Case Reports in Gastroenterology

Case Rep Gastroenterol 2018;12:566–569

DOI: 10.1159/000492460
Published online: September 18, 2018

Single Case

Acute Abdomen with Ileus: A Heralding Presentation of Neuroleptic Malignant Syndrome

Chukwunonso Chime Ahmed Alemam Kishore Kumar Manjeet Dhallu

Bronx Care Health System – Affiliate of Mount Sinai Hospital System, Bronx, NY, USA

Keywords
Acute abdomen · Neuroleptic malignant syndrome · Ileus

Abstract
The pathophysiology of neuroleptic malignant syndrome (NMS) with use of psychotropic drugs is still unclear. Although a rare event with an incidence of 0.02–3.2%, when not promptly recognized and managed, it carries a high mortality (10–20%) and morbidity rate. Presentation can be either typical, with muscle rigidity and hyperpyrexia, or atypical, the latter posing diagnostic and early management challenges in clinical practice. Our patient presented with delayed fever and ileus, making early diagnosis difficult. We propose that NMS be considered an alternate diagnosis in patients using psychotropic medications and manifest ileus and delayed fever, especially after other differentials have been excluded.

Introduction

Neuroleptic malignant syndrome (NMS), an idiosyncratic drug reaction, is a rare and life-threatening clinical entity encountered in patients on anti-dopaminergic medications or after rapid withdrawal of dopaminergic agonists. NMS is rare with a pooled data incidence of 0.02–3.2% and early diagnosis is critical due to its high morbidity and high mortality (10–20%) rate if not promptly recognized [1]. Furthermore, incidence has been steadily declining with increased awareness and use of newer antipsychotics, [2] but can still occur with any

Dr. Chukwunonso Chime
1650 Selwyn Avenue, Suite 10C
Bronx, NY 10457 (USA)
E-Mail Cchime@bronxleb.org

neuroleptic, regardless of class. According to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria, NMS is typically characterized by development of severe muscle rigidity and elevated temperature associated with use of neuroleptic medications [3, 4]. Broadly, typical symptoms are muscle rigidity, elevated temperature, autonomic instability, mental status alteration, and abnormal metabolic changes [5]. Autonomic instability can have a wide range of presentations including ileus, a symptom easily overlooked but can be a precursor for NMS, especially in the absence of fever. We present an unusual case of NMS presenting as acute abdomen with ileus and delayed fever.

Case Report

A 61-year-old man with a history of schizoaffective disorder on trifluoperazine, presented with a 2-day history of colicky abdominal pain associated with multiple episodes of vomiting and inability to pass stool or flatus. On presentation, he had a blood pressure of 174/99 mm Hg, heart rate of 130 beats per minute, respiratory rate of 22 per minute, and initial temperature of 99.1°F. Abdomen was distended, there were no postoperative scars, and bowel sounds were hypoactive with mild generalized tenderness. Investigations showed hemoglobin 13.7 g/dL, white cell count 12.4×10^9/L (76.1% neutrophils), serum sodium 140 mEq/L, potassium 4.0 mEq/L, creatinine 0.8 mg/dL, bilirubin 0.4 mg/dL, alanine transaminase 26 U/L (normal 5–40), and aspartate transaminase 53 U/L (normal 9–43). Computed tomography scan showed distended fluid-filled stomach, dilated loops of small bowel with gradual transition to normal caliber, and collapsed distal ileum. He was started on broad-spectrum antibiotics intravenously and taken for emergent exploratory laparotomy, with intraoperative findings of small patches of ischemia and creeping fat throughout much of the small bowel. He remained intubated postop and was admitted under the surgical intensive care unit.

