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CASE REPORTS

Acute Drug-Induced Symptoms of Restless Legs Syndrome in an Emergency Department

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Restless legs syndrome is a chronic disorder that is characterized by an urge to move the legs and unpleasant sensations in the lower extremities. Its symptoms develop slowly and a sudden onset is very unusual, which may be confusing for the emergency physician. We describe a case of an abrupt presentation of restless legs syndrome symptoms induced by infusion of metoclopramide during treatment of a migraine attack in settings of an emergency department. The patient shortly after infusion of metoclopramide started to experience rapid movements of the legs, claiming that it was the only way to relieve extremely unpleasant sensations in her legs. The symptoms subsided after saline infusion and did not appear again.

Keywords: antiemetic, ferritin; migraine, metoclopramide, restless legs syndrome

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INTRODUCTION

Restless legs syndrome (RLS) is a chronic disorder that is characterized by an urge to move the legs and unpleasant sensations in the lower extremities. The symptoms develop during rest and in the night, and subside during voluntary leg movements. Idiopathic RLS is likely caused by iron metabolism disorders and/or disturbed dopaminergic transmission.[1] Secondary RLS may be caused by iron deficiency, pregnancy, or end-stage renal disease,[2] and may be an adverse effect of pharmacotherapy (eg, antipsychotic drugs). We report the case of a woman who experienced acute symptoms of RLS after a single dose of metoclopramide that was given to manage an attack of migraine in an emergency department. The acute appearance of symptoms of RLS may be confusing for emergency physicians; therefore, we present the following case.

REPORT OF CASE

A 32-year-old woman with a 15-year of history of migraine without aura was admitted to our emergency department (ED) in October 2016 because of a migraine attack. She was not pregnant at the admission and had not been receiving drug-based treatment, although she had taken 400 mg of ibuprofen by mouth for her symptoms. The headache had begun 6 hours before her admission, and she had also experienced nausea, vomiting, and photophobia. The headache's severity decreased before the admission, and the most problematic symptom at the ED was nausea. The patient did not have focal neurological signs during a neurological examination, and we administered antiemetic treatment (10 mg of intravenous metoclopramide).

However, the patient reported experiencing strange sensations in her legs within 5 minutes after the infusion, such as an urge to move that was localized to her calves and feet, as well as an unpleasant inner "creepy-crawly" sensation in her lower extremities. The patient had never experienced these symptoms before and voluntarily performed vigorous leg movements that provided relief from the symptoms during the movements, although the symptoms returned after she stopped the movements. The sensations were exacerbated when the patient intentionally kept still, although the patient did not experience general restlessness, anxiety, or a generalized need to move. Laboratory testing revealed normal findings, with the exception of low ferritin levels (**Table 1**), and the patient did not have a history of anemia, iron deficiency, or chronic renal disease.

An intensive saline infusion (500 mL/20 min) was performed to flush the D2 blockade, and her RLS, nausea, and headache resolved within 1 hour after the infusion. The patient was discharged, and follow-up telephone calls after 12 hours and 3 months revealed that she had not experienced any further symptoms involving her legs.

DISCUSSION

This patient exhibited symptoms that were typical of RLS (ie, a focal urge to move the legs with unpleasant sensations), which were relieved by movement and reappeared when the movements ended. Furthermore, the symptoms were exacerbated when the patient attempted to lie still. However, there are two novel aspects of this case. The first is the abrupt onset of the RLS symptoms, as the natural course of this condition is considered slow and progressive. An unexpectedly acute onset may be problematic for emergency specialists or neurologists, and it is important to determine the factors that may have influenced the acute course. The acute onset in the current case was likely related to the patient's low ferritin levels and the

Table 1—The patient's clinical data.

Sex	Female
Age	32 years
Body mass index	21.8 kg/m^2
Blood pressure admission	127/70 mmHg
Heart rate at admission	62/min
O_2 saturation at admission	99%
Pain intensity at admission (VAS)	4/10
C-reactive protein	3.4 mg/L
Blood Na^+	141 mEq/L
Blood K^+	4.7 mEq/L
Serum creatinine	1.0 mg/dL
Hemoglobin	12.5 g/dL
Red blood cell count	4.5 × 10^{12}/L
White blood cell count	6.7 × 10^9/L
Serum iron	61 µg/mL
Ferritin	22.27 ng/mL

VAS = visual analog scale.

metoclopramide infusion. The second novel aspect is the clear role of metoclopramide, as it is widely accepted that antiemetic drugs can induce RLS, although few studies have specifically evaluated whether metoclopramide treatment leads to RLS. One study revealed that chronic metoclopramide treatment was associated with the risk of RLS,[3] whereas another study found that metoclopramide did not induce RLS symptoms.[4] To the best of our knowledge, ours is the first report of acute RLS symptoms induced by a single dose of metoclopramide. Hoque and Chesson published a comprehensive review focusing on drug-induced RLS. The authors analyzed numerous publications describing induction of RLS symptoms with various drugs (especially neuroleptics and antidepressants) though no data on induction of RLS with metoclopramide were found.[5]

Metoclopramide is a D_2 dopamine receptor antagonist that acts on the central nervous system.[6] These receptors are critical in RLS, as the most potent dopaminergic drugs used to treat RLS are D_2 and D_3 agonists.[7] However, our case involved two overlapping major pathogenic mechanisms that led to the RLS: a preexisting iron metabolism disorder (low ferritin levels) and acute iatrogenic blockade of D_2 receptors using metoclopramide. These mechanisms led to the acute appearance of RLS, which resolved after stopping the D_2 blockade and providing an intravenous saline infusion. Therefore, caution should be exercised when administering metoclopramide therapy.

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DISCLOSURE STATEMENT

Work for this study was performed at Medical University of Gdansk, Department of Emergency Medicine. All authors have seen and approved the manuscript. The authors report no conflicts of interest.