

CASE REPORT

Atypical neuroleptic malignant syndrome
presenting as severe paralytic ileus following
procyclidine withdrawal: A case reportMinhal Fatemah^{1†}, Areeba Ghaffar^{1†*}, and Muhammad Affan Baig²¹Department of Anesthesia, Rawalpindi Medical University Allied Hospitals, Rawalpindi, Punjab, Pakistan²Department of Surgery, Holy Family Hospital, Rawalpindi, Punjab, Pakistan

Abstract

Neuroleptic malignant syndrome (NMS) is a rare but potentially life-threatening condition that has been reported in some patients following the administration of anti-dopaminergic agents or the rapid withdrawal of dopaminergic medications. Here, we report a case of a hypertensive male in his 60s who presented with fever, altered sensorium, rigidity, tremors, constipation, and significant abdominal distension. He had been on procyclidine 5 mg twice daily for 3 years, which was abruptly discontinued 10 days prior. Laboratory investigations revealed elevated creatinine phosphokinase, hypokalemia, and neutrophilic leukocytosis. Imaging showed massive bowel distension without signs of mechanical obstruction. A diagnosis of NMS was established based on Levenson's criteria. Despite initial conservative management and optimization, the patient succumbed, highlighting a rare and fatal presentation of NMS following procyclidine withdrawal and presenting with paralytic ileus.

Keywords: Neuroleptic malignant syndrome; Procyclidine; Paralytic ileus; Case report

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1. Background

Neuroleptic malignant syndrome (NMS) is a rare but potentially life-threatening idiosyncratic reaction with a mortality rate of approximately 10%.¹ Incidence rates range from 0.01% to 3.20% of patients taking neuroleptic medications.² Beyond mortality, NMS can result in significant morbidity, including residual catatonia, Parkinsonism, neurocognitive deficits, such as memory impairment and amnesia, and cardiopulmonary or renal complications, with some cases of acute kidney injury requiring hemodialysis.²⁻⁴

NMS is characterized by a clinical tetrad of hyperthermia, muscular rigidity, altered mental status, and autonomic dysregulation. Key laboratory indicators include elevated white blood cell count and increased creatinine phosphokinase (CPK) levels.⁵ Although diagnosis is primarily clinical, imaging studies, such as muscle magnetic resonance imaging (MRI), have demonstrated myopathic changes in NMS,⁶ suggesting that while NMS predominantly manifests with neurological and systemic symptoms, atypical presentations can occur, posing diagnostic challenges.

Acute abdomen and intestinal obstruction are uncommon and under-recognized complications of NMS. These gastrointestinal manifestations may result from profound dysautonomia, severe rigidity affecting the smooth muscles, or secondary complications, such as ileus.⁷ NMS arises due to severe blockage of dopamine receptors in the central nervous system, which can occur following the administration of low-potency psychotropic drugs or the sudden discontinuation of dopaminergic medications. In addition, drugs like the antiemetic metoclopramide, the tricyclic antidepressant amoxapine, lithium, and phenelzine have been known to trigger NMS, likely due to their dopamine-blocking effects.⁸ The withdrawal of anticholinergic agents, such as procyclidine, which are often used as adjunctive therapy for Parkinsonism, may further exacerbate NMS symptoms due to unopposed cholinergic activity.⁹

This case report highlights a rare presentation of NMS with acute abdomen and intestinal obstruction following the abrupt cessation of procyclidine. Through this case, we aim to emphasize the importance of recognizing atypical gastrointestinal manifestations of NMS, particularly in the context of medication withdrawal.

2. Case presentation

A South Asian male in his 60s, with a known history of hypertension and an estimated weight of 75 kg, presented to the surgical emergency with fever, altered sensorium, generalized rigidity, tremors, constipation, and abdominal distention. The patient had been on procyclidine (5 mg twice daily) for the past 3 years for Parkinsonism, which was abruptly discontinued 10 days before presentation. There was no history of recent antiemetic or antipsychotic medication usage. On admission, he was vitally stable, with a blood pressure of 120/80 mmHg, a pulse of 80 bpm, a respiratory rate of 20/min, and a temperature of 38.3°C. Central nervous system examination revealed a Glasgow Coma Scale of 13/15, down-going plantar reflexes, 4/5 power in all limbs, and absent reflexes.

Laboratory investigations showed elevated CPK levels (1,161 IU/L; normal range: < 171 IU/L), hypokalemia (2.8 mEq/L), and a neutrophilic predominance (84.9%) in the complete blood count. Renal function tests were deranged with a serum creatinine level of 1.8 mg/dL and a serum urea level of 157 mg/dL. In contrast, liver function tests, clotting profile, and blood cultures were unremarkable. [Table 1](#) lists the trend of key laboratory parameters of the patient during his hospital stay.

As the patient presented to the surgical emergency with significant abdominal distension and absent bowel

Table 1. Trend of key laboratory parameters of the patient over hospital stay

Parameters	Reference ranges	Day 1	Day 2	Day 3	Day 4
Urea	15–50 mg/dL	132.00	157.00	143.28	160.97
Creatinine	0.7–1.2 mg/dL	1.6	1.8	2.5	2.7
Potassium	3.5–5.0 mEq/L	2.18	2.80*	3.65	4.29
CPK	<171 IU/L	1,161	266	189	-

Note: *Patient received 40 mmol of potassium chloride on day 2.

Abbreviations: CPK: Creatinine phosphokinase.

sounds, initial evaluation focused on ruling out an acute surgical abdomen. The erect abdominal X-ray revealed diffuse, severe gaseous distension of bowel loops with no identifiable transition point to suggest mechanical obstruction. Notably, no air-fluid levels were observed, and there was no free subdiaphragmatic air to indicate perforation, raising concern for a functional obstruction such as paralytic ileus rather than a mechanical cause. The X-ray of the chest was clear, and the computed tomography scan of the brain was unremarkable, ruling out any intracranial pathology.

