A Case Report on Atypical Presentation of Neuroleptic Malignant Syndrome

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Background

Neuroleptic Malignant Syndrome (NMS) is a condition of unknown etiology, hypothesized to be a result of dopamine receptor blockade in the hypothalamus and disturbance in dopamine neurotransmission in the nigrostriatal pathway [2]. The classic presentation is fever, rigidity, mental status changes and autonomic instability [1] following the use of a first generation, high potency antipsychotics such as fluphenazine and chlorpromazine. Second generation antipsychotics, such as risperidone, have also been implicated in the development of NMS, although in the latter, the classic tetrad may be absent. This atypical presentation of NMS is more commonly seen with the use of low potency antipsychotic medications or earlier diagnosis. In the case of early diagnosis, the four cardinal symptoms may present individually, and diagnosis can be made if two of the four symptoms are present [5]. Additionally, isolated signs of dysautonomia, hyperthermia, Parkinson-like rigidity and creatinine kinase (CK) elevations may be the only presenting signs. CK elevations, leukocytosis, liver function test (elevated ALT/AST), basic metabolic panel showing hyponatremia and hypocalcemia can help support the diagnosis of atypical NMS in suspected cases. CK elevation is a reflection of the amount of rigidity occurring, therefore if rigidity is not well developed, CK levels may lower than expected. Additional characteristics of NMS are myoglobinuria, indicative of rhabdomyolysis [5]. Dehydration is a risk factor for the development of NMS [1] and was present in 92% of cases [5]. The main goals of treatment include immediate discontinuation of the offending agent, adequate fluid resuscitation to prevent renal impairment and the use of benzodiazepines to control agitation with dantrolene in moderate-severe cases, followed by the addition of bromocriptine or amantadine. Other treatment measures include maintaining cardiorespiratory stability, temperature and blood pressure reduction, if elevated and heparin to prevent DVT [5]. Atypical NMS, although infrequent, is a useful differential to have in the setting of a patient on antipsychotic therapy who presents with isolated symptoms of NMS as will be discussed in this case.

Case Report

Initial Presentation

A 67-year-old male with a past medical history significant for Bipolar I Disorder on Risperidone 1mg PO BID and Carbamazepine 600mg PO QD presented to the ED for altered mental status (AMS). The week before current admission Risperidone 1mg PO BID was added to his bipolar 1 medications. At presentation, he was mostly non-verbal with a GCS of 13. On physical exam, he had tachycardia, dry mucous membranes as well as tremors in his upper and lower extremities. No rigidity or hyperpyrexia was present. He was otherwise hemodynamically stable. A head CT without contrast excluded the possibility of acute hemorrhage, mass effect or large infarct. His CXR was unremarkable. He was subsequently admitted for acute on chronic kidney injury, dehydration and AMS and treated in the ED with 2 L of NS and 1 gram of Rocephin due to mild elevations in WBC count. It is not known how long he was in a state of dehydration and AMS prior to arrival at the ED.

Initial Presentation Tests & Results:

CBC: WBC: 12.3 RBC: 4.57 Hct: 37.5 Hgb: 12.9
BMP: Na: 149 K: 5.1 Cl: 112 CO2: 19 Ca: 9.4 BUN:114 Cre: 3.7 Gluc: 369
Anion Gap: 18 mmol/L (7-15)
Urinalysis: small amount of blood, no RBC, no WBC, nitrate negative. Few bacteria.
Urine Myoglobin: 91 (<=21)
Urine Drug Screen: Negative
Serum Osmolality: 336 MOSM/KG H2O
Ammonia: 26 UMOL/L (9-35)
Carbamazepine Level: <2.1 (4-12) uG/ML
Glasgow Coma Scale: 12
EKG: Sinus tachycardia, nonspecific ST abnormality
Echo: EF 65-70% with no regional wall motion abnormalities.
Head CT: No acute hemorrhage, significant mass effect or large infarct.

Case Report Cont.

Course:

Day 1 & 2: Bilateral upper and lower extremity tremors present. In the ED, patient was started on Lactated Ringers 150mL/hour and given 1g Rocephin and Benadryl 50mg IV. Antipsychotic medications were held. Psychiatry, Nephrology and Neurology were consulted. Ativan 1mg IV q6hours scheduled and IV hydration.

Day 3: Patient continued to have tremors in upper and lower extremities. Rigidity present in upper extremities. IV fluids (Lactated Ringers) decreased from 150 mL/hr to 100 mL/hr. Ativan 1mg IV q6hours scheduled.

Day 4 & 5 : Patient more awake and oriented. Tremors reduced. Rigidity present in upper extremities. 90 degree abduction of both upper extremities reduced. Ativan dosage reduced from 1mg q6hours scheduled to 0.75mg IV q6hours scheduled. Propranolol restarted on Day 5 for blood pressure management, tremors and anxiety.

