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Atypical Treatment Response Of Neuroleptic Malignant Syndrome - A Rare Case Report

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Abstract
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 . Here we present a case of nms which didn't response to bromocriptine but later responded to lorazepam.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.

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I. Introduction

"Neuroleptic Malignant Syndrome (NMS) is an idiosyncratic reaction to certain psychotropics", with a death rate of up to 10%.[1] It is most commonly related to antipsychotics (typical>atypical). It is generally characterized by "muscular rigidity, fever, altered mental status & autonomic dysfunction" [1]. There is increased danger within the initial 7 days (28 days with the depot) of greater initial dosage, quick rising titration, "polypharmacy of antipsychotics" & simultaneous systemic disease[2]. NMS generally quickly evolves over days & lasts up to 2 weeks, if untreated.[1]Here we present a case of NMS that didn't respond to bromocriptine but later responded to "lorazepam".

II. Case Report

A 26 year old male, with a past of "Bipolar Affective Disorder" on tablets Sodium Valproate at divided dosage of 1000 mg & Haloperidol at divided dosage of 10 mg for past 3 months with questionable compliance presented to a psychiatric hospital with elevated self esteem, reduced need for sleep for 10 days. He was diagnosed to be in mania as per DSM 5 criteria. Patient was started only on Ziprasidone at dosage of 40 mg at night 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 relatives claimed that patient improved symptomatically r 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 Complete Blood Count , Urine for culture and sensitivity , Creatine Phosphokinase, Na+, K+, Ca++, Mg++, urea, creatinine, LFT, TSH, Typhidot, NS1 Antigen for dengue. Urine was sent for routine and microscopic examination as well as culture and sensitivity. An ECG & chest X-ray were done which 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 as per DSM 5 criteria. The patient was put on Bromocriptine 5mg TDS, infusion of normal saline, cold sponging, moist oxygen through mask @ 4 litre/min, injection Furosemide (to control BP), Syrup Promethazine- 2 tsf single dose. 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 with Lorazepam 12mg/day, Valproate 1000 mg/day. Bromocriptine was tapered & stopped. CPK level was 280 IU/ml.

III. Discussion

"NMS is a rare, life-threatening condition, that is missed in patients who present with fever" [2]. In our subject, the beginning of rigidity, perspiration & fever without any definitive cause, made us suspect non-infectious etiology. We noticed that the patient was on several medicines, recognized as activating agents for "NMS". "High potency 1st generation antipsychotics", like "Haloperidol", are most generally implicated in producing NMS; further agents like atypical antipsychotics, & centrally acting antiemetics may cause NMS[3].

"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 NMS [1.] Leucocytosis & electrolyte imbalance may be seen. Typically, NMS develops over days to weeks, & shows a sluggish neuromuscular response, characterized 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 the 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 on the basis of Naranjo algorithm [6]. There are case reports in the literature where ziprasidone was the culprit behind NMS [7,8].

In our case, there was a decrease in CPK levels, & a decrease in rigidity, with an increased dose of Lorazepam tablet, and a rise in CPK again when Lorazepam was tapered down. This showed that there was a definite causal benefit of Lorazepam. Such cases have been reported in literature [9,10]. For controlling agitation and reversing catatonic symptoms in NMS [9] benzodiazepines have been suggested. When other treatments failed to work in certain circumstances, benzodiazepines were shown to be successful 10. We used supportive care and lorazepam to handle all three patients in a similar manner. In 24-72 hours, both fever and muscle stiffness subsided and disappeared. These results suggest that lorazepam may be helpful for treating NMS brought on by both conventional and atypical antipsychotic medications. This is also one of the rare cases where bromocriptine failed to control the same. Despite Dantrolene having the best efficiency in treating NMS we could not use that because of its unavailability in our institution

IV. 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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