Six hours postoperatively, the patient was noted with a spike in temperature of 101.9°F and this maintained an upward trend during his hospital course. Infectious disease team was consulted and extensive workup for etiology of fever included a negative chest radiograph, five blood cultures, three urine cultures, and a fungal culture, all of which yielded no growth. He continued to be febrile and developed asymmetric rigidity and repetitive tongue protrusion movements. On day four of admission, he became more hemodynamically unstable with hypotension, heart rate above 170 beats per minute, and atrial flutter pattern and spiked a temperature of 107.4°F, so neurology and cardiology teams were consulted. At this stage, his investigation also revealed worsening renal function, creatinine of 2.9 mg/dL, leukocytosis ($28.4 \times I0^9$/L), and elevated creatine phosphokinase (CPK) of 4,800 U/L. He failed 3 attempts at cardioversion and was started on amiodarone and norepinephrine. For a suspicion of NMS, in addition to cooling measures, he received dantrolene 2.5 mg/kg as loading dose and another dose 6 h later of 1 mg/kg with resolution of fever. On day five after initial presentation, the patient became bradycardic and hypotensive, progressed to asystole, and was pronounced dead.

Discussion

Dopamine receptor blockage by antipsychotics is the common etiology for NMS and the pathophysiology is still being debated. Although the typical antipsychotics have the greatest risk and are frequently associated with NMS, there are also many reported cases with atypical

neuroleptics but the risk appears reduced [6]. DSM-IV NMS diagnostic criteria include severe muscle rigidity, elevated temperature, associated with use of neuroleptic medications, and any two of the following: diaphoresis, dysphagia, tremor, incontinence, changes in level of consciousness ranging from confusion to coma, mutism, tachycardia, elevated or labile blood pressure, leukocytosis, and laboratory evidence of muscle injury (for example, elevated CPK), after exclusion of other drug-induced psychiatric or systemic illness [3, 4]. In the updated DSM-V, NMS is classified as hyperthermia, rigidity, mental status alteration, CPK elevation, sympathetic nervous system lability, and hypermetabolism after exposure to dopamine antagonist or dopamine agonist withdrawal, with a negative examination for infectious, toxic, metabolic, and neurologic causes [7].

A hypothesis, proposed as being responsible for most, if not all the clinical features of NMS, is sympathoadrenal hyperactivity [8]. Among the presentations of autonomic instability is ileus. This rarely observed symptom can have fatal consequences especially when not considered as a complication of the neuroleptic therapy. In a review by Nielsen and Meyer [9] of 26,720 cases of schizophrenia between the years 1996 and 2007, 123 cases of ileus were noted with 9 cases (7.3%) having a fatal course. The use of high-potency first-generation antipsychotics, anticholinergics, opiates, tricyclic antidepressants, increasing age, and female sex were associated with increased risk of developing ileus in patients with schizophrenia [9]. According to Palmer et al. [10], review of literature showed that antipsychotic clozapine can affect the entire gastrointestinal system and may cause bowel obstruction, through a mechanism likely to be anticholinergic and antiserotonergic.

Our patient on presentation did not show the typical features of fever and rigidity, rather acute abdomen with ileus, necessitating exploratory laparotomy. During the course of admission, he eventually manifested delayed fever and rigidity, but valuable hours had been lost due to the early diagnostic challenge. Our goal is to highlight the importance of having a high clinical suspicion for NMS even with atypical presentations, given that with this disease entity, timely recognition is essential. Furthermore, we also want to emphasize vigilance for the afebrile or delayed fever variant of NMS, as was the case with our patient. This approach does not diminish the importance of recognizing typical clinical symptoms and laboratory investigations that define NMS. Attempts should also be made to pursue and exclude other differential etiologies of ileus and/or fever. In our case, other causes of fever were excluded, and review of anesthetic notes did not reveal any medications used during general anesthesia that could cause malignant hyperthermia.

