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AMISULPRIDE INDUCED NEUROLEPTIC MALIGNANT SYNDROME: A CASE REPORT

Emergency Medicine

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ABSTRACT

Neuroleptic malignant syndrome (NMS) is rare but lethal complication of neuroleptics. An atypical antipsychotic like amisulpride may be associated with NMS by blocking dopamine receptors. Conventional presentations include hyperthermia, muscle rigidity and elevated creatine kinase level. The syndrome often occurs after sudden increase in dosage of neuroleptic drug or in state of dehydration. Treatments of NMS is mainly supportive and include withdrawal of potentiating neuroleptic or antipsychotic medication and administration of directly acting skeletal muscle relaxant like dantrolene and centrally acting dopamine agonist like bromocriptine. Complications of NMS include acute renal failure and acute respiratory failure. In this article we report a case of 47 years old male suffering from schizophrenia who is on neuroleptic medication for last 20 years presented with signs and symptoms consistent with NMS.

KEYWORDS

Neuroleptic malignant syndrome, schizophrenia, neuroleptics, amisulpride, atypical antipsychotic.

Case report:
A 47 years old male with schizophrenia was admitted to emergency medicine department who has been taking,

- Tab. Clonazepam(100mg) daily,
- Tab. Aripiprazole(15mg)daily,
- Tab. Lorazepam (4mg) daily since last 20 years.

Before 15 days, He was started with Tab. Amisulpride (100mg) and Tab.Quetiapine (200mg) addition to his daily regimen for worsening of symptoms. After which patient developed high grade fever, muscle rigidity and altered mental status in a span of 10 to 12 days.

On admission patient's temperature was 104 f, had tachycardia (100/min), high blood pressure (160/90mmhg). On CNS examination, patient was drowsy and not following verbal command, terminal neck rigidity was absent, pupils were bilateral equal size & reacting to light, lead pipe rigidity and hypereflexia were present.

Laboratory investigation revealed leucocytosis (WBC- 36.13/mm3) with elevated CRP (32.3 mg/l), hyperkalemia (5.40 mEQ/L). Creatine kinase level was markedly elevated (19,290 IU/L) with normal renal function, liver function and CSF study.

His body temperature was elevated but source of infection was not evident. Strong suspicion of NMS was made according to diagnostic criteria. Neuroleptic medication was stopped. Patient was treated with IV hydration, external cooling measures, other supportive treatment and Tab. Bromocriptine (2.5mg 3 times a day through RT) and inj. Dantrolene (60 mg iv qid) was started.

On the next day, patient became breathless and saturation was dropped so patient was intubated and put on the ventilatory support. Patient was gradually weaned off from the ventilatory support over a period of few days. Serial CPK levels were sent which were in decreasing titre (19,290 IU/L->2119 IU/L->528 IU/L). Over a period 10 days patient fully regained lucidity and no hyperreflexia. Fever was improved. After 12 days, patient was discharge from the hospital without any complications.

Discussion:
NMS is an infrequent but potentially life threatening neurological emergency associated with use of neuroleptic or antipsychotic medication. It was first declared with use of neuroleptic medication haloperidol in 1960. Incidence rate of NMS ranges from 0.02 to 3% among the patient taking neuroleptic drug.[1,2] Amisulpride is an atypical antipsychotic. Only two cases of amisulpride induced NMS have been reported till date.[8]

The pathogenesis of NMS is still unclear. Dopamine receptor blockade play an important role in two major theories of NMS: 1) alteration of central neuro-regulatory mechanism. 2) Abnormal reaction of predisposed skeletal muscle.

The four definitive features that characterize NMS are:
1) Motor symptoms: rigidity (lead pipe), akinesia, bradykinesia, dystonia, dysarthria, tremors [1]
2) Altered metal status
3) Hyperthermia
4) Autonomic instability: respiratory irregularity, cardiac arrhythmias, varying blood pressure, incontinence, diaphoresis [1,4].

The laboratory abnormalities that are present in NMS are elevated creatine kinase, leucocytosis, elevated LDH, increase alkaline phosphatase, increase ALT, electrolyte abnormalities like hypocalcaemia, hypomagnesaemia, hypo/hyper natremia, hyperkalemia and metabolic acidosis are frequently observed. Low serum iron concentration is seen is sensitive but not specific for NMS. Pharmacological risk factors of NMS include high dose of neuroleptic medication, parenteral administration and rapid dose titration. Other risk factors include high ambient temperature, male sex, young age, past history of NMS, trauma , alcohol intake, female in premenstrual phase and thyrotoxicosis.[5]

Diagnostic criteria for NMS [6]

Major	Fever >38 c, measured orally on at least two occasion Lead pipe muscle rigidity Psychomotor slowing and altered mental status Sympathetic nervous system liability (2 or more features) • Elevated blood pressure • Blood pressure fluctuation

	• Diaphoresis • Urinary incontinence Recent dopamine antagonist exposure or dopamine agonist withdrawal
Minor	Increase creatine kinase level (>4*upper limit) or myoglobinuria Tachycardia Tachypnea Hypersalivation Tremor Muscle cramps
Exclusionary criteria	No other infectious, toxic, metabolic, or neurologic cause identified

NMS usually develop in the first 2 weeks of neuroleptic therapy. Amisulpride induced NMS develop earlier, in range of 1-4 days after exposure. Amisulpride Induced NMS also resolved within 2 weeks, similar to typical NMS.

Complication associated with NMS [5,7]

- Rhabdomyolysis
- Acute renal failure
- Acute respiratory failure
- Seizure
- Brain damage
- Myocardial infarction
- DIC
- Hepatic failure
- Sepsis
- Escherichia coli fasciitis

Treatment of NMS [6]

- Withdrawal any antipsychotic and potentiating drug, such as anticholinergic, antihistaminic or lithium
- IV hydration to restore circulating volume and maintain urine output
- Reduce the patient's temperature with external cooling measures
- Sedation with benzodiazepines, such as lorazepam, 1-2 mg iv every 2-4 h as needed
- Airway protection: consider early intubation, especially if hypersalivation is present
- Nondepolarizing neuromuscular blocking agent
- Consider agent to reduce severe muscle rigidity
- Dantrolene, 1.0-2.5 mg/kg IV load, f/b 1 mg/kg IV 6h or
- Bromocriptine, starting with 2.5 mg PO 3-4 times a day or
- Amantadine, 100 mg PO 3 times a day

Conclusion:

As we are working in a region which is endemic to so many disorders causing altered sensorium and high grade fever. History taking, physical examination and disease specific knowledge play a major role to establish diagnosis. Neuroleptic malignant syndrome commonly occurs with typical antipsychotic but it may also occur with atypical antipsychotics. Neuroleptic malignant syndrome is a medical emergency. The prognosis is best when identified early and treated aggressively.

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