Case Report

Atypical treatment response of a neuroleptic malignant syndrome - a rare case report

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Introduction

Neuroleptic Malignant Syndrome (NMS) is an idiosyncratic reaction to certain psychotropics, with a fatality rate of up to 10%. It is most commonly associated with antipsychotics (typical>atypical).It is commonly characterised by muscular rigidity, fever, altered mental status & autonomic dysfunction. There is increased risk within first 7 days (28 days with depot) of high starting dose, rapid upward titration, polypharmacy of antipsychotics & concurrent systemic disease. NMS generally rapidly evolves over days & lasts up to 2 weeks, if untreated.[1]Here we present a case of NMS with atypical treatment response

Case Report

A 26 year old, obese (110 Kg) man, with a history of Bipolar Affective Disorder on tablets Sodium Valproate & Haloperidol presented to a psychiatric hospital with big talks, elevated self-esteem, and reduced need for sleep for 10 days. He was diagnosed to be in mania as per DSM 5 criteria. Ziprasidone at dosage of 40 mg at night was started, to alleviate mood symptoms. Within 1 week of starting Ziprasidone at a dosage of 40 mg at night for 3 days, it was then increased to 80 mg in divided dosage. The manic symptoms reduced but the patient had difficulty in walking. On presentation to the Emergency Department of our institution, patient was very much rigid, was not able to move his limbs fully, was unable to swallow even water, complained of respiratory distress. His oxygen saturation fell to 88-90% (without moist oxygen), temperature was 103 degree F, BP=180/100 mmHg, Pulse=140/min, Respiratory Rate=40/min; there was severe perspiration, hyporeflexia & nasal intonation of voice. Patient was then shifted to ICU. Blood was sent for CBC, C/S, CPK, Na+, K+, Ca++, Mg++, urea, creatinine, LFT, TSH, MPDA, Typhidot, NS1 Antigen for dengue; Urine was sent for R/E, C/S; ECG & chest X-ray were done.All were found to be in normal range.CPK level was 1470 IU/ml; TLC was increased to 18,500. A diagnosis of NMS was made. The patient was put on Bromocriptine 5mg TDS, infusion of NS, cold sponging, moist oxygen through mask @ 4 litre/min, injection Furosemide (to control BP), Syrup Promethazine- 2 tsf single dose (to overcome symptoms of laryngopharyngeal dystonia). As the patient was unable to swallow even water, Ryle's tube was introduced. And, as the patient was not fully conscious (GCS-12), Foley's catheter was introduced. Dose of Bromocriptine was increased to 10 mg TDS after 3 days. Neurological, General Medicine, ENT opinions were sought. Amantadine was started in dosage of 100 mg TDS. HRCT thorax was done and found to be normal. But patient showed no clinical improvement. Rather, CPK level was found to be raised to 5500 IU/mL.Then, Lorazepam tablet was started in the divided dosage of 6 mg/day and was increased to 12mg/day. Urine myoglobin was sent. As urea and creatinine showed a gradual rise (though within normal range), hourly urine output was monitored, to intervene at the earliest, for impending renal failure. Positive balance was maintained.

After initiation of Lorazepam, CPK came down to 1550 IU/mL. Rigidity of the patient was reduced. But the fever continued. Blood was sent for C/S, malaria, dengue, chikungunya, typhoid, serology; sputum for H1N1; Chest X-Ray; urine R/E, C/S were done, all being negative. Then, we removed the central venous catheter, after which, the fever subsided. Finally, he was discharged owith Lorazepam 12mg/day, Valproate 1000 mg/day. Bromocriptine was tapered & stopped. CPK level was 280 IU/ml.

Discussion

NMS is a rare, life threatening condition, that is missed in patients who present with fever 2.In our patient, onset of rigidity, perspiration & fever without any definitive cause, made us suspect non-infectious etiology. We noticed that the patient was on multiple medications, identified as triggering agents for NMS. High potency 1st generation antipsychotics, like Haloperidol, are most commonly implicated in causing NMS; other agents like atypical antipsychotics, & centrally acting antiemetics may cause NMS3.

The pathogenesis behind the cause of NMS is only speculative[2]. The classical lead pipe rigidity noted on physical examination[4] is defined by increased resistance in all limbs, to all ranges of motion.Elevated CPK is most commonly seen; typically >1000, but can reach up to 10,000 or more, in severe NMS1. Leucocytosis & electrolyte imbalance may be seen.Typically, NMS develops over days to weeks, & shows a sluggish neuromuscular response, characterised by rigidity & hyporeflexia[3].When NMS is suspected, all antipsychotics are stopped. Intramuscular injections are stopped, & patient has to be well hydrated, to prevent ARF. Though not much supported in literature, Paracetamol is often used for fever. Antihypertensives & anxiolytics are indicated to manage autonomic hyperactivity.Though not tested in large clinical trials, Dantrolene & Bromocriptine are used for 7-10 days[2]. Clinical improvement starts within a few days, & usually resolves within 2 weeks. ECT can be given; it reduces mortality. Though prognosis of NMS has improved now, but still, mortality remains ~10%. Complete recovery occurs in most cases[5]. ARF & disease severity are the most important factors for mortality. Early suspicion, leading to early detection & treatment, is crucial to reduce mortality in NMS.

Coming to our case,

Ziprasidone was found to be the causative agent behind NMS.There are case reports in literature where ziprasidone was the culprit behind NMS [6,7].

In our case, there was decrease in CPK levels, & decrease in rigidity, with increased dose of Lorazepam tablet, and rise in CPK again when Lorazepam was tapered down. This showed that there was a definite causal benefit of Lorazepam. Lorazepam was the drug that lead to reducing it. Such cases have been reported in literature [8,9]. Benzodiazepines have been recommended for managing agitation and reversing catatonic symptoms of NMS [8]. In some cases, benzodiazepines were found to be effective when other medications failed [9] .We employed a similar management in our three patients, using supportive care and lorazepam. Both fever and muscular rigidity improved and resolved in 24–72 hours. These findings indicate that lorazepam may be useful for management of NMS precipitated by both typical and atypical antipsychotic agents.This is also one of the rare cases where bromocriptine failed to control the same.

Conclusion

NMS is a life threatening and deadly situation for any psychiatrist. It is one of the handful cases where it was successfully controlled with lorazepam. Because of its easy availability and comparative safety and efficacy of other anti NMS agents, it can be used more frequently in practice. As more case reports, & more research emerge, more can be known about NMS & its treatment.

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