CASE REPORT

Neuroleptic malignant syndrome: A case report

Muhammad Kashif, Asad Tamizuddin Nizami, Kainat Kareem Mirza

Abstract

Neuroleptic malignant syndrome is a serious adverse drug reaction associated with antipsychotic medications. The cause is dopamine blockade caused by these drugs. We are presenting the case report of a 25-year old male patient, who presented to our psychiatry emergency facility, with post-ictal behavioural disturbances. He required rapid tranquilization and subsequently developed symptoms of NMS due to the first-generation antipsychotics. His creatinine phosphokinase levels were markedly elevated, reaching 89900 and 105000 at different points. Early diagnosis and prompt management played an important role in his recovery. This case emphasizes the importance of early diagnosis and treatment to reduce mortality and morbidity associated with NMS. The withdrawal of antipsychotics is the mainstay of management, along with supportive treatment.

Keywords: Neuroleptic Malignant syndrome (NMS), Creatinine Phosphokinase level (CPK), 4 times a day (QID).

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Introduction

Neuroleptic malignant syndrome is an adverse drug reaction associated with antipsychotics. It presents with classic clinical features i.e., muscle rigidity, hyperthermia, autonomic dysregulation and altered mental state. Laboratory findings include myoglobinuria, leucocytosis and electrolyte imbalance.[1] The pathophysiology is not completely understood, but the cause may be decreased dopamine levels. The first-generation antipsychotics cause a stronger D2 antagonism as compared to the second-generation antipsychotics.[2] The prevalence of NMS due to neuroleptics was previously reported to be 0.2-3.2%. However, with increased awareness of the syndrome and the availability of new antipsychotic agents, the figure has decreased to 0.01-0.02%. Despite being rare, it is a potentially fatal and life-threatening condition, which requires early recognition and prompt medical management to reduce mortality.[3]

Institute of Psychiatry, Benazir Bhutto Hospital, Rawalpindi, Pakistan.
Correspondence: Kainat Kareem Mirza.
e-mail: kainatkareemmirza946@gmail.com
ORCID ID: ORCID ID: 0000-0000-0000-0000

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This case is presented to highlight the importance of prompt diagnosis and management of NMS. This patient had high level of creatinine kinase but he improved with early diagnosis and treatment.

Case Report

A 25-years old male patient presented to the emergency department of the Institute of Psychiatry, Benazir Bhutto Hospital, Rawalpindi in June 2023. It was the patients' first presentation to any psychiatric facility.

The patient, a known case of epilepsy for the past 6 years and non-compliant with medication, was brought in by his family due to physical and verbal aggression that started after an epileptic seizure. The seizure had occurred 10 days prior, followed by loss of consciousness. The patient became aggressive after he regained consciousness.

The patient was admitted to the in-patient psychiatric facility, and was given an injection of haloperidol 5mg and an injection of promethazine 25mg intramuscularly to tranquillize him. However, he remained aggressive and the tranquilizers were repeated after 6 hours of admission, after which the patient was sedated. The general physical examination was unremarkable.

At the time of admission, the patient was vitally stable with a blood pressure of 130/70 mmHg, a pulse rate was of 80 beats per minute, a respiratory rate of 19 breaths per minute, and was afebrile.

The treatment given was, sodium valproate 500mg BD, haloperidol 10mg BD, procyclidine 5mg thrice a day and clonazepam 2mg at night, all in the form of oral tablets.

On the second day of admission, the patient was drowsy but remained oriented and vitally stable.

His vitals were monitored after every 4 hours. By evening, the patient developed a fever of 104ºF, his blood pressure was 90/60 and became unresponsive. He was started on intravenous fluids, injection paracetamol and cold sponging was done to reduce the body temperature. The blood pressure rose to 100/60, but the fever persisted. The laboratory investigations are shown in Table 1.

The patient was immediately shifted to the medical emergency and later to the medical ward for further management. All psychotropic medications were withheld

Table-1: Laboratory investigations.

Blood Complete Picture	23/6/2023	Normal Range
WBC count (10^3/ uL)	16.1	4.0-11.0
RBC Count (10^6/ uL)	4.19	3.50-5.50
Haemoglobin (g/dL)	14.5	12.0-16.0
HCT (%)	39.5	35.0-55.0
MCV (fL)	94.2	76.0-96.0
MCH (pg)	34.7	26.0-32.0
MCHC(g/dL)	36.8	32.0-36.0
Platelet (10^3/ uL)	297	150.0-450.0
Differential Leukocyte Count		
Lymphocytes	6.4%	20.0-40.0
ELECTROLYTES	135-145	
Sodium (mEq/L)	148	3.5-5.0
Potassium(mEq/L)	4.24	95-108
Chloride(mEq/L)	112	
Liver Function Tests		
AST (u/L)	133.0	8-33
Total Bilirubin	0.6	upto 1.2
Alkaline Phosphate(U/L)	64.4	Adults(30-171)
Alanine transferase(u/l)	35.6	Upto 43
Renal Function Tests		
Serum Urea(mg/dl)	109.98	15-50
Serum Creatinine(mg/dl)	2.5	0.7-1.2
Creatinine Kinase (U/L)		
23/6/2023	6910	30-145U/L for Male
27/6/2023	89900	
3/7/23	105000	
7/7/23	2853	

immediately. The creatinine kinase levels were sent for analysis. There was no rigidity on physical examination.

