

Case Report

Neuroleptic Malignant Syndrome – A medical emergency in a psychiatric patient

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Abstract:

With an estimated incidence of 0.02 to 3.23%¹, neuroleptic malignant syndrome (NMS) is a rare idiosyncratic reaction to antipsychotic drugs; having a relatively high fatality rate of about 10%². Here, we are reporting, a 38 years old female schizoaffective patient, presented with fever, muscle rigidity and altered sensorium who had started tablet risperidone (an atypical antipsychotic drug) 11 days prior to hospital admission. After initial sepsis work up and neuroimaging, infective causes and acute cerebrovascular incidents were ruled out and a presumptive diagnosis of NMS was made. Immediate discontinuation of suspected causative agent, along with the provision of supportive care leads to complete resolution of all the symptoms in our patient.

Keywords: Neuroleptic Malignant Syndrome (NMS), Antipsychotic drug, Risperidone.

Introduction:

Neuroleptic malignant syndrome is a relatively uncommon but potentially fatal idiosyncratic reaction characterized by the development of hyperthermia, muscular rigidity, autonomic dysfunction, and altered consciousness, either on exposure to antipsychotic³ and some other psychotropic medications⁴ or due to an abrupt withdrawal of anti-parkinsonism drugs⁵. It is essentially a diagnosis of exclusion, and treatment is mainly supportive along with the instant withdrawal of the causative neuroleptic agents and starting of dopaminergic drugs. NMS presents a clinical challenge and a high index of suspicion is necessary to diagnose a case as the patient outcome depends on its early recognition and prompt implementation of appropriate management. This article reports, a case of a 38-year-old female patient with schizoaffective disorder who presented with typical features of NMS after initiation of risperidone (an atypical antipsychotic drug).

Case report:

A 38-year-old housewife, mother of one child, was admitted to the intensive care unit (ICU) of Bangladesh Medical College Hospital on September 2016, with the history of high grade continued fever for 4 days, rigidity of all four limbs and altered level of consciousness for 1 day. According to her husband, two days prior to hospital admission she was also showing unusual behavior, altered sleep pattern and resting

tremor. She had no history of trauma, drug abuse or recent traveling to home and abroad. Her previous medical history revealed, she was a diagnosed case of schizoaffective disorder for last 2 years and was on tablet Quetiapine (100 mg thrice daily), Escitalopram (10 mg daily), with questionable adherence to treatment. As her psychotic symptoms were not responding well, 11 days prior to this hospital admission tablet risperidone 2 mg was started and gradually increased to 4 mg/day. She had no other documented organic co-morbidity.

On admission, a thorough physical examination demonstrated, the patient was disoriented with Glasgow coma score 8/15 (E3M4V1); temperature 102o F and was tachycardic (110 beats/min) with blood pressure 90/60 mm of Hg. Increased spasticity and tremulousness in all extremities were present. Other systemic examinations were unremarkable. Routine laboratory investigations showed Haemoglobin 11.5 gm/dL, leukocyte 6,000/mm³, platelets 3,00,000/mm³; serum creatine phosphokinase (CPK) was 2,388 U/L, but her level of blood urea nitrogen, serum creatinine, serum electrolytes, serum transaminases and blood gases were all within normal limit. The finding of the MRI of brain and chest X-ray were unremarkable. A provisional diagnosis of NMS was made. All antipsychotic drugs were withheld instantaneously. To rule out the possibility of central nervous system (CNS) infection, lumbar puncture was done and the CSF studies were found normal. Blood, urine, and sputum cultures showed no growth in 48 hours. Supportive cares including adequate hydration were maintained to prevent acute kidney injury (AKI); to lower body temperature tepid sponging with ice water and acetaminophen were used as required. Tablet Bromocriptine was started at a dose of 2.5 mg thrice daily and increased to 15mg/day. On the 5th day, patient's temperature was subsided, her level of consciousness and muscle rigidity improved. On the 8th day, she was shifted to ward. After normalization of her CPK level, the dose of bromocriptine was slowly tapered and withdrawn subsequently. On the 13th day, she was discharged from hospital without further complication. On subsequent follow-up, in order to control her ongoing psychotic

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symptoms, tablet olanzapine was prescribed, starting at a dose of 2.5 mg daily and gradually increased up to 10 mg per day. For preventing extrapyramidal side-effects, tablet procyclidine hydrochloride was also given. With these treatments, her depressive and psychotic symptoms improved considerably without any notable adverse effects, till date.

