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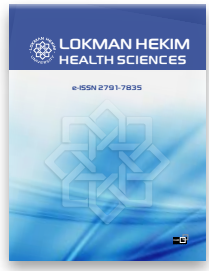

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LETTER TO THE EDITOR

Metronidazole-Associated Delirium: A Case Report

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Dear Editor,

Adverse drug reactions account for approximately 3–5% of all hospital admissions.[1] Among antibiotics, neuropsychiatric side effects such as dizziness, tremor, and hallucinations have been reported in about 9–11% of patients treated with fluoroquinolones or nitroimidazoles. Although metronidazole is widely used and generally well tolerated, rare central nervous system adverse events – including encephalopathy, confusion, depression, and psychosis – have been described.[2] Here, we present a case of acute delirium temporally associated with intravenous metronidazole administration.

A 45-year-old male was admitted to the emergency department with a 3-week history of diarrhea, lower abdominal pain, and syncope. His past medical history included coronary artery disease. On admission, his blood pressure was 70/40 mmHg, heart rate 120 bpm, body temperature 37°C, and oxygen saturation 95%. He reported watery, non-bloody, non-mucoid diarrhea occurring 5–6 times daily, along with nausea and vomiting, leading to reduced oral intake. Physical examination revealed mild diffuse abdominal tenderness without guarding or rebound. He denied recent travel or contact with individuals with gastroenteritis. Laboratory findings showed leukocytosis (white blood cell 21,000/μL), serum creatinine 2.2 mg/dL, sodium 131 mmol/L, potassium 3.8 mmol/L, and C-reactive protein 236 mg/L. Parasite eggs were observed in stool sample. The patient was diagnosed with acute gastroenteritis and acute kidney injury, and hospitalized for intravenous hydration and empiric antimicrobial therapy with metronidazole 500 mg TID intravenously.

On the 2nd day of hospitalization, despite improvement in gastrointestinal symptoms, the patient developed confusion characterized by repetitive and incoherent speech, disorientation to place and time, and nocturnal agitation. Neurological examination revealed a confusional state with limited cooperation and apathy. The patient exhibited perseveration – repeating the same phrases in response to different questions – while cranial nerves and motor function were intact. There was mild truncal ataxia, but no focal deficits or cerebellar dysfunction. Metabolic, endocrine, and infectious causes of acute cognitive change were excluded through laboratory testing, and a non-contrast brain computed tomography was unremarkable. Given these findings, delirium was suspected, and low-dose haloperidol was initiated; however, no improvement was observed. Subsequently, metronidazole was discontinued, and within 24 h, the patient's neuropsychiatric symptoms completely resolved.

Metronidazole readily crosses the blood–brain barrier, and both the drug and its metabolites may reversibly bind to neuronal RNA, leading to direct or indirect neurotoxic effects.[3] Metronidazole-related neuropsychiatric reactions

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are considered rare; however, to our knowledge, no precise incidence rate for metronidazole-associated delirium has been reported in the literature. The abrupt onset of delirium following drug initiation, in conjunction with rapid resolution after withdrawal, supports a probable causal relationship. In our case, the patient had taken a total of 2000 mg of metronidazole when delirium developed. Although delirium can occur at any age, it is more common in older adults. When delirium develops in younger patients, medication-induced toxicity or severe systemic illness should be strongly considered.[4] Therefore, a detailed review of all current medications is essential when evaluating acute confusional states.

In conclusion, clinicians should remain vigilant for neuropsychiatric adverse reactions associated with metronidazole, particularly when new-onset delirium or cognitive changes arise during therapy. Early recognition and prompt drug discontinuation can prevent unnecessary diagnostic testing and facilitate rapid recovery.

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