

Neuroleptic Malignant Syndrome (Case Presentation)

Terad Talmesany M.D

(Department of Family and Community Medicine, Faculty of Medicine, AlBaha University, Kingdome of Saudi Arabia)

Abstract: Neuroleptic malignant syndrome (NMS) is an uncommon but potentially fatal adverse effect of neuroleptic drugs. It is commonly characterized by muscular rigidity, fever, altered mental status, and autonomic dysfunction. Its pathophysiology is not clearly understood, but the blockade of dopamine receptors appears to be the central mechanism. The presented case is for a patient who suffered from severe depression and was getting worse despite being on treatment. Being on many neuroleptic medications of high dosages and presenting with agitation and being combative against the medical staff in the Emergency Department, the patient got exposed to high doses of antipsychotic medications. The patient condition got complicated with NMS and multi-organ failure due to undiagnosed severe Aortic stenosis and cardiogenic shock.

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I. Introduction

There are various sets of criteria to aid in the diagnosis of NMS. These are primarily useful as research tools to help assure consistent diagnosis of NMS. However, the clinical diagnostic standard is set by DSM-IV-TR criteria. For a diagnosis of NMS, the required criteria are the development of severe muscle rigidity and elevated temperature associated with the use of neuroleptic/antipsychotic medications not caused by other substances, medical conditions, or mental disorders. Additionally, ≥ 2 of the following symptoms must be present: diaphoresis, dysphagia, tremor, incontinence, changes in the level of consciousness, mutism, tachycardia, labile blood pressure, leukocytosis, and evidence of muscle injury (elevated CK).

II. Case Presentation

A 60-year-old male presented to the Emergency Department (ED) with confusion and agitation. According to family members who were with him he had a worsening depression over four months. He was started on paroxetine, amitriptyline, and risperidone by his primary care physician over the same period, while maximizing the dose of each of the provided medication since the patient did not experience any improvement of his symptoms. In the ED, he was treated with haloperidol 5 mg IV x 2, loaded with Benadryl 100mg and morphine 4 mg IV x 2 per the ED physician since the patient was very agitated and combative. Pertinent physical exam findings were, BP: 89/54, HR: 99 bpm, RR: 20/min, temp:36.9C, O2 sat 99% RA, agitated at the beginning but sleepy and unresponsive after the was given the IV medications in the ED.

His course during hospitalization after he was admitted to the intensive care unit (ICU) was complicated with respiratory distress then failure that required ventilation, a fever 41.6 C for which the patient was given Dantrolene and all neuroleptic/ antipsychotic medications were stopped, and later the patient newly diagnosed with severe Aortic Stenosis and developed a cardiogenic shock, Renal, and hepatic failure. The patient was on supportive measures but was deteriorating and died during hospitalizations.

III. Laboratory Result

Table no 1: Shows Blood investigations parameters of the patient with the NMS.

CBC		Chemistry		LFTs		Other Labs	
WBC	13.2	Sodium (Na)	135	T.Bili	2.7	Serum iron	12
Hgb	14.3	Potassium (K)	5.5	T.Protein	7.9	Iron Saturation	4
Hct	49	Chloride (Cl)	98	Alk Phos	86	LDH	229
Plt	100	CO2	25	AST	56	CPK	844
MCV	95	BUN	65	ALT	24	Procal	0.17
Seg	80.2	Creatinine	2.23	Albumin	3.6	CRP	4.60
Lymph	9.7	Glucose	143	-	-	TSH	0.58

IV. Discussion

Serotonin Syndrome (SS) can present as a change in the mental status, a disturbance of the autonomic nervous system, neurologic abnormality, and hyperthermia. Similarly, NMS presents as muscle rigidity, hyperpyrexia, mental status changes, and autonomic instability. However, the clinical laboratory profile of elevations in CK, liver function tests (LDH, AST), and WBC, with a low serum iron level, can help in differentiating NMS from SS among patients taking neuroleptic and serotonin agonist medications simultaneously. For both SS and NMS, immediate discontinuation of the causative agent is the primary treatment, along with supportive care.

All dopamine-blocking drugs are capable of precipitating NMS. Even Clozapine, an antipsychotic with a very low affinity for dopamine-2 (D2) receptors in the nigrostriatal tracts. Additionally, the abrupt withdrawal of dopaminergic agonist drugs used to treat Huntington's disease and Parkinson's disease, such as Levodopa and Amantadine has been shown to produce NMS-like conditions.

Numerous hypotheses have been proposed to explain the pharmacologic mechanisms of NMS. However, the distillation of these hypotheses results in 2 different explanations of NMS pathophysiology. The first emphasizes CNS neurotransmission aberrations and the role of dopaminergic hypofunction in particular. The second endorses peripheral sympathetic autonomic nervous system hyperactivity as the primary culprit. Regardless, none of the hypothesized mechanisms fully explain the signs and symptoms of NMS.

Muscle rigidity, hyperpyrexia, mental status changes, and autonomic instability are all known cardinal symptoms of NMS, where patients suffering from the condition can present with most of these symptoms but not necessarily all of them. "Lead pipe" rigidity is the most common neurologic finding, but rigidity may present in a less severe form, such as akinesia, dyskinesia, waxy flexibility, or cogwheel rigidity. Fever or hyperpyrexia usually exceeds 38°C and occasionally exceeds 41°C.

Elevated serum CK is typically more than 1000 IU/L. Other nonspecific lab findings are Leukocytosis, with a WBC typically 10,000 to 40,000. Mild elevations of LDH, ALP, and liver transaminases. Electrolyte abnormalities like hypocalcemia, hypomagnesemia, hypo and hypernatremia, hyperkalemia. Myoglobinuric acute renal failure can result from rhabdomyolysis. Low serum iron is a sensitive (92 to 100 %).

Management includes Supportive management, Maintaining cardiorespiratory stability, and the administration of Dantrolene. Complications are Rhabdomyolysis, Renal failure, Cardiovascular arrhythmias and collapse, Hepatic failure, and Death.

V. Conclusion

NMS is a rare but life-threatening idiosyncratic reaction to neuroleptic medications characterized by fever, muscular rigidity, altered mental status, and autonomic dysfunction. It often occurs shortly after the initiation of neuroleptic treatment or after dose increases. In the absence of rhabdomyolysis, renal failure, or aspiration pneumonia, and with good supportive care, the prognosis for recovery is good. The mortality rate is reported at 20-30%. Rises to about 50% if complicated by renal failure.

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