Discussion:

In 1960 Delay and colleagues, a group of French clinicians, first described an akinetic hypertonic syndrome in a group of patients using haloperidol⁶; they named it "syndrome malin des neuroleptiques", from which the term 'neuroleptic malignant syndrome' is derived.⁷ Since then numerous case reports of this syndrome have been published from different countries and the incidence rate was estimated from 0.2 to 3.23%^{1,7}. It was identified in the literature that, in a susceptible individual, both typical and atypical antipsychotic drugs, at any dose, can induce symptoms of NMS^{8,9}. But, initiation of a new neuroleptic, the rapid increase in dosage, use of high potency or long-acting intramuscular depot formulation, all raise the possibility of developing NMS. Other suspected risk factors are dehydration, iron deficiency, hyperthyroidism, malnutrition, alcoholism, male gender, younger age, increased ambient temperature, previous episode of NMS, concomitant use of other psychoactive substances (especially lithium), and presence of structural or functional brain disorders such as encephalitis, tumor, delirium, or dementia¹⁰⁻¹³. Sudden withdrawal of dopaminergic drugs in a Parkinson disease patient may also provoke NMS^{5,14}. In our patient, risperidone, a potent antipsychotic drug was started and the dose was also increased rapidly in a view to controlling her schizophrenic symptoms, all these seem to trigger her to develop NMS.

The exact pathophysiology of neuroleptic malignant syndrome is still not well elucidated; among several theories, the most enduring one is excessive blockage of D2 dopamine receptor within the nigrostriatal, hypothalamic, and mesolimbic/cortical pathways, leading to a marked and sudden reduction in central dopaminergic activity, plays a pivotal role in this condition^{15,16}. Another group of experts advocate that, increase release of calcium from the sarcoplasmic reticulum of muscle fibers with antipsychotic usage, may be responsible for exaggerated muscle contraction, rigidity and break down¹⁷.

Although the clinical presentation of NMS is often heterogeneous, the cardinal manifestations are high-grade fever, generalized rigidity, altered level of consciousness (from confusion to coma) and autonomic instability in the form of blood pressure fluctuation, tachycardia, tachypnoea, profuse sweating, flushing, excessive salivation and urinary incontinence¹⁷⁻¹⁹. Infrequently observed features are dysphagia, tremor, chorea, tonic-clonic seizure, mutism, trismus, oculogyric crisis, positive babinski's sign and opisthotonus. The symptoms may develop within one to thirty days after exposure to antipsychotic medications but typically appear within two weeks²⁰. Due to rhabdomyolysis, creatine phosphokinase (CPK) is characteristically found elevated and

threatens to cause acute kidney injury. Mild leukocytosis and increased serum transaminases levels are commonly reported. Unfortunately, none of these are either specific for the syndrome or universally present in all cases. So, a number of other fatal conditions presenting with similar clinical scenario must be excluded. Apart from central nervous system infection, septicaemia, acute intoxication and cerebrovascular accidents, the important neuropsychiatric differential diagnoses are serotonin syndrome, malignant hyperthermia, and lethal catatonia. Careful history taking, especially drug history and detailed physical examinations are helpful to distinguish between these life-threatening conditions. However, laboratory investigations such as CSF studies, blood, and urine culture, toxicology screening and neuroimaging are essential in the evaluation of other etiologies.

Neuroleptic malignant syndrome is a medical emergency; if the diagnosis is delayed the case fatality could be as high as 30%²¹. Widespread awareness among clinicians regarding the syndrome has thankfully reduced the rate near to 10% in recent years². As antipsychotic drugs are strongly protein-bound, they cannot be removed by dialysis, so early discontinuation of offending agents along with the provision of supportive therapy is the crucial strategy in the management of suspected NMS. To prevent dehydration and AKI from myoglobinuria, vigorous fluid resuscitation is mandatory. Antipyretics are less effective in lowering body temperature in NMS, manual cooling with ice water and cold blankets are usually employed. Correction of hypoxaemia, electrolyte imbalance and acidosis and maintenance of nutrition is necessary. Fulminant cases may require intensive care monitoring and ventilatory support. Although data supporting the efficacy of adjunctive pharmacotherapy is insufficient, several drugs are being administered empirically to alleviate acute symptoms. Bromocriptine, amantadine, and other dopaminergic drugs; dantrolene a muscle relaxant, and benzodiazepines are frequently tried alone or in combination in different case studies²²⁻²⁴. In refractory cases, electroconvulsive therapy may be beneficial to hasten recovery. If appropriate interventions are not taken immediately, disease course may prolong with serious complications like DIC, renal failure, aspiration pneumonia, sepsis, deep vein thrombosis, pulmonary embolism, adult respiratory distress syndrome, arrhythmia, cardiorespiratory failure^{1,24}; and surviving patients may have life-long morbidity secondary to cognitive impairment, cerebellar neuronal degeneration, residual catatonia or parkinsonism^{25,26}. After complete resolution of an episode (within 2-14 days) of NMS, because of compelling indication, it is often required to restart antipsychotic drugs. But it should preferably be done at least after two weeks, with an alternative low potency agent at a low dose and titrated gradually with great caution as recurrent cases are reported in literatures^{17,26}.

Conclusion: Although majority of cases of neuroleptic malignant syndrome follow an indolent course, lack of clinical vigilance may lead to life-threatening complications As there are no pathognomonic sign or gold standard

investigation for NMS and timely initiation of management is critical for favorable outcome; when there is a dilemma about etiology, it is prudent to withhold all neuroleptic drugs in a psychotic patient until rigorous investigations reveal a conclusive diagnosis.

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