

## A Case of medication withdrawal induced neuroleptic malignant syndrome

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### Abstract

Given the severity of symptoms and life-threatening nature of Neuroleptic Malignant Syndrome (NMS), it is important for clinicians to be aware of its features. This case also demonstrates the importance of obtaining a thorough history when caring for a patient, as well as properly reconciling home medications, thereby expanding the differential to include NMS and ultimately initiation of proper care for the patient. Thus, when obtaining full medication reconciliation, it is not only crucial to get a list of medications but to ask when the last dose was given.

### Keywords

neuroleptic malignant syndrome; baclofen withdrawal; dantrolene

### Abbreviations

NMS: Neuroleptic Malignant Syndrome; CPK: Creatinine Kinase; ORIF: Open Reduction and Internal Fixation; ECG: Electrocardiogram; CT: Computed Tomography; IV: Intravenous; GABA: Gamma Aminobutyric Acid; CBC: Complete Blood Count; CMP: Comprehensive Metabolic panel

### Introduction

Neuroleptic Malignant Syndrome (NMS) is an extremely rare but life threatening phenomenon associated with certain medications. Prevalence is noted to be anywhere between 0.02%-3%. NMS is more common in men than women [1]. Symptoms include fever, autonomic instability, diaphoresis and blood pressure fluctuation. Elevated creatinine kinase (CPK) is a common laboratory finding. Mortality today is anywhere between 10%-20%, which is a huge decline from the estimated 75% mortality seen in the early 1960's. This decrease in mortality is due to the early recognition in the syndrome and subsequent early treatment; thus illustrating the importance of having a low threshold for suspicion so treatment can be initiated in a timely manner [2,3]. The most discussed cause of NMS is the association with taking "typical" and "atypical" anti-psychotics. There appears to be less published discussion, relatively, about the withdrawal of medication. There have been a few cases published in which withdrawal of medication in perioperative management have been thought to be causes of NMS. Perhaps the rarity of the phenomenon is why abruptly stopping medications continues to occur. The following case will attempt to illustrate how abrupt cessation of anti-spastic medications could have potentiated NMS and thus why it is important to be cautious of stopping medications, especially in peri-operative

management.

## Case Presentation

We present a case of a 17-year-old male with a past medical history of paraplegic immobility syndrome following previous motor vehicle accident with subsequent spasticity, back pain, neurogenic bladder, autonomic and temperature instability. The patient was admitted to the general pediatric service for acute onset of hypotension, fever and hypoxia status post open reduction and internal fixation (ORIF) of right femur fracture. Two hours post-op, a rapid response was initiated when the patient acutely developed temperature of 105 F, tachycardia, hypotension, and hypoxia. He was alert, responsive and diaphoretic. Fluid resuscitation and anti-pyretic control was initiated with a normal saline bolus and acetaminophen. Initial labs, an electrocardiogram (ECG) and a chest x-ray were reassuring, and computed tomography (CT) of chest negative for pulmonary embolus. Upon arrival to the pediatric floor, the patient was alert, warm to touch, diaphoretic, tachycardic and with strong distal pulses, requiring no supplemental oxygen. He exhibited spontaneous clonus in bilateral lower extremities. Family reported this to be the patient's neurological baseline. Upon obtaining further history, mother revealed that he did not receive any of his home medications for four days leading up to surgery, including his anti-spastic medications: Dantrolene and Baclofen. Due to concern for NMS, he was immediately given a one-time dose of IV Dantrolene. His home regimen of Dantrolene and Baclofen were then resumed. Lab work revealed CPK of 1097 with following CK 1547. Aggressive hydration and scheduled anti-pyretic control were initiated. He remained hospitalized for 48 hours with gradually improving symptoms and CPK trends.

## Discussion

NMS is an uncommon phenomenon; but when seen, it is often associated with initiating "typical" antipsychotic medications and anesthesia. The cause of NMS is not well understood. Multiple theories have been published and much of the literature focuses on the correlation with neuroleptic therapy and anesthesia. Less emphasis has been on the withdrawal of medication that can also cause NMS. Withdrawal of Baclofen not only increases muscle tone but also decreases gamma aminobutyric acid (GABA) activity. Decrease in GABA typically causes dysautonomia, altered mental status and fever.

In this particular case, when the rapid response was called, clinicians were appropriately concerned with pulmonary embolism and sepsis. Therefore, work up included Spiral CT, ECG and complete blood count (CBC) with differential and comprehensive metabolic panel (CMP). All of which were within normal limits. Once the patient was transferred, mom provided the accepting pediatric team with a list of the patient's medications, which included Baclofen and Dantrolene. This prompted a more thorough history to be obtained, which unveiled that the patient's Baclofen and Dantrolene had been discontinued four days prior to surgery. Prior to obtaining a more thorough medication history when the patient was transferred, NMS had not been in the differential. Although patient's initial presentation of fever, tachycardia, hypotension and hypoxia could be seen in sepsis or pulmonary embolism, associated spasticity and elevated CPK would point more towards NMS. Once consideration of NMS was made, the patient's management then focused on hydration, anti-pyretics, and IV Dantrolene. His home dose of Dantrolene and Baclofen were also restarted.

An elevated CPK may be due to a multitude of causes, including recent surgery. Rhabdomyolysis has been associated with surgical procedures, specifically orthopedic procedures. Theoretically, the prolonged periods of muscle compression that may be required during orthopedic procedures is believed to lead to an elevated CPK with possible progression to rhabdomyolysis post-op [4]. While this could certainly be the case in our patient, as he had his ORIF hours prior to presentation, there are other aspects of his history and presentation, as discussed above, which prompt the primary team to assess for other causes. In the setting of high fever, spasticity and associated mortality seen in NMS, decision to initiate Dantrolene was made. Dantrolene's effect on hyperthermia is thought to be due to the disassociation of the excitation-contraction coupling effect and thus preventing the dissipation effect created by muscle contraction. Neuroleptic Malignant Syndrome is a diagnosis that is based clinically. Our patient's symptoms of fever, tachycardia, rigidity and clinical history of sudden cessation of Dantrolene and Baclofen certainly fit the criteria of NMS. Resolution of symptoms and elevated CPK with initiation of IV Dantrolene and aggressive hydration also supports the diagnosis of NMS. Our patient's neurological dysautonomia also complicates the picture. Disruption of the sympathetic nervous system can affect thermal regulation via vasomotor changes that can lead to decrease heat dissipation, as well as fluctuations in blood pressure and heart rate [5].

## Conclusion

The case demonstrates the importance of a proper medication reconciliation, especially when considering anesthesia and potential discontinuation of medication prior to various procedures, operations or induction of anesthesia. It is imperative to make the diagnosis of NMS promptly as early detection and intervention has decreased mortality and morbidity.

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