Neuroleptic Malignant Syndrome in the Setting of Severe Hypernatremia: A Diagnostic Challenge

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Abstract

Neuroleptic malignant syndrome (NMS) is a rare, life-threatening reaction to dopamine antagonists that can be difficult to recognize in medically complex patients. A 39-year-old incarcerated male presented with altered mental status and severe hypernatremia. Mental status partially improved with sodium correction; however, persistent delirium led to antipsychotic initiation. The patient subsequently developed NMS. Antipsychotics were discontinued, and supportive management resulted in clinical improvement. In this case, initial improvement after correction of hypernatremia obscured the development of neuroleptic malignant syndrome. Worsening symptoms despite laboratory improvement should prompt reconsideration of the diagnosis, as early recognition and discontinuation of the offending agent are critical.

Introduction

- NMS is a rare, life-threatening reaction to dopamine antagonists
- Presents with hyperthermia, rigidity, autonomic instability, altered mental status
- Diagnosis is difficult in medically complex patients
- Metabolic derangements (e.g., hypernatremia) may make diagnosis difficult

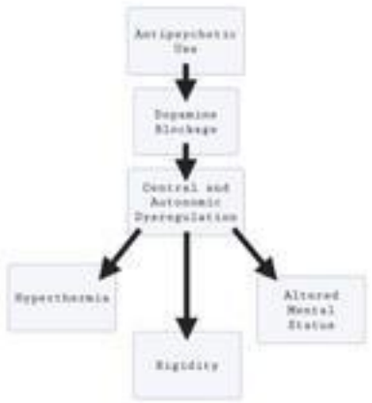

Figure 1. Pathophysiologic mechanisms of neuroleptic malignant syndrome, including central dopaminergic dysfunction and its clinical manifestations.

Results

B.

Phase	Key Events	Clinical Interpretation
Presentation	AMS, dehydration, agitation Na 158–166, AKI, leukocytosis	Severe metabolic derangement + hypernatremia causing encephalopathy
Early Hospitalization	IV fluids initiated, sodium corrected Na + to ~160	Partial improvement supports metabolic cause
Persistent Symptoms	Ongoing delirium despite improving labs	Hypernatremia alone insufficient
Psychiatric Management	Antipsychotics initiated	New dopamine blockade exposure
Clinical Deterioration	Fever, tachycardia, diaphoresis, rigidity + CK + (~1000)	Classic NMS features emerging
Intervention	Antipsychotics discontinued and supportive care initiated	Treatment of NMS
Recovery	CK downtrending, mental status improves	Confirms NMS diagnosis
Disposition	Stabilized, discharged, antipsychotic restarted	Safe recovery

Figure 2. Clinical timeline of the patient's hospital course demonstrating initial presentation with hypernatremia and altered mental status, followed by partial improvement with sodium correction, and subsequent clinical deterioration after antipsychotic initiation leading to neuroleptic malignant syndrome.

C.

D.

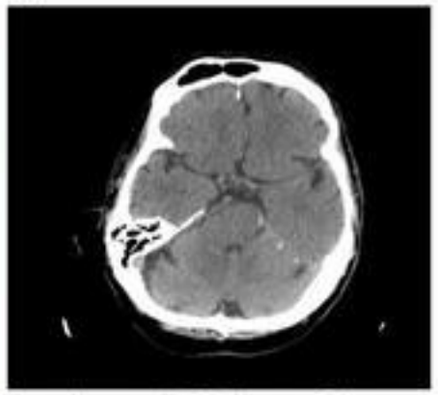

Figure 3: Medical causes of altered mental status ruled out **C.** Sinus rhythm and nonspecific ST changes **D.** No acute intracranial pathology and no cerebral edema

E.

Parameter	9/2/24 (ED)	9/2/24 (evening)	9/3/24	9/5/24	9/6/24	9/11/24	9/9/24-9/10/24
WBC ($10^3/\mu L$)	24.2	—	—	—	—	—	—
Sodium (mmol/L)	**158**	**166**	**160**	**—**	**—**	**—**	**140-145**
Potassium (mmol/L)	4.1	5.3	3.4	—	—	—	—
Chloride (mmol/L)	118	127	125	—	—	—	—
BUN (mg/dL)	97	92	70	—	—	—	—
Creatinine (mg/dL)	**2.3**	**2.9**	**1.5**	**—**	**—**	**—**	**—**
Creatine Kinase (U/L)	—	—	—	**1000**	**545**	**559**	**371**

Figure 4: Laboratory trends over the hospital course demonstrating initial severe hypernatremia with subsequent correction, followed by delayed elevation in creatine kinase corresponding to the onset of neuroleptic malignant syndrome.

Discussion

- The patient's initial altered mental status was likely due to severe hypernatremia, consistent with metabolic encephalopathy
- Early improvement with sodium correction supported this working diagnosis and led to a focus on a metabolic cause
- However, continued and later worsening symptoms despite improving labs signaled that something else was going on
- After starting antipsychotic therapy, the patient developed fever, rigidity, autonomic instability, and an elevated creatine kinase
- This clinical picture was concerning for neuroleptic malignant syndrome (NMS) as a superimposed process rather than ongoing metabolic encephalopathy
- Underlying dehydration, acute kidney injury, and overall physiologic stress may have increased the patient's risk for developing NMS
- The overlap between metabolic encephalopathy and NMS made the diagnosis more difficult and likely delayed recognition

Conclusion

- Neuroleptic malignant syndrome can be difficult to recognize when metabolic abnormalities like hypernatremia are present at the same time
- Early improvement after correcting electrolyte abnormalities may be misleading
- When clinical symptoms don't improve as expected, the diagnosis should be reconsidered
- Prompt recognition of NMS and stopping the offending medication are key to improving outcomes

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