Atypical presentation of Neuroleptic Malignant Syndrome in a middle-aged female receiving Ziprasidone for Autism Spectrum Disorder

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Case Presentation

•26-year-old female with history of Autism Spectrum Disorder and seizure disorder (last seizure 2 weeks prior) presented to the emergency department with agitation, combativeness and tachycardia.

• Home Medications: Lorazepam, Desvenlafaxine, Fluoxetine, Ziprasidone, Clomipramine, Buspirone

•Patient placed into restraints in the ER. Administered medications: Haldol 10 mg IM, Versed 2 mg IM, Cogentin (Benztropine) 1 mg IM. After 90 minutes, patient continued to be awake, agitated and combative. Geodon (Ziprasidone) 20 mg IM was administered. Subsequently, patient fell asleep for 20 minutes and then became more agitated with noted rigidity of the upper extremities. Versed 5 mg IM was administered.

• At time of admission: Temperature: 38.2 C, Respiratory rate: 18, Heart Rate: 123, Blood Pressure: 127/71. Physical exam noted to have rigidity, especially in upper extremities. No diaphoresis, neurological exam was intact.

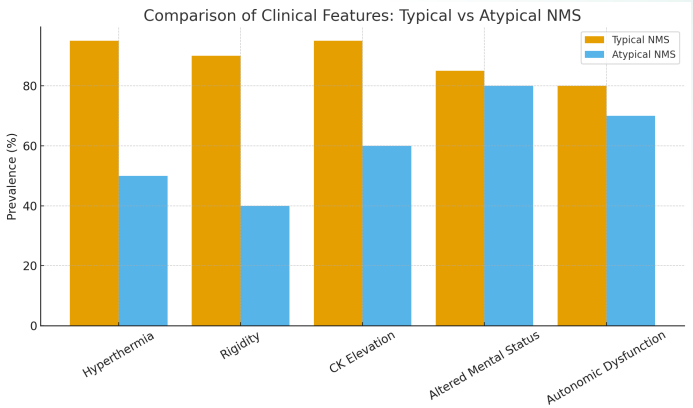
• Neurology was consulted and noted the patient to be extremely restless and agitated. Cranial nerve examination: pupils were 4 mm, equal and reactive. Extra ocular movements were intact. Motor examination and muscle tone were within normal limits. Reflexes were 2/4. Sensory exam was intact.

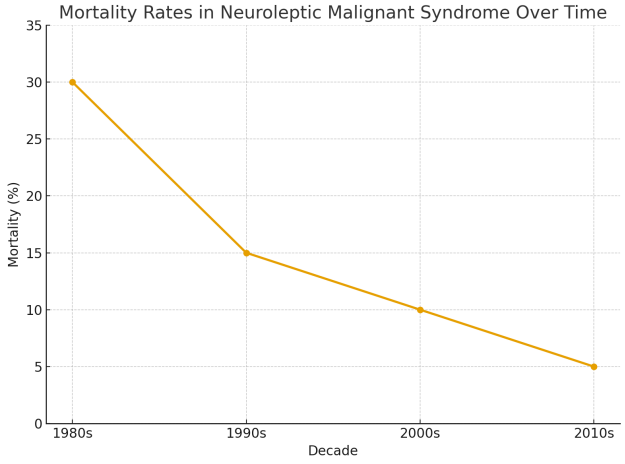
• She remained afebrile and had no muscle rigidity throughout the hospitalization. Labs revealed elevated creatine kinase levels > 2,000 IU/L over a 3 day hospital stay.

• Symptoms improved with immediate discontinuation of antipsychotics and supportive treatment, supporting a diagnosis of atypical NMS.

• https://pmc.ncbi.nlm.nih.gov/articles/PMC7953912
• https://pmc.ncbi.nlm.nih.gov/articles/PMC11268033
• https://pmc.ncbi.nlm.nih.gov/articles/PMC9392844

Clinical features of typical vs. atypical NMS





Results

•Creatinine Kinase Trend (IU/L): 2,902–> 2,246—>3,073—>4,195—> 2,752—>3,130—>2,478

• EEG: No epileptic activity

• MRI Brain: Normal brain morphology

Discussion

- Neuroleptic Malignant Syndrome is a rare, potentially fatal reaction to dopamine antagonists, particularly first-generation antipsychotics with an incidence of approximately 0.01–0.02% in patients treated with antipsychotics.
- Classical tetrad by using diagnostic criteria such as DSM-5 and Levenson's criteria includes: hyperthermia, generalized muscular rigidity, altered mental status, autonomic dysfunction (e.g., tachycardia, BP fluctuations).
- Emergence of Atypical NMS with the increased use of second-generation (atypical) antipsychotics (e.g., clozapine, quetiapine, olanzapine) with reported absent or minimal rigidity, no hyperthermia, normal or mildly elevated CK levels, slow or insidious onset.
- In this particular case, addition of atypical antipsychotic medication Ziprasidone may have caused atypical NMS.
- Failure to diagnose atypical NMS may lead to **increased morbidity or mortality**. Raising awareness through **case reports** is essential for updating diagnostic approaches and consideration.
- Atypical NMS should be considered even in **non-classic** scenarios, especially with **recent changes in antipsychotic therapy**.