Case Report

A Case of Aripiprazole-Induced Neuroleptic Malignant Syndrome

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Abstract

Neuroleptic malignant syndrome (NMS) is a serious medical emergency with significant fatality rates if not recognized and treated early. High-potency first-generation antipsychotics are reported to have more incidence of NMS. Aripiprazole-induced NMS is very rare, and here we report the case of a 38-year-old woman with bipolar illness disorder. The disorder started after escalating the dose and resolved after stopping the medicine.

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Introduction

An acute idiosyncratic reaction to drugs with disturbed thermoregulation and autonomic dysfunction, neuroleptic malignant syndrome (NMS), is a serious medical emergency with significant fatality rates if not recognized and treated early.[1] The syndrome first reported about 50 years ago with high-potency antipsychotics such as haloperidol, presents with altered consciousness, autonomic dysfunction, fever, sweating, rigidity, leukocytosis, raised creatine phosphokinase (CPK) levels, and disturbed liver function test (LFT).[1,2] There can be significant variation in the clinical presentation and outcome, and all signs and symptoms may not be present in every patient.[1,2] Initially, fatality rates reported were 10%–20%, but recent studies have put the figures at 3–4 mainly due to early recognition and treatment.[3,4] High-potency first-generation antipsychotics (FGAs) are reported to have more incidence of NMS, especially with a high dose and rapid escalation of dosage. Other risk factors reported include male gender, dehydration and other medical condition. Although NMS with second-generation antipsychotics (SGAs) is less common, it is reported with almost every SGA with variable severity, signs, and symptoms. Against this background, we report a case of aripiprazole-induced NMS that developed 5 days after dose escalation but resolved completely with treatment.

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Case Report

A 38 year old lady known to have had multiple episodes of bipolar disorder in the previous 10 years was admitted to the hospital with a new episode of mania. Prior to the admission, she had received lithium and aripiprazole 15 mg in the previous 2 weeks on an outpatient treatment basis. The admission was necessitated due to increased agitation and aggression with active psychotic symptoms. Her biological functions were disturbed grossly. In her previous episodes of illness, she was treated with lithium and olanzapine and was maintained on prophylactic lithium. Because she had put on significant weight with olanzapine, it was decided to use aripiprazole along with lithium, and injection lorazepam was kept for PRN. She was afebrile, and reports of complete blood counts (CBCs), LFT, renal function test (RFT), and Vitamin B12 and urine analysis were normal. Serum lithium was 0.6 mEq/l. In view of the increased symptoms, especially psychotic symptoms, it was decided to escalate her aripiprazole dose to 30 mg daily. There was no significant change in her behavior in the initial 5 days after the escalation of aripiprazole.

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On the 6th day, the patient suddenly turned delirious with restlessness, confusion, irrelevant muttering, and urinary incontinence. On examination, her body temperature was 39°C, pulse rate was 118, and respiratory rate was 31/min. There was significant cogwheel rigidity in the body. Suspecting NMS, we sent for CPK levels along with the repetition of CBC, LFT, and RFT. The results showed leukocytosis (15,500), and CPK levels were 2100. Serum lithium was 0.8 mEq/l. No marked changes were seen in electrocardiogram, and computed tomography head was normal. With confusion, fever above 39°C, and CPK levels 2100, our case was diagnosed as moderate-to-severe NMS according to Hynes criteria.[5]

The patient was shifted to the intensive care unit. Aripiprazole and lithium were stopped immediately, and she was treated with intravenous fluids, injection lorazepam, and tepid sponging. She made gradual recovery over the next 1 week. CPK level came down to 471 after 7 days. The patient was discharged from the hospital after 2 weeks with full recovery from NMS, and her CPK level was 42 at the time of discharge. Lithium was restarted at discharge. Quetiapine 25 mg per day was started with a plan of very gradual escalation of dose. One month after discharge, she returned for follow-up with few psychotic symptoms persisting. She was on quetiapine 200 mg per day with normal CPK levels.

Discussion

In France, *syndrome malin* was a nonspecific medical term used to describe a fulminant, neurovegetative state that preceded collapse and death. It had many etiologies and was often associated with fever and fatal infectious processes. The term *syndrome malin des neuroleptiques* was used for similar findings in neuroleptic-treated patients by Delay *et al*. in 1960. The English translation of the syndrome – "neuroleptic malignant syndrome" – first appeared in 1968.[6] The pathogenesis of NMS is still not known. Two main mechanisms are suggested: one, central D2 receptor blockade causing an abnormal reaction in skeletal muscle and second, sympathoadrenal hyperactivity leading to autonomic dysfunction.[4] NMS is often reported in patients with antipsychotics with lithium, as in the present case. Here, NMS could be due to the concomitant use of antipsychotic or due to independent lithium induced. Lithium alters neurotransmitter activity and reduces the effects of dopamine by preventing the accumulation of cyclic adenosine monophosphate at the intracellular level. Dopamine underactivity has been widely accepted as a hypothesis for the occurrence of NMS.[3] Our case of NMS developing in a young female after several weeks of initial aripiprazole has many interesting points. Many cases of aripiprazole-induced NMS are reported with no hyperthermia, no tachypnea, and diaphoresis.[6,7] Our case had hyperthermia with temperatures running above 39°C, diaphoresis, as well as tachypnea. Mortality rates are less with SGAs than with FGAs. Rigidity and fever may be less common in the clinical presentation of NMS induced by the SGAs.[6,7] NMS caused by aripiprazole use could be related to its pharmacodynamic profile, or allelic variants altering CYP2D6-mediated metabolism may cause an increased risk of NMS.[8] On an average, NMS develops 14 days following the initial administration of aripiprazole with a mean prescribed dosage of 5–30 mg/day. In our case, it developed after 5 days with dose escalation to 30 mg.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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