After a diagnosis of NMS has been made, the general principles of management include biological approach and parallel supportive therapy [11]. Supportive therapy starts with withdrawal of offending agent, cooling measures to manage hyperpyrexia, adequate intravenous hydration, and antihypertensive and/or anxiolytics for autonomic hyperactivity. Biological approach has traditionally been with dantrolene, a skeletal muscle relaxant, and bromocriptine, a dopamine agonist, with varying results [12]. Our patient had improvement of fever and rigidity with dantrolene, but cardiorespiratory status continued to decline until he expired. Acute respiratory failure is the strongest independent predictor of mortality [13]. Other prognostic factors include acute renal failure, coexisting heart failure, and infections [5].

Conclusion

NMS, though rare, has had a declining incidence, partly due to more recognition by physicians of typical presentations of fever and muscle rigidity. Atypical NMS remains a diagnostic

challenge. Delay in diagnosis due to unusual presentation, as in our index case, ileus with acute abdomen, and delayed fever can result in delay in appropriate management. We want to encourage physicians to have a high index of suspicion and vigilance in patients on antipsychotics and consider the wide range of sympathoadrenal hyperactivity symptoms that can herald NMS. Management still involves symptomatic or supportive therapy, bromocriptine, and dantrolene. The role of a multidisciplinary team in management, cardiology, neurology, infectious disease, psychiatry, critical care, and surgery can also not be overemphasized. The majority of patients will improve within days to weeks of therapy [12], but complications like end organ damage can progress to fatalities.

Statement of Ethics

There were no ethics violations in the writing of this case report; patient confidentiality was maintained.

Disclosure Statement

The authors have no conflicts of interest and no competing interests to disclose.

References

1 Patel U, Agrawal M, Krishnan P, Niranjan S. Neuroleptic malignant syndrome presenting as pulmonary edema and severe bronchorrhea. J Natl Med Assoc. 2002 Apr;94(4):279–82.
2 Stübner S, Rustenbeck E, Grohmann R, Wagner G, Engel R, Neundörfer G, et al. Severe and uncommon involuntary movement disorders due to psychotropic drugs. Pharmacopsychiatry. 2004 Mar;37 Suppl 1:S54–64.
3 Caroff SN, Mann SC. Neuroleptic malignant syndrome. Med Clin North Am. 1993 Jan;77(1):185–202.
4 American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC: American Psychiatric Association; 2000 2013. https://doi.org/10.1176/appi.books.9780890425596.
5 Oruch R, Pryme IF, Engelsen BA, Lund A. Neuroleptic malignant syndrome: an easily overlooked neurologic emergency. Neuropsychiatr Dis Treat. 2017 Jan;13:161–75.
6 Khan FY, Qusad MJ. Neuroleptic malignant syndrome. Neurosciences (Riyadh). 2006 Apr;11(2):104–6.
7 American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington (VA): American Psychiatric Publishing; 2013. https://doi.org/10.1176/appi.books.9780890425596.
8 Gurrera RJ. Sympathoadrenal hyperactivity and the etiology of neuroleptic malignant syndrome. Am J Psychiatry. 1999 Feb;156(2):169–80.
9 Nielsen J, Meyer JM. Risk factors for ileus in patients with schizophrenia. Schizophr Bull. 2012 May;38(3):592–8.
10 Palmer SE, McLean RM, Ellis PM, Harrison-Woolrych M. Life-threatening clozapine-induced gastrointestinal hypomotility: an analysis of 102 cases. J Clin Psychiatry. 2008 May;69(5):759–68.
11 Al Danaf J, Madara J, Dietsche C. Neuroleptic Malignant Syndrome: A Case Aimed at Raising Clinical Awareness. Case Rep Med. 2015;2015:769576.
12 Reulbach U, Dütsch C, Biermann T, Sperling W, Thuerauf N, Kornhuber J, et al. Managing an effective treatment for neuroleptic malignant syndrome. Crit Care. 2007;11(1):R4.
13 Modi S, Dharaiya D, Schultz L, Varelas P. Neuroleptic Malignant Syndrome: Complications, Outcomes, and Mortality. Neurocrit Care. 2016 Feb;24(1):97–103.