Day 6: B/L upper extremity rigidity improved from Day 5 with minimal tremors present. Ativan 0.75 IV q6hr scheduled.

Day 7 & 8: B/L upper extremity rigidity and tremor both improving, similar to Day 5. Patient has LLE stiffness. Ativan 0.75 IV q6hr scheduled.

Day 9: Muscle rigidity in upper extremities improved. Ativan decreased from 0.75mg IV q6hours to 0.5mg PO q6hours per psych recommendation.

Day 10: Muscle rigidity in upper extremities and tremor improved. Carbamazepine (Tegretol) 300mg QHS started. Ativan 0.5mg PO q6hours.

Day 11: Muscle rigidity in upper extremities and tremor improved. Carbamazepine (Tegretol) increased from 300mg QHS to 600mg QHS per psych recommendations. Ativan 0.5mg PO q6hours.

Day 12: Muscle rigidity in upper extremities and tremor improved. Ativan tapered from 0.5mg q6hours to 0.5mg q8hours.

Day 13 to Day 28: patient continued to improve, and psychiatry continued to be consulted. Per psychiatry recommendations, patient was discharged on 0.5mg Lorazepam.

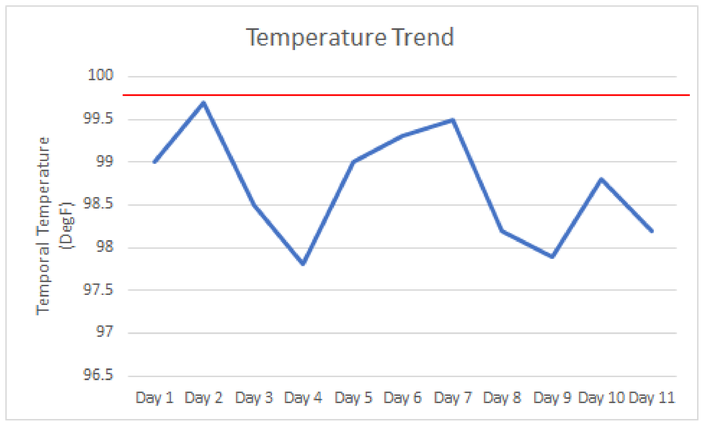

Figure 1: Temperature Trend

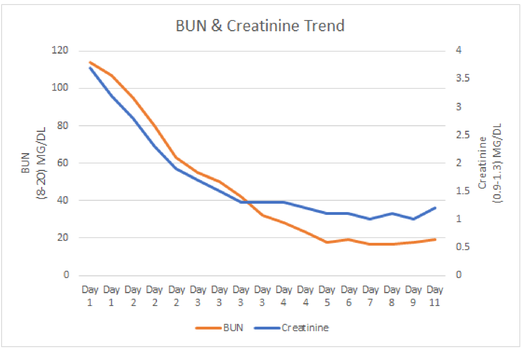

Figure 2: BUN and Creatinine Trend

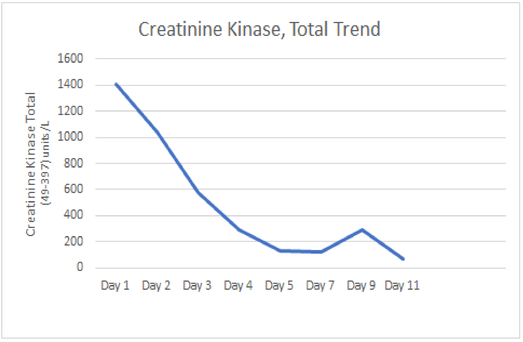

Figure 3: Creatinine Kinase Total Trend

Learning Points

- NMS has an unknown etiology but is thought to occur due to dopamine receptor blockade in the hypothalamus and disturbance in dopamine neurotransmission in the nigrostriatal pathway.
- Atypical NMS does not always present with a high fever.
- Second generation antipsychotics are more likely to precipitate an atypical presentation in which only two of the four symptoms are required to make a diagnosis.
- The main goal of treating NMS includes discontinuing the offending agent(s), fluid resuscitation and the use of benzodiazepines (lorazepam or diazepam), with dantrolene in moderate-severe cases, followed by the addition of bromocriptine or amantadine.
- Lastly, it is recommended to wait at least 2 weeks to begin antipsychotic medications [4]. It is recommended to start at low doses or switch the offending agent.

Conclusion

Our case demonstrates that NMS has varying presentations. If healthcare professionals are not vigilant of atypical NMS, a delay in treatment can have severe consequences such as renal failure. The goal in treatment is to stop the offending agent, fluid resuscitation and benzodiazepine administration. With adequate treatment, NMS should resolve within two weeks, as seen in this case.

References

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