

# Antipsychotic Drug Emergency: Neuroleptic Malignant Syndrome

Dr. V. Santhosh <sup>1</sup>, Dr. J. John Samuel Weizman <sup>2</sup>, Dr. A. Khadeja Bi <sup>3</sup>

<sup>1,2,3</sup> Department of Biochemistry, Karpaga Vinayaga Institute of Medical Sciences and Research Centre, Chengalpet, Tamilnadu, India.

Email: santhoshviswan13@gmail.com<sup>1</sup>

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## Abstract

**Introduction:** Neuroleptic Malignant Syndrome is rare and potentially life-threatening reaction due to antipsychotic drugs. Over the last decade 1000 cases of neuroleptic malignant syndrome have been reported worldwide and the first case was reported in 1950. **EPIDEMIOLOGY:** Neuroleptic malignant syndrome is a life-threatening complication. First mortality was reported in the year 1960 and it accounts to 76 percentage. In recent years due to the awareness on its complications the mortality rate has declined to 10-20 percentage. **Clinical features:** Neuroleptic Malignant Syndrome is a clinical phenomenon exhibiting high fever, unstable mental state, autonomic dysfunction, rigidity of muscles, tachycardia, hypertension or hypotension, diaphoresis, tremor, incontinence, tachypnoea or hypoxia. **Case discussion :** A 28 years old male who is a known case of bipolar affective disorder with episodes of mania, was started on Inj. Haloperidol 5mg and Tab. Olanzapine 10mg. He presented with tachycardia, muscle rigidity, fever and increased serum creatine kinase levels after 4 days of administration of drugs and was diagnosed as Neuroleptic Malignant Syndrome. **Conclusion:** Neuroleptic Malignant Syndrome is a life-threatening condition, if not attended to may end up fatal. Awareness about Neuroleptic malignant syndrome due to neuroleptic medication, its early diagnosis, prompt treatment and follow up by physician on neuroleptic drugs has shown prevention of complications and better therapeutic outcomes.

**Keywords:** Neuroleptic malignant syndrome (NMS), Antipsychotics.

## INTRODUCTION

Neuroleptic Malignant Syndrome is rare and potentially life-threatening condition due to antipsychotic drugs. Over the last decade 1000 cases of neuroleptic malignant syndrome have been reported worldwide and the first case was reported in 1956.

Neuroleptic malignant syndrome (NMS) is an adverse condition by antipsychotic medications with anti-dopaminergic properties or associated to dopaminergic drug withdrawal. The first ever adverse event of NMS was reported after the administration of antipsychotic medication chlorpromazine<sup>1</sup>. In 1960 study, French Physicians had documented the adverse events of the new antipsychotic drug haloperidol and these events were named as 'syndrome malin des neuroleptiques'<sup>2</sup>

## EPIDEMIOLOGY:

Neuroleptic malignant syndrome is a life-threatening complication. First mortality was reported in the year 1960 and it accounts to 76 percentage. In recent years due to the awareness on its complications the mortality rate has declined to 10-20 percentage.

## CLINICAL FEATURES:

The symptoms of NMS occurs within few hours or within few days after the administration of the drug, most of which occurs

within two weeks and not exceeding 30 days.

Neuroleptic Malignant Syndrome is a clinical phenomenon exhibiting high fever, unstable mental state, autonomic dysfunction, rigidity of muscles, tachycardia, hypertension or hypotension, diaphoresis, tremor, incontinence, tachypnoea or hypoxia.

The clinical course of NMS starts with rigidity of the muscles followed by very high temperature within few hours of administration of antipsychotics which might be followed with unstable mental state, once the symptoms appear, it is rapid, progressive and intensifies in three days.

The diagnosis of Neuroleptic malignant syndrome is mainly thorough clinical history, examination of patients and laboratory investigations.<sup>3,4</sup> Increased creatine phosphokinase (CPK) are sequelae to leucocytosis and rhabdomyolysis. Findings might not be typical and not seen in all cases<sup>5</sup>. Renal impairment is evident in those with rhabdomyolysis and mostly need hemodialysis<sup>6</sup>. Acidosis mainly metabolic and deficiency of iron are additional findings<sup>7</sup>. Imaging studies and cerebrospinal fluid analysis are within physiological limits, but an electroencephalogram (EEG) study has reported nongeneralized slowing.

## CASE HISTORY:

A 28 years old male who is a known case of bipolar affective disorder for past three years on irregular medication had come with the episodes of mania. No History of Head injury/ Trauma. He is not a smoker but alcoholic for past four years takes alcohol occasionally. On General examination Patient is moderately built and nourished. Vitals were normal and systemic examination were normal. He was treated with Inj. Haloperidol 5mg (stat and SOS), Tab. Olanzapine 10mg OD HS and Tab. Divalproex sodium 500mg BD.

