Neuroleptic malignant syndrome in a patient with stable dose of olanzapine

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ABSTRACT

Neuroleptic malignant syndrome (NMS), a potentially fatal consequence due to typical neuroleptics, has been described so far. In the past few years, there has been increased use of atypical antipsychotic drugs. Cases of NMS related to atypical neuroleptics, such as olanzapine, are less common in spite of increasing cases reported in literatures. Here, we report a case of NMS in a patient with bipolar affective disorder on maintenance treatment with 5 mg olanzapine for the last 7 year. He was successfully treated with bromocriptine and discharged in stable condition in 10 days.

Keywords: Bipolar affective disorder, neuroleptic malignant syndrome, olanzapine

Introduction

Neuroleptic malignant syndrome (NMS) is a potentially life-threatening idiosyncratic reaction generally associated with neuroleptics. NMS is characterized by hyperthermia, extrapyramidal symptoms, elevated creatinine kinase (CK), altered mental state, leukocytosis, and problems with vegetative functions. Till now, NMS has been described as a potentially fatal consequence due to typical neuroleptics. In the past few years, there has been increased use of atypical antipsychotic drugs. Nowadays, olanzapine is widely used by primary care physicians for various other indications such as dementia, anxiety, and depression.¹,² Due to its lower affinity for dopaminergic receptors and higher affinity for serotonin receptors, olanzapine-associated atypical NMS was less common than typical neuroleptics. Cases of NMS related to olanzapine are less common in spite of increasing cases reported in literatures.³-⁷ Here, we report a case of NMS in a patient with bipolar affective disorder (BPAD) on maintenance treatment with 5 mg olanzapine for the last 7 years. He was successfully treated with bromocriptine and discharged in stable condition in 10 days.

Case Report

A 30-year-old male patient, a case of BPAD was stable on combination of tablet olanzapine 5 and 400 mg of tablet sodium valproate for the last 7 years. Three weeks before admission to our hospital, he had fever with rigors of 3–4 days duration, which subsided with over the counter medication. During this period, he continued to take tablet olanzapine and sodium valproate. He remained apparently asymptomatic for 2 weeks and again developed fever with rigors, for which he was admitted in a local hospital for 4 days. While in hospital, he developed increased frequency of passing urine, loose stools, and inability to sleep at night. He went into altered sensorium and was unable to recognize his relatives, stopped feeding on the 4th day, for which he was referred to our hospital as he showed no improvement. His antipsychotics were stopped during his stay in the local hospital.

On admission to our hospital, the patient was febrile with temperature of 103°F had pulse rate 122/min. He was mute. Examination of central nervous system revealed Glasgow Coma Scale of 8/15 (E3M4V1), lead pipe rigidity in all four limbs, neck, tremors in the left hand and jaw, brisk deep tendon reflexes, and equivocal plantar response. His total leukocyte count was...
8300/cumm. Malarial parasite was not found on peripheral smear and paracheck was negative. His blood urea, serum creatinine, serum electrolytes, TSH, serum calcium, urine routine and culture, blood culture, and X-ray chest were normal. His viral markers (HBsAg, anti-HCV antibodies, and anti-HIV 1 and 2 antibodies) were nonreactive. His random blood sugar (RBS) was 412 mg/dl and his liver function test revealed raised enzymes. Examination of cerebrospinal fluid (CSF) revealed clear fluid with 6 lymphocytes, proteins 67.9 mg/dl, sugar 59 mg/dl (corresponding RBS 112 mg/dl), and ADA 2 U/L. There was no evidence of microorganisms on Gram-stain, fungal elements, and acid-fast Bacilli on Zeil Neilson’s stain. Contrast-enhanced computed tomography (CT) of the brain was normal.

A provisional diagnosis of meningocencephalitis was made with the above reports and treated with aciclovir 500 mg three times a day (tid) intravenously (IV), ceftriaxone 2 g BD IV, dexamethasone 4 mg tid, Ryle’s tube feed in addition to other supportive measures. On the 3rd hospital day, his fever persisted. He developed generalized tonic seizures, tremors became generalized, and rigidity worsened. He developed autonomic disturbances in form of intermittent profuse diaphoresis. The patient was transferred to high dependency unit for close monitoring. His repeat total white blood cell count now showed leukocytosis of 13,300/cumm with 85% neutrophils. Blood for creatinine phosphokinase (CPK) and lactate dehydrogenase (LDH) was sent considering the possibility of NMS. His CPK and LDH were 1192 U/L (normal range 24–195 U/L) and 934 U/L, respectively. In view of persistent high-grade fever, no response to initial treatment and history of use of olanzapine with leukocytosis and elevated CPK, the diagnosis of NMS was made. He was started on bromocriptine 2.5 mg tid PO (through Ryle’s tube), lorazepam 1 mg BD, trihexyphenidyl 1 mg thrice daily, aripiprazole 5 mg once daily, and levetiracetam 500 mg BD on the 4th day of hospital admission. Supportive measures were continued. Injections of aciclovir and ceftriaxone were stopped. He was marginally better on the 2nd day of starting bromocriptine. Dose of bromocriptine was increased to 5 mg tid after 48 h. On the 4th day of starting bromocriptine, all the symptoms and signs including rigidity, tremors, diaphoresis settled, and patient became afebrile. He became responsive, oriented, and started taking orally. His repeat CPK levels gradually decreased through 934–423 U/L. His RBS on day 10 was 142 mg/dl. He was finally discharged on request on day 10 with advice to continue bromocriptine, trihexyphenidyl, aripiprazole for 1 week, and follow-up in psychiatry outpatient department.

**Discussion**

Several diagnostic criteria are used for NMS worldwide, including the Levenson criteria, and the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision criteria, sharing quite similar main content. Typical symptoms are hyperthermia, autonomic dysfunction, altered consciousness, muscular rigidity, and an elevation of CK. In the present case, the patient had generalized rigidity, hyperthermia, altered consciousness, tremors, tachycardia (122 bpm), leukocytosis (13,300 cumm), raised CK (1192 U/L), and good response to bromocriptine supported the diagnosis of NMS. Definite diagnosis of NMS is based on clinical manifestation, so differential diagnosis is of prime importance. Viral infection of the central nervous system, brain lesions, toxic, drug-induced acute idiosyncratic reaction, hyperthyroidism other causes should be excluded from the study. In the present case, brain CT and CSF values, blood and urine cultures, thyroid function tests, and chest X-ray were all normal. No medications used were related to the symptoms presented in this patient, except olanzapine. Although the patient was on 5 mg of olanzapine for the last 7 years, the current medical conditions such as loose stools, decrease oral intake in scorching heat might have precipitated NMS. Although there are various case reports of olanzapine-related NMS, NMS after such a longtime usage with same dose is rarely reported.

**Conclusion**

This case demonstrates the fact that NMS can occur with atypical antipsychotics such as olanzapine even in lower doses, especially in the presence of risk factors. We should pay attention to this rare but potentially fatal complication as olanzapine is commonly used by primary care and other physicians. NMS remains a dangerous condition and has also been described in nonpsychiatric settings. It is often unrecognized, underdiagnosed, or inappropriately treated. A better understanding of this syndrome would be helpful in reducing its fatalities.

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**Conflicts of interest**

There are no conflicts of interest.

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