading to dysregulated motor output (Waln & Jankovic, 2019). In patients with renal impairment, reduced clearance of metoclopramide results in elevated plasma levels and prolonged central exposure, effectively mimicking higher cumulative dosing even during short-term use.[6] This mechanism may explain the rapid onset of dyskinetic movements observed in the present case.

Nusantara Hasana Journal
Volume 5 No. 7 (Desember 2025), Page: 208-212
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Diabetes mellitus further compounds the risk of TD. Experimental and clinical studies suggest that chronic hyperglycemia induces oxidative stress and neuroinflammation, which may sensitize dopaminergic neurons to pharmacological insults. Epidemiological data consistently demonstrate higher TD prevalence among patients with diabetes, independent of antipsychotic exposure duration.[5] In this patient, poor glycemic control likely amplified susceptibility to dopamine receptor dysregulation.

Differential diagnosis in this context includes acute dystonia, akathisia, seizure disorder, metabolic encephalopathy, and structural central nervous system pathology. The predominance of choreoathetoid orofacial movements, absence of altered mental status, normal neuroimaging, and clear temporal association with metoclopramide strongly support the diagnosis of TD rather than other extrapyramidal syndromes.[10]

Although valbenazine is currently the recommended standard therapy for tardive dyskinesia, early recognition and prompt discontinuation of the offending agent remain the cornerstone of management.[11] While tardive dyskinesia may become persistent or irreversible, particularly with delayed intervention, early-onset cases identified promptly are more likely to resolve, as observed in this patient. This underscores the importance of clinician awareness.

From a preventive standpoint, this case emphasizes the need for individualized risk assessment prior to prescribing metoclopramide. Dose adjustment in renal impairment and preferential use of alternative antiemetics with minimal dopaminergic activity—such as serotonin 5-HT3 antagonists—should be strongly considered in high-risk populations. Education of non-psychiatric clinicians is essential to reduce preventable drug-induced neurological morbidity.

CONCLUSION

This case demonstrates that tardive dyskinesia can occur even after short-term use of metoclopramide, particularly in patients with predisposing factors such as diabetes mellitus and renal impairment. The findings emphasize that tardive dyskinesia is not limited to long-term exposure to dopamine receptor antagonists and may present acutely in susceptible individuals. Early recognition and prompt discontinuation of the offending agent remain the cornerstone of management and may prevent persistent neurological complications. Careful risk assessment, dose adjustment, and consideration of alternative antiemetic therapies are essential to reduce the likelihood of this preventable adverse drug reaction.

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