NEUROLEPTIC MALIGNANT SYNDROME: A POTENTIAL MIMIC OF ACUTE ENCEPHALITIS SYNDROME

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ABSTRACT

Neuroleptic malignant syndrome (NMS) is a neurological emergency due to neuroleptic medications which is characterized by fever, muscle rigidity, autonomic instability, and altered mental status. Here we report a case of a 74 years old female who presented with complaints of fever, altered sensorium, restlessness, self-muttering, irritation, muscular rigidity, decreased mobility and diaphoresis. She was under medication olanzapine for schizoaffective disorder. It is a diagnosis of exclusion after detailed examinations and investigations. The patient was managed with bromocriptine and supportive measures. NMS may mimic acute encephalitis syndrome. Therefore, NMS should be included in differential diagnosis with presentation as in our case.

KEYWORDS

Bromocriptine, neuroleptic malignant syndrome, olanzapine

***Received on**: February 28, 2023*
***Accepted for publication**: June 26, 2023*

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DOI: https://doi.org/10.3126/nmcj.v25i3.59024

INTRODUCTION

Neuroleptic malignant syndrome (NMS) is a life-threatening adverse reaction to neuroleptic medications which is characterized by fever, muscle rigidity, autonomic instability, and altered mental status.[1] The incidence has declined to about 0.01% to 0.02% from 0.2% to 3.2% as physicians have become more aware of the syndrome.[2] The central and peripheral manifestations of NMS ultimately coalesce in a diffuse encephalopathic process that can mimic as viral encephalitis.[3] Here we report a case of NMS found at Nepal Medical College Teaching Hospital which was diagnosed on the basis of history of intake of neuroleptic medication, clinical, and laboratory findings.

CASE REPORT

A 74 year old female, resident of Besigaun presented to Emergency Department in October, 2021 with chief complaints of high-grade fever, acute onset of altered sensorium, restlessness, self-muttering, irritation, suspiciousness, disturbed sleep, disinhibited behavior, vomiting, muscular rigidity, decreased mobility, and diaphoresis. She was under medication olanzapine (10 mg/day) for 4 years for the treatment of schizoaffective disorder. However, she was not compliant to the treatment. On examination, her vital signs were: temperature of 104 degree F, blood pressure 100/50 mmHg, heart rate 110 beats/min, regular and respiratory rate 20 breaths/min, regular. Serial blood pressure measurement was fluctuating indicating labile hypertension. On neurological examination, higher mental function tests revealed confusion, irritability, auditory hallucination and delusion of persecution along with symmetrical limb rigidity, bilateral resting tremor of limbs with no signs of meningism. No remarkable findings were found during the chest examination, precordial examination, and per abdomen examination. Laboratory studies showed leukocytosis (13,700/cumm) with neutrophilic predominance and no significant findings were found in liver function test, renal function test, chest xray PA view, arterial blood gas analysis, cerebrospinal fluid analysis and MRI of the head. However, sinus tachycardia was present in ECG and creatine kinase was 646 U/L (24-190U/L). Therefore, we suspected NMS and discontinued tablet olanzapine after consultation with the psychiatry department. She was prescribed tablet bromocriptine at a dose of 5 mg once a day for treatment of NMS along with supportive treatment for high grade fever.

On day two, her symptoms and signs subsided and complete blood count and renal function test was within normal range. She was discharged on the third day of admission on request. She was followed up after 2 weeks in medicine and psychiatry OPD and she was doing well.

DISCUSSION

NMS is a life threatening idiosyncratic adverse reaction to neuroleptic medications which is manifested by a variety of clinical features, including hyperpyrexia, muscle rigidity, autonomic instability, and altered mental status.[1] The first reported case of NMS appeared shortly after the introduction of the antipsychotic drug (thorazine) in 1956. In a 1960 study, French physicians gave the syndrome its name following side effects of haloperidol and characterized it as a "syndrome malin des neuroleptiques".[2] The frequency of this syndrome varies from 0.1% to 2.2% among patients receiving neuroleptic medications.[4]

Very few studies have reported olanzapine-induced NMS making it a rare diagnosis.[5,7] We have also encountered a similar case of NMS in our setting. After initiation of neuroleptic medications, NMS develops within 24 hours in 16.0%, within the first week in 66.0%, and virtually all cases within 30 days and the recovery time is within 7-10 days. NMS is a diagnosis of exclusion due to a variety of confounding factors such as male gender, age, restlessness, physical exertion, dehydration, and neurological defects.[5,8] In our context, she was under medication for 4 years but was non-compliant to medication. This may be one of the reasons for her late presentation of NMS. The patient was schizoaffective in our case. There are two theories to explain the syndrome: central dopamine receptor blockade and skeletal muscle defect. The first theory explains antagonism of dopaminergic receptors by neuroleptics can disrupt the normal role of dopamine in central thermoregulation. Heat is generated by serotonin stimulation in the hypothalamus and dopamine inhibits this process. The second theory explains pathophysiology of NMS is similar to that of malignant hyperthermia.[9] Thus, the first theory seems to have worked in our patient. Our patient had met all the DSM-5 criteria for NMS:[10] exposure to dopamine-blocking agent (olanzapine), muscle rigidity, elevated temperature, diaphoresis, bilateral tremors of the limbs, tachycardia, leukocytosis, and high creatine kinase.

The treatment of NMS includes risk factors reduction, prompt recognition, stoppage of neuroleptic medication, and provision of intensive medical care that focuses on hydration, temperature reduction, and support of cardiac, respiratory, and renal functions. Vigilant monitoring for complications such as aspiration pneumonia, thromboembolism, and renal failure is important.[11]

DGPPN S3 schizophrenia treatment guideline (2019) differentiates the NMS into 5 severity levels, with grade 3–5 being termed "early/moderate/severe NMS" and our patient falls under moderate NMS for which standard protocol include discontinuation of antipsychotics, intensive care, lorazepam (up to 8 mg/day), bromocriptine (up to 15 mg/day), or amantadine (up to 300mg/day) and ECT as a second line therapy.[10] Our patient was treated with tablet bromocriptine.

Prompt improvement of the patient within a day after holding tablet Olanzapine and treating with tablet bromocriptine may have supported our diagnosis of NMS in this case. Similar finding was supported by Javed *et al.*[12] Our patient did not develop any complications of NMS which might be due to early diagnosis and immediate medical interventions.

In conclusion, early detection and treatment of NMS is crucial and therefore proper medication history and being vigilant about side effects of the drugs are important. The signs and symptoms of NMS may mimic like acute encephalitis syndrome. Therefore, NMS should also be included in differential diagnosis of patient taking neuroleptic medications with similar presentation as in our case.

Conflict of interest: None

Source of research fund: None

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