Following consultation with medicine and psychiatry, a diagnosis of NMS was suspected based on Levenson's criteria, according to which the presence of all three major criteria (fever, rigidity, and elevated CPK) or two major and four minor criteria (altered mental status, autonomic instability, leukocytosis, or tachycardia) strongly supports the diagnosis. In our patient, fever, rigidity, and elevated CPK were present alongside altered mental status and leukocytosis, fulfilling all three major and two minor criteria, thereby supporting the diagnosis of NMS.

Due to the severity of abdominal distension and risk of complications, such as ischemia or perforation, surgical intervention was considered. However, the patient was declared unfit for anesthesia and was admitted to the medical ward for conservative management and optimization for surgery. The patient received intravenous (IV) fluids, potassium replacement, IV antibiotics, and cold sponging to manage fever and muscle rigidity. His condition was closely monitored, with frequent vital signs and serial checks of CPK and potassium levels.

Despite partial biochemical improvement (CPK reduced to 189 IU/L) and stabilization of potassium levels, the patient's abdominal distension worsened. Surgical intervention was reconsidered. However, the patient's condition rapidly deteriorated before any procedure could be undertaken. He was shifted to the surgical intensive care unit for intensive monitoring but ultimately succumbed

the following day, likely due to NMS-related complications, including multiorgan dysfunction and sepsis.

3. Discussion

NMS is a rare but potentially fatal adverse reaction to antipsychotic medications, marked by high fever, altered mental status, severe muscle rigidity, and autonomic instability. Our case is distinctive in two aspects: first, NMS was precipitated by the abrupt withdrawal of procyclidine, an anticholinergic agent rarely reported as a trigger; and second, it manifested predominantly with severe paralytic ileus mimicking intestinal obstruction, an under-recognized complication. The timely diagnosis of NMS, as determined by Levenson's criteria, allowed for prompt management. However, the patient's condition ultimately proved fatal, highlighting the severe nature of NMS and the need for heightened awareness of its atypical presentations.

The relationship between NMS and anticholinergics remains elusive. While anticholinergics, such as procyclidine, are not commonly implicated in the development of NMS, reports have emerged highlighting this relationship. Interestingly, there have been reports of NMS responding to rapid IV administration of procyclidine.^{10,11} Another case reported the development of a typical episode of NMS following the abrupt withdrawal of long-acting neuroleptic combined with anticholinergic, interestingly responding to procyclidine administration.¹¹ Other instances of NMS responding to bromocriptine administration¹² and intramuscular administration of the anticholinergic agent, biperiden, have also been reported.¹³ This suggests that abrupt discontinuation of anticholinergics could potentially lead to a cholinergic surge, which may disrupt the dopaminergic–cholinergic balance, potentially leading to the development of NMS. These findings highlight that a complex relationship between the two does exist and warrants further research and vigilance.

Although hyperthermia and rigidity are hallmark features of NMS, it may also involve gastrointestinal complications, such as colonic pseudo-obstruction,¹⁴ gastrointestinal bleeding and hepatic injury,¹⁵ and, as in our case, paralytic ileus.^{7,16,17} The mechanisms underlying these complications are still speculative. In the present case, the development of paralytic ileus is likely related to autonomic dysregulation, compounded by hypokalemia, leading to intestinal dysmotility and potentially leading to paralytic ileus. While hypokalemia is a known cause of paralytic ileus, the persistence of ileus despite potassium

correction, in conjunction with hallmark features, such as fever, rigidity, altered mental status, and elevated CPK, strongly suggested NMS as the primary underlying etiology. Although rare, cases of paralytic ileus in NMS have been reported both before¹⁶ and after^{17,18} other NMS symptoms. In any case, ileus has been suggested for inclusion in the list of NMS symptoms.⁷

The atypical presentations of NMS, combined with its diagnostic challenges, demonstrate a need for improved diagnostic approaches. In some cases, muscle MRI has shown findings suggestive of myopathic changes.⁶ While these findings are not specific, emerging biophysical tools, such as magnetic force microscopy, may enable ultra-sensitive detection of nanoscale tissue changes¹⁹ and offer novel insights into NMS pathophysiology in the future. Taken together, there is a need for ongoing research into both the unusual manifestations of NMS and innovative diagnostic approaches to improve outcomes in this potentially fatal syndrome.

4. Conclusion

This case illustrates both an uncommon presentation of NMS as paralytic ileus, as well as an unusual precipitant, that is, the abrupt withdrawal of procyclidine rather than an antipsychotic initiation. It adds to the body of atypical presentations of NMS, highlighting that clinicians should maintain a high index of suspicion for NMS in patients presenting with altered mental status, fever, rigidity, and autonomic dysfunction, even in the absence of antipsychotic use, and should consider NMS in the differentials for paralytic ileus. Given the rapidly fatal potential of NMS, early recognition and multidisciplinary management are critical to improving clinical outcomes.

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Conflict of interest

The authors declare that they have no competing interests.

Author contributions

Conceptualization: Minhal Fatemah, Areeba Ghaffar

Investigation: All authors

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Writing—review & editing: All authors

Ethics approval and consent to participate

Informed consent was obtained from the patient's legally authorized representatives before the preparation of the case report.

Consent for publication

The patient's legally authorized representatives provided informed consent for the publication of the findings derived from this study. Where applicable, the legally authorized representatives gave explicit permission for the publication of any data, images, or information that could potentially reveal the patient's identity. The authors affirm that all relevant consent forms have been obtained and are available upon request.

Availability of data

Not applicable.

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