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Case Report

Hold off That Olanzapine! The Development of Neuroleptic Malignant Syndrome in a Dehydrated Pediatric Patient

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INTRODUCTION

Neuroleptic Malignant Syndrome (NMS) is a rare and life-threatening complication of treatment with antipsychotic medications.[1] NMS most commonly develops from antipsychotics and other medications that interfere with dopamine transmission.[2] While typical antipsychotics like haloperidol and fluphenazine more commonly cause NMS, atypical antipsychotics such as olanzapine and aripiprazole also can precipitate this condition.[3-5] A multitude of risk factors can increase risk for NMS, including dehydration, sudden increase or withdrawal of medication, use of restraints, and exhaustion.[6-8] Its complex clinical presentation most often involves some combination of altered mental status, elevated blood pressure, tachycardia, tachypnea, muscle rigidity, and diaphoresis.[6,7] Common sequelae include cardiac arrhythmia, disseminated intravascular coagulation, and respiratory failure.[3,6] Laboratory studies often reveal elevated creatine kinase (CK) levels, myoglobinuria, leukocytosis, and elevated liver function tests.[7,9] If not recognized early, NMS may result in death.

Though well-characterized in adult populations, few reported cases of pediatric NMS exist in the literature. The following case discusses NMS developing in a severely dehydrated pediatric patient after receiving a single dose of olanzapine.

CASE REPORT

An eight-year-old male with a past medical history of autism with severely impaired expressive language, not on any medication, who came to the Emergency Department (ED) with the complaint of nausea, vomiting (non-bloody, non-bilious), and diarrhea (non-bloody) for two days. On physical exam, the patient appeared ill, pale, and fatigued. Initial labs showed an elevated white count and increased anion gap metabolic acidosis. After ruling out appendicitis with an abdominal X-ray and CT scan, the hospital physicians administered a bolus of intravenous (IV) fluids and started him on maintenance fluids, then admitted him for further management given chronic poor oral intake and dehydration.

During his stay in the ED, the patient became physically aggressive, ripping out his IV, pulling his mom's hair, biting her, and attempting to bite the nurse. He received 5 mg of olanzapine oral dissolving tablet (ODT) as a sedating measure, but he soon grew increasingly aggressive and had a dystonic reaction involving an oculogyric crisis and stiffening of his legs. The medical team transferred him to the inpatient unit to observe if he would improve with oral fluid intake.

During this time, the patient continued to have diarrhea and worsening muscle rigidity. Within a few hours, he became tachycardic and tachypneic. His mental status acutely worsened to the point of obtundation. Labs revealed severe metabolic acidosis, leukocytosis, thrombocytosis, and a critically low glucose.

Following transfer to the Pediatric Intensive Care Unit (PICU), his hypoglycemia resolved with a 5 mL/kg D10 bolus, though his acidosis worsened. Repeat laboratory studies showed lactic acid increasing from 7.5 to 9.3, as well as a CK of 12,039. Elevated INR and transaminitis prompted a workup for acute liver failure that did not elucidate a specific cause; likewise, blood cultures demonstrated no growth of any microorganisms, and a head CT was unremarkable. Extensive genetic testing did not reveal any diseases of metabolism. Excluding these other causes indicated that NMS secondary to olanzapine likely caused his clinical deterioration.

He received sodium bicarbonate to correct his acidosis, an empiric dose of vancomycin and ceftriaxone, as well as Vitamin K, Rifaximin, and emergent plasma exchange. His hypotension required three vasopressors (epinephrine, norepinephrine, and vasopressin) to correct. After three days in the PICU, he achieved medical stability. Discharge occurred after one week of hospital stay.

DISCUSSION

NMS is a fatal complication that most commonly happens after initiating antipsychotic medications, taking anywhere from a few hours to weeks to develop.[6,10] Increased dopaminergic D2 receptor antagonism in the central nervous system creates a series of dysregulated homeostatic responses like fever, altered mental status, and muscular rigidity.[8]

Prior studies have noted that dehydration can predispose towards NMS.[6-8,11] In one case, a two-year-old girl presenting with nausea, vomiting, and dehydration received high-dose metoclopramide (dopamine D2 receptor antagonist) and developed NMS within two hours.[10] In another, a six-year-old girl with dehydration developed NMS after receiving the typical antipsychotic thioridazine.[12]

Our eight-year-old patient received a single 5 mg dose of olanzapine for acute agitation. After this, the patient developed tachycardia, tachypnea, altered mental status, and muscle rigidity, classic symptoms of NMS. Furthermore, our patient exhibited increased CK levels and leukocytosis, important diagnostic features of NMS, as well as characteristic electrolyte abnormalities, increased anion gap metabolic acidosis, acute kidney injury, acute liver failure, hypotension, and coagulopathy.[1,4,6,7,13,14]

During episodes of acute agitation, pediatric patients can receive three classes of medications: antihistamines, benzodiazepines, and atypical antipsychotics.[15] Though the FDA only has approved risperidone and aripiprazole for irritability in patients with autism, many EDs administer olanzapine to pediatric patients who exhibit such severe agitation that they pose a danger to themselves or others, as occurred in this case.[16,17] However, while 5 mg of olanzapine is a reasonable dose for acute agitation in most individuals, it triggered NMS in this antipsychotic-naïve, underweight, and severely dehydrated patient. It is vital to assess for environmental risk factors on a case-by-case basis before prescribing antipsychotic medications to reduce risk for this potentially deadly sequela.

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Keywords: Neuroleptic Malignant Syndrome, autism, agitation, dehydration, antipsychotics