

LETTERS TO THE EDITOR
CASE REPORTS**Neuroleptic malignant syndrome associated with only one dose of metoclopramide in an older adult**

Dear Editor,

Neuroleptic malignant syndrome (NMS) is a potentially life-threatening complication of neuroleptic medications, which are dopamine-receptor antagonists, and is characterized by a distinctive clinical syndrome of mental status change, rigidity, fever and dysautonomia. In contrast, blocking central dopamine pathways, such as metoclopramide, which is widely used to treat nausea and emesis of different origin in any age group, can be related to NMS. Although NMS is a rare condition, the reports related to NMS underscore the need for specific attention to elderly patients because of predisposing factors, such as comorbidities, polypharmacy, dehydration, malnutrition and electrolyte abnormalities. In the present report, we present an NMS case that developed after only one i.v. dose of metoclopramide in an older adult.

A 74-year-old man was brought to the emergency department because of nausea, emesis, dysuria, pollakuria, alteration in level of consciousness and a lack of appetite for the previous 2 days. His medical history showed Alzheimer's disease and sleep disorder, and he had been taking rivastigmine 18-mg patch, memantine 20 mg and trazodone 50 mg for the past 1 year. In the emergency department, a urinary tract infection was detected, and levofloxacin was empirically initiated at 500 mg/day p.o., and a single dose of 10 mg metoclopramide was given i.v. for emesis. Then, he was discharged. After 12 h, he was admitted to a geriatric outpatient clinic due to the fact that his mental status had become worse and he became stiff.

On physical examination, stupor was prominent without cooperation and orientation. The patient had a temperature of 38.2°C, blood pressure of 110/80 mmHg, respiratory rate of 30/min and heart rate of 54 b.p.m. He was dehydrated. There was generalized muscular rigidity characterized by lead pipe rigidity. He also had diaphoresis, a fluctuating level of consciousness and urinary incontinence. Leukocyturia was detected in urinalysis. Laboratory findings showed leukocytosis, elevation of Aspartate aminotransferase (AST) (98 U/L), Lactate dehydrogenase (LDH) (413 U/L), Creatine

phosphokinase (CPK) (4184 U/L), creatinine (1.39 mg/dL), sodium (166 mmol/L) and C-reactive protein (103.2 mg/L). Because after exposure to metoclopramide all these positive findings, including lead pipe rigidity, mental status alteration, elevation of creatine kinase more than fourfold the upper limit of normal and tachypnea, and negative findings for toxic, metabolic or neurological causes, were taken into account, NMS was diagnosed according to NMS diagnostic criteria.¹

Immediately, cardiorespiratory monitoring was provided. Intravenous fluid therapy was started, and low-molecular weight heparin was given to prevent deep venous thrombosis. The patient started bromocriptine treatment, a dopamine agonist, 2.5 mg four times daily, and lorazepam 0.5 mg three times daily by nasogastric feeding tube. Levofloxacin therapy was continued. The levels of CPK, sodium, AST, LDH and C-reactive protein levels progressively dropped in 9 days (Fig. 1). Lorazepam and bromocriptin were gradually reduced and stopped after the normalization of CPK levels. His consciousness and rigidity had completely improved. On the 12th day of admission, he was discharged from the hospital.

In the present case, NMS developed in an older adults after only one dose of metoclopramide.

NMS is a life-threatening condition, and it can occur either with the use of dopamine receptor antagonists or by the withdrawal of dopamine receptor agonists. If not promptly recognized and treated, the mortality rate is 3.3–27.7%. Major complications are rhabdomyolysis, acute kidney injury, systemic infections and venous thromboembolism.²

Although metoclopramide – a dopamine antagonist – is the first choice of drug and is often used for emesis, especially in emergency departments, treatment with metoclopramide can cause severe adverse effects, including tardive dyskinesia, dystonia and parkinsonism.^{1,2} Furthermore, metoclopramide is also related to NMS in older adults on rare occasions, and a few cases have been reported.^{3–5} In one of these cases, the patient received three 10-mg tablets of metoclopramide for nausea.³ In another report, metoclopramide (six 5-mg tablets daily)

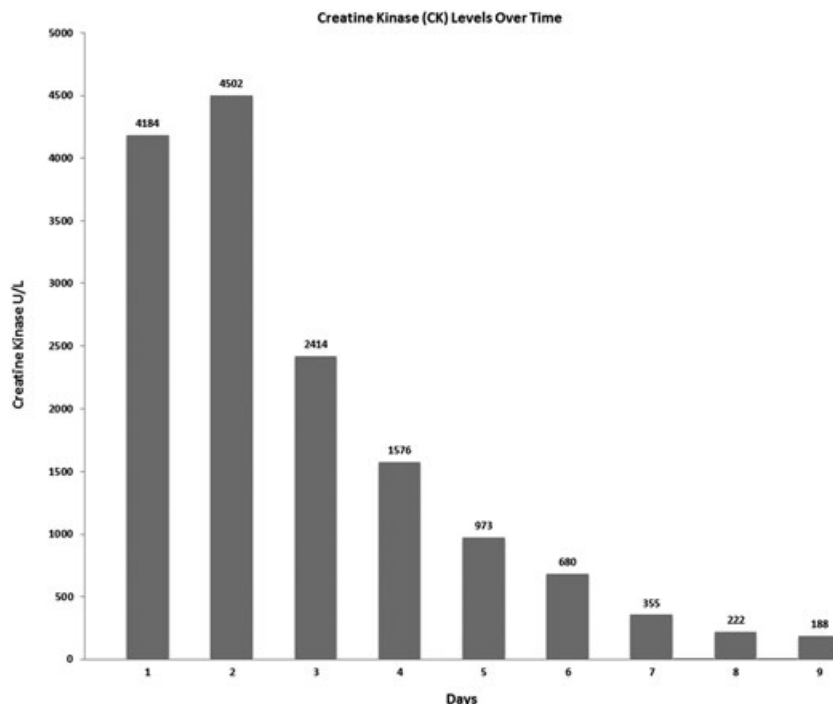


Figure 1 Changes of serum creatine kinase levels (the findings of the emergency department are shown as day 0).

was used for gastroparesis for 1 week.⁴ Finally, another older adult was treated with metoclopramide 10 mg twice a day for gallbladder empyema for 4 days.⁵ In all these cases, the repeated doses of metoclopramide resulted in NMS, and two of them were fatal.^{3,5} Unlike these aforementioned cases, the present report has shown that NMS can develop after only one 10-mg dose of metoclopramide, and the patient fully recovered without any complications after early diagnosis and treatment. In contrast, NMS diagnosis is generally difficult as a result of the concomitant precipitating events in older adults, therefore showing the reduction of dopamine transporter ligand-binding by dopamine transporter single-photon emission computed tomography or metaiodobenzylguanidine scintigraphy could be useful for diagnosis of NMS in these patients.⁶

Although metoclopramide-induced NMS is extremely rare, it should be kept in mind that this drug is widely used in clinical practice, and that only single dose can be enough to cause NMS. Therefore, NMS should be suspected in every case of unexplained mental alterations, muscular rigidity and fever after initiation of treatment with metoclopramide.

Disclosure statement

The authors declare no conflict of interest.

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