

## NEUROLEPTIC MALIGNANT SYNDROME – A CASE REPORT

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**Abstract :** Neuroleptic malignant syndrome (NMS) is an uncommon condition, a purely clinical entity, characterised by hyperthermia, muscle rigidity, autonomic instability and altered mental status. Autonomic dysfunction is characterized by tachycardia, labile blood pressure, profuse diaphoresis, dyspnoea and urinary incontinence. Extrapyramidal dysfunction is characterized by catatonic behaviour, dystonia, generalised rigidity and pseudoparkinsonism. NMS occurs after use of potent neuroleptics like haloperidol, thiothixene or piperazine, phenothiazines. The exact mechanism of NMS is not known but could be (i) dopaminergic blockade at various levels (ii) glutaminergic excitatory amino acids influencing dopaminergic activity and (iii) low serum iron. The differential diagnosis is from serotonin syndrome, malignant hyperthermia, infection and alcohol withdrawal. Prevention is better than treatment, which is carried out by use of bromocriptine and dantrolene sodium.

### INTRODUCTION

Neuroleptic Malignant Syndrome (NMS) which though rare, is treatable, if diagnosed early. The 'criteria' for diagnosis of NMS are (a) history of treatment with neuroleptic drug (s) within 7 days of onset of symptoms (2-4 weeks for depot preparation), (b) hyperthermia equal to or more than 38°C, (c) muscle rigidity, (d) exclusion of other drug induced, systemic or neuropsychiatric illnesses, and (e) any five of the following: change in mental status, tachycardia, hypertension or hypotension, tachypnoea or hypoxia, diaphoresis or sialorrhoea, tremors, urinary incontinence, raised CPK or myoglobinuria, leucocytosis or metabolic acidosis.

### CASE REPORT

A 40 years old female was admitted with complaints of high grade fever with chills, stiffening of body and altered sensorium since one day. There was no history of headache, vomiting, seizures and loss of consciousness. Her clinical examination revealed pulse 112/min, blood pressure 160/94 mmHg, temperature fluctuating between 102-103°F, respiratory rate 32/min. She was drowsy to stuporous. She had no signs of meningeal irritation but had generalised rigidity with a characteristic waxy flexibility in the limbs suggestive of catatonic rigidity. Within four hours, her blood pressure came down to 106/60 mmHg. CSF examination for meningitis was non-contributory. Other investigations included Hb 10.2 g%, TLC 14200/mm<sup>3</sup>, DLC P72, L28, E0, M0, ESR 10 mm/1 hour, urine C/E NAD and MP slide negative. PBF showed microcytic hypochromic anemia. Blood glucose was 80 mg%, blood urea 30 mg%, serum creatinine 1.3 mg%, LFT's normal, X-ray chest NAD, widal test negative, blood culture negative and HIV non-reactive. Further questioning of her husband revealed that his wife (index patient) was a known case of endogenous depression since 2 years and was taking imipramine 75 mg/day off and on, till 6 months ago. For the last 8-10 days, she had restarted taking the drug on her own with thrice the original dose. In view of clinical presentation and drug history, a provisional diagnosis of NMS was made on the third day of admission. Her CPK levels were 110 U/L. The offending drug i.e. imipramine was stopped immediately. She was put on IV fluids and tablet bromocriptine 5 mg thrice daily. Fever subsided after 72 hours of initiating therapy and she became asymptomatic within four days.

### DISCUSSION

It is a rare but serious complication of treatment with phenothiazines, as well as butyrophenones especially haloperidol and rarely metoclopramide and pimozide<sup>2</sup>. The sites at which these drugs act are hypothalamus (causing fever), corpus striatum and basal ganglia (causing extrapyramidal syndrome), mesolimbic system and mesocortical pathway (alteration of mental status) and spinal cord (dysautonomia and altered sympathetic tone). Schizophrenia is the most common disease reported with NMS<sup>2</sup>. NMS has been reported in a patient of systemic lupus erythematosus<sup>3</sup>. Only rare case reports describe NMS after tricyclic antidepressants like imipramine<sup>4</sup>, as described in the present case and others also<sup>5</sup>. The chances of

developing NMS with the use of neuroleptics are 0.02 – 3.23%. It occurs in young and middle aged adults and is more common in males (M:F 2:1). Predisposing risk factors include organic brain disorders, psychomotor activity or agitation, underlying genetic factors, dehydration, physical exhaustion and past history of NMS<sup>1</sup>. The exact pathophysiology of NMS is not fully known but is attributed to neurohormonal disruption within brain dopaminergic system. The central dopaminergic blockade within basal ganglia leads to extrapyramidal rigidity while hyperthermia, mental changes and dysautonomia are attributed to dopaminergic blockade in the hypothalamus. In addition hyperthermia occurs as a result of increased muscular activity. A peripheral mechanism also seems to play a role in which dopamine mediated skeletal muscle contraction is inhibited by neuroleptics<sup>1,6</sup>. Even low serum iron has been reported to be responsible for NMS<sup>7</sup>. The differential diagnosis includes infection, malignant hyperthermia, alcohol withdrawal state as well as serotonin syndrome (SS). The clinical picture of NMS usually resolves within 1 to 3 days and lasts for 5 to 10 days after withdrawal of the offending drug whereas mortality is 20-25% if untreated. Death is due to renal failure, arrhythmias, acidosis, hypercalcaemia, myocardial infarction, aspiration pneumonia, pulmonary embolism, rhabdomyolysis (with acute renal failure), DIC or ARDS. Prognosis is poor in patients with underlying brain disorder, hypotension, rhabdomyolysis and acute renal failure. Regarding treatment, prevention is always better. The awareness about NMS, during neuroleptization, early recognition by careful observation of signs and symptoms is of utmost importance. Once the clinical diagnosis is made, immediate omission of offending drug and institution of specific and supportive measures are helpful. Treatment is to increase dopamine activity by giving bromocriptine 2.5 to 5.0 mg thrice daily (as high as 10 mg tds). Amantidine 100-200 mg twice a day can be given. Skeletal muscle relaxants like dantrolene 1-3 mg/kg 8 hourly are advocated<sup>1</sup>. Neuromuscular paralysis may need ventilation.

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