The nasogastric tube and urinary catheter were inserted. The patient was started on injection ceftriaxone 2gram IV BD, injection dexamethasone 4gm QID, Injection dextrose water 5%, injection paracetamol and injection valproic acid 500mg BD. Tablet bromocriptine 2.5mg and tablet baclofen 10mg BD were added to the treatment on 26/6/2023, due to the rising creatinine kinase levels.

The psychiatry department was in liaison with the medical department and prescribed clonazepam drops 2mg at night for his irritability.

The patients' condition deteriorated further, with laboured breathing and he was transferred to medical ICU, where he remained for 5 days. The patient was given injection diazepam 10mg TDS in addition to the ceftriaxone and sodium valproate. The injection omeprazole and heparin were administered OD. Patient was continued on tablet bromocriptine 2.5mg TDS.

The patient's condition gradually improved. He was shifted back to the medical ward and was later discharged on medication. During a follow up psychiatric evaluation, the patient was oriented to place, person and time. The patient had ictal and post-ictal amnesia but had no mood symptoms and no psychotic features on mental state examination.

Tablet valproic acid 250mg in morning and 500mg at night was prescribed. informational care regarding epilepsy was given to the patient and his family. Additionally, the family was psycho-educated about drug compliance for the management of epileptic seizures. The patient was referred to a neurologist for the management of epilepsy.

Discussion

NMS was described by Frank. J Ayd in 1956, as Fatal hyperpyrexia, after the antipsychotics were introduced.[4] Despite the reduction in incidence, it remains one of the significant causes of morbidity and mortality in psychiatric patients.[5]

The elevated serum creatinine kinase level is the hallmark for NMS. It leads to rhabdomyolysis, which results in leucocytosis and myoglobinuria, resulting in acute renal failure.[6] The DSM-5 diagnostic criteria for NMS is mentioned in Table 2.[7]

In one reported case, a patient on atypical antipsychotics for 12 months had creatinine kinase level raised to 26,152U/L.[8] whereas our patient developed NMS within 24 hours of antipsychotic treatment.

Table-2: Diagnostic Criteria of Neuroleptic Malignant Syndrome.[7]

- **Hyperthermia**
  >100.4°F or >38.0°C measured twice
- **Profuse diaphoresis**
- **Rigidity,**
  "lead pipe"
- **Altered mental state**
  From stupor to comatose state
- **Autonomic dysregulation**
  - Increased heart rate (>25% above baseline)
  - BP systolic (>25% above baseline) or fluctuation (change >20 mmHg--- diastolic BP or change of >25 mmHg systolic BP within 24 hours)
  - Tachypnea
- **Respiratory distress --- metabolic acidosis**
  - Sudden respiratory arrest

Neurological symptoms

- Tremor
- Sialorrhoea
- Akinesia
- Dystonia
- Trismus
- Myoclonus
- Dysarthria
- Dysphagia
- Rhabdomyolysis

Laboratory Investigations

- **Elevated Creatine kinase level**
  Four times the upper limit

Supportive care is the cornerstone of treatment. The dopamine agonist and benzodiazepines can be used along with the muscle relaxant dantrolene. Bromocriptine should be continued 10 days after symptom resolution and should be tapered slowly.[9]

NMS should be differentiated from serotonin syndrome, malignant hyperthermia or encephalitis. The management aims to reduce the CPK levels. The intravenous fluids are essential for lowering the CPK level, preventing renal failure caused by rhabdomyolysis. Early diagnosis and prompt treatment improve outcomes significantly, whereas delays could lead to complications thus increasing the mortality rate.[10]

Conclusion

Neuroleptic malignant syndrome is a life-threatening medical emergency. This case report highlights the successful recovery of a patient with significantly raised CPK level which improved through prompt medication and intensive care. The physicians must be aware of the serious adverse effects of antipsychotics. Early diagnosis and prompt treatment can play a pivotal role in the treatment of neuroleptic malignant syndrome.

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Author Contribution:
MK: Design, data interpretation and critical review.
ATN: Review, important intellectual content and final approval.
KKM: Attended the patient, documenting the case report based on the severity of the condition and subsequent recovery of the patient.