His laboratory investigation showed Hb-12.3gm%, TLC-10300cells/cumm, RBS-121mg/dl,

urea-27mg/dl, creatinine-2.1mg/dl, Total bilirubin-0.5mg/dl, Bilirubin Direct-0.3mg/dl,

Bilirubin Indirect-0.2mg/dl, Protein Total 7.3mg/dl, Albumin-3.6mg/dl, Globulin-3.7mg/dl,

SGOT-80U/L, SGPT-20U/L, ALP-95U/L, GGT-12U/L. Sodium-146mmol/L,

Potassium-3.9mmol/L, Chloride 113mmol/L, Bicarbonate-17mmol/L.

After 4 days of administration of drugs he had presented with tachycardia, muscle rigidity, fever and increased serum creatine kinase levels

**CPK->1000 on dilution it shows 2068U/L.**

He was diagnosed as Neuroleptic Malignant Syndrome.

## DISCUSSION:

Neuroleptic malignant syndrome has been evidenced with drugs like haloperidol, prochlorperazine, chlorpromazine, trifluoperazine, and fluphenazine. These drugs have greater risk when compared to atypical antipsychotics and are said to be frequently causing NMS<sup>8</sup>. There is also been evidenced of NMS with common atypical neuroleptic drugs including olanzapine, ziprasidone, clozapine, quetiapine, risperidone and aripiprazole<sup>9-14</sup>

In Parkinson disease the sudden cessation or reducing therapy with levodopa is known to induce Neuroleptic malignant syndrome<sup>15</sup>

The most common differential diagnosis of Neuroleptic Malignant Syndrome is heat stroke, toxic encephalopathies, infections

of CNS, status epilepticus, agitated delirium and extrapyramidal symptoms caused by benign drugs<sup>16,17</sup>. Intoxication syndromes due to drug abuse such as cocaine, 3,4-Methylenedioxymethamphetamine (MDMA), methamphetamine, amphetamine and phencyclidine are known to cause hyperthermia, disturbed mental status and causes functional disturbances in autonomic nervous system and are said to mimic Neuroleptic Malignant Syndrome<sup>17</sup>. Alcohol withdrawal syndrome and certain drugs like benzodiazepine can alter mental stability with associated rigidity of muscles. Neuroleptic malignant syndrome can also mimic baclofen withdrawal<sup>18</sup>

Other diseases which mimic NMS is Serotonin Syndrome which is because of increased serotonin have common clinical features like NMS.<sup>19</sup>

Lethal catatonia is said to be life threatening and clinically present as fever, mental status changes, rigidity and akinesia<sup>20</sup>. Lethal catatonia and Neuroleptic Malignant Syndrome are difficult to be differentiated as clinical motor features are a continuation of behavioural changes within weeks which includes ambivalence, automatism, apathy, withdrawal, psychotic agitation and extreme negativism<sup>21</sup>.

## TREATMENT:

First step is cessation of the suspected antipsychotic drug, correction of dehydration, ice pack or cooling blanket to the groin and axilla for hyperthermia and correction of metabolic abnormalities if any.

Increased risk of morbidity and mortality in patients with Neuroleptic malignant syndrome is due to disseminated intravascular coagulation (DIC) secondary to rhabdomyolysis and renal failure<sup>17</sup>. Pulmonary embolism and deep venous thrombosis due to immobilization and dehydration, aspiration pneumonia resulting from difficulty in swallowing with mental status changes, other medical complications such as seizures, cardiopulmonary failure, myocardial infarction, sepsis and arrhythmias. Many patients may require intensive care support and monitoring<sup>16</sup>

Drugs like dantrolene sodium and bromocriptine mesylate improves outcomes of NMS, reducing the morbidity and mortality. A dopamine agonist bromocriptine mesylate and a muscle relaxant. Dantrolene sodium act by inhibiting release of calcium from sarcoplasmic reticulum. Many studies have reported that these drugs when used alone or in combination have proven to have better therapeutic compliance leading to reduction in morbidity and mortality<sup>22,23</sup>. Oral administration of bromocriptine or when administered through NG tube have reversed the hypodopaminergic state, with an initial dose of 2.5 mg twice or thrice daily and increasing the dose by 2.5 mg every day to a maximum of 45 mg/day<sup>22,23</sup>. Intravenous administration of Dantrolene sodium (1 to 2.5 mg/kg) then subsequently with 1 mg/kg sixth hourly to a maximum of 10 mg/kg/day<sup>22,23</sup> can be administered. In less severe cases oral dantrolene therapy is used. Oral dantrolene therapy is also used in order to taper IV administration. Dantrolene is hepatotoxic and hence should be used wisely and stopped once the symptoms are reduced. Therapy with bromocriptine mesylate is continued for ten days minimum in NMS which is because of oral neuroleptics and two to three weeks for injectable neuroleptics.

## CONCLUSION:

Neuroleptic Malignant Syndrome is life threatening, if not attended to may end up fatal. Awareness about neuroleptic malignant syndrome due to neuroleptic medication, its early diagnosis, proper treatment and regular follow up by physicians has shown to prevent complications and aids to achieve better therapeutic outcome.

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