



Neuroleptic Malignant Syndrome and Anaesthesia: A Case Report

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Neuroleptic Malignant Syndrome (NMS) is a life threatening, neurological disorder most often caused by an adverse reaction to neuroleptic or anti psychotic drugs. We report a case of Neuroleptic Malignant Syndrome who was posted for an incidental surgery and its anaesthetic management.

Key Words: Neuroleptic Malignant Syndrome, anti psychotics, hyperthermia

Neuroleptic Malignant Syndrome (NMS) is a rare but potentially life threatening idiosyncratic reaction to neuroleptic drugs. It causes hyperthermia, muscular rigidity, altered mental status, elevated creatine phosphokinase (CPK) and autonomic dysfunction. The underlying pathological abnormality is thought to be the central dopamine D2 receptor blockade or dopamine depletion in the hypothalamus, nigrostriatal and spinal pathways. The condition shares many features with the serotonin syndrome and malignant hyperthermia. Anaesthesia for an incidental surgery in such a patient poses unique challenges to an anaesthesiologist.

Case Report: An 18 year old male, a known case of Bipolar mood disorder on antipsychotics was admitted to our Intensive Care Unit with complaints of high grade fever (106⁰F) for 2 days, agitation and involuntary movements for 8 days and vomiting with altered sensorium for 1 day. Patient was immediately intubated to protect his airway, intensive measures to bring down temperature commenced and investigations including haematological, biochemical, brain imaging and cerebrospinal fluid sent for evaluation. Investigations revealed:



leukocytosis (TLC 19,000/mm³), elevated liver enzymes (SGOT 477 IU/l, SGPT 190 IU/l); progressively increasing Creatine Kinase (1004; 2040; 3270; 39794 U/l), Serum Creatinine (1.3; 1.5; 1.8 mg/dl) and Serum K⁺ (4.8, 4.9, 5.5 meq/l). Computed tomography of brain and cerebrospinal fluid examination were normal. So a diagnosis of neuroleptic malignant syndrome was made. All antipsychotic medications were then stopped. Tab. Bromocriptine 1.25 mg thrice daily and Tab. Alprazolam 0.25 mg four times daily were started and other intensive care measures continued. Patient was gradually weaned off ventilator support and extubated on 6th day.

Unfortunately patient developed a bed sore on the buttock which needed a flap cover He was posted for surgery on 15th day of admission. A pre-anaesthetic check up revealed a responsive patient, hypertonia present in all limbs and restricted mouth opening (just 2 fingers due to hypertonia). Investigations revealed elevated CPK 829 U/l, S. K⁺ 4.9 meq/l, INR = 1.54; rest of examination and investigations were within acceptable limits.

Anaesthetic management included avoidance of following drugs perioperatively: Inj. droperidol, succinylcholine, prochlorperazine, promethazine and metoclopramide. Patient received premedication with alprazolam 0.25 mg at 10 p.m. before the day of operation and at 6 a.m. on day of surgery. Consent taken and patient shifted to operation theatre. Drip started with 16 G intravenous cannula and standard monitoring established. Fentanyl 1.5 µg/kg and midazolam 1 mg IV was administered. Anaesthesia induced by thiopentone sodium 4 mg/kg IV slowly, after pre-oxygenation for 5 minutes and adequacy of mask ventilation confirmed, muscle paralysis achieved with atracurium 0.5mg/kg. Airway secured with 34Fr cuffed armoured endotracheal tube orally and anaesthesia maintained with 50% of O₂ + N₂O + Isoflurane < 0.4%, fentanyl was used for analgesia and atracurium for muscle paralysis assisted by neuromuscular monitoring. Surgery was conducted in prone position; procedure lasted 2½ hours during which 2 units of whole blood, 2 units of FFP and 1.5 litres crystalloid were infused. Patient remained haemodynamically stable throughout procedure. At end of surgery, neuromuscular blockade was reversed with neostigmine and glycopyrrolate. Trachea was extubated in prone posture itself as requested by surgeons to avoid pressure on flap after patient was awake; Ondansetron 4mg IV was used as antiemetic.

Post operatively patient was shifted to post anaesthesia care unit with O₂ supplementation and then towards after 2 hrs. Patient was discharged from hospital on 7th post operative day with psychiatry referral.

Discussion: Neuroleptic Malignant Syndrome (NMS) was first described by Delay et al during early trials of haloperidol¹. The incidence is estimated to range from 0.02–2.4% with



conventional anti-psychotics and a much lower incidence for atypical antipsychotics² The Diagnostic criteria are:

- Administration of neuroleptics
- Hyperthermia (> 38°C)
- Muscle rigidity
- Five of following: mental status change, tremor, tachycardia, incontinence, labile blood pressure, metabolic acidosis, tachypnoea/hypoxia, CPK elevation, diaphoresis/sialorrhea, leukocytosis.
- Exclusion of other central and systemic causes of hyperthermia.

Although NMS has a variable onset and sometimes evolves rapidly, rigidity and altered mental status usually occur early, followed by autonomic changes and hyperthermia³. No laboratory tests are pathognomonic of diagnosis. Serum creatine kinase is frequently elevated reflecting rhabdomyolysis, with resultant risk of myoglobinuric renal failure. CT scan brain and cerebrospinal fluid examination and sepsis evaluation are negative in NMS and allow for the exclusion of other causes of fever and neurological deterioration. Other frequently described laboratory abnormalities include metabolic acidosis, hypoxia, low serum iron, electrolyte abnormalities, elevated serum catecholamines and coagulopathies

Differential Diagnosis of NMS: Infectious encephalitis^{4,5}, structural lesion of brain, rare cases of status epilepticus⁶, lethal catatonia⁷, heat stroke, endocrinopathies, drugs, autoimmune disorders, thyrotoxicosis, pheochromocytoma, malignant hyperthermia, serotonin syndrome⁸. Volatile anaesthetics and succinylcholine are associated with malignant hyperthermia during surgery, which can be confused with NMS if neuroleptics are administered⁹

The basic management of NMS remains risk reduction, early diagnosis, cessation of neuroleptic medications and institution of Intensive, medical and nursing care^{10,11}. Benzodiazepines, bromocriptine, amantadine or other dopamine agonists may be a reasonable next step in patients with moderate symptoms of NMS. Dantrolene may be beneficial in cases of NMS with extreme rigidity and hyperthermia. Electro convulsion therapy (ECT) is used if NMS is refractory to other measures or who remain psychotic after NMS is resolved. Since a common pathophysiology has been suggested between NMS and malignant hyperthermia (MH)^{12,13} the possibility that patients with a history of NMS may be vulnerable to developing MH is an important factor when considering general anaesthesia, especially succinylcholine administration. To date, there is no report in the literature of (MH) as a complication of ECT in NMS patients. However, until the association between



NMS and MH is conclusively disproved, careful metabolic monitoring of general anaesthesia is necessary.

Conclusion: Neuroleptics are highly effective medications that have achieved wide spread use in medicine and psychiatry. However they have been associated with NMS in about 0.2 percent of patients. Awareness of diagnosis, cessation of medications, early medical intervention and consideration of specific remedies can reduce morbidity and mortality when NMS occurs. This case report has been published to increase familiarity with the diagnosis and management of this unusual but fascinating drug reaction and anaesthetic management of a incidental surgery in a patient of NMS.

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