Successful Treatment of a Complicated Case of Neuroleptic Malignant Syndrome with a Higher Dose of Bromocriptine and Lorazepam

ABSTRACT
A 53-year-old patient of schizoaffective disorder developed neuroleptic malignant syndrome (NMS) following treatment with haloperidol, clozapine and parenteral fluphenazine. He showed full recovery with immediate discontinuation of potential offenders and prompt treatment with a higher dose of bromocriptine and lorazepam along with management of aspiration pneumonia. Need for early recognition of NMS and treatment by a multidisciplinary team is discussed.

Keywords: Neuroleptic malignant syndrome, Bromocriptine, Lorazepam, Fluphenazine, Haloperidol, Clozapine.


Source of support: Nil

Conflict of interest: None

INTRODUCTION
Neuroleptic malignant syndrome (NMS) is a potentially fatal but rare side effect of neuroleptics. It is characterized by altered consciousness, rigidity, fever, autonomic instability and elevated serum creatinine phosphokinase (CPK) and leukocytosis.1,2 Neuroleptic malignant syndrome may lead to hepatic and renal failure, rhabdomyolysis, acute respiratory syndrome and disseminated intravascular coagulation. It is seen in 0.07 to 2.2% of patients receiving neuroleptics and carries a mortality risk of 10 to 30%.2 Bromocriptine, dantrolene sodium, amantadine and levodopa carbidopa, benzodiazepines and electroconvulsive therapy (ECT) have been shown to be effective in its management.3,5 Neuroleptic malignant syndrome may be difficult to diagnose and manage in the presence of serious medical comorbidities like central nervous system (CNS) infections, toxicencephalopathies, agitated delirium, heat stroke, etc.6,7 and associated complications, such as acute renal failure, venous thromboemboli, multiple system failure and aspiration pneumonia.8 Therefore, it is essential to adopt a multidisciplinary management in such cases. We are reporting a case who developed NMS following addition of fluphenazine to haloperidol and clozapine. This case is primarily reported to highlight the efficacy of early institution of higher dose of bromocriptine and lorazepam and need for multidisciplinary care in averting this potentially fatal condition.

CASE REPORT
A 53-year-old patient of schizoaffective disorder was admitted in psychiatry ward with acute exacerbation. His symptoms stabilized with haloperidol 10 mg/day, divalproex sodium 1000 mg/day, clozapine 400 mg/day, trihexyphenidyl 4 mg/day and clonazepam 2 mg/day. However, in view of chronic course and poor drug compliance in the past, he was also given two injections of 25 mg fluphenazine decanoate each, after 3 and 4 weeks of admission. He was discharged on above medicines after 4 weeks. About 12 days after discharge, the patient started worsening and was ultimately admitted under medicine with the complaints of altered consciousness, body stiffness, urinary incontinence and loss of appetite.

On examination, patient appeared dehydrated; he was febrile (101.6ºF), diaphoretic, stuporose, had salivary effortless, coarse lung crepitations. His pulse rate was 126 beats/minute, respiratory rate 24 breaths/minute and blood pressure 100/60 mm Hg. In view of chronic course and poor drug compliance in the past, he was also given two injections of 25 mg fluphenazine decanoate each, after 3 and 4 weeks of admission. He was discharged on above medicines after 4 weeks. About 12 days after discharge, the patient started worsening and was ultimately admitted under medicine with the complaints of altered consciousness, body stiffness, urinary incontinence and loss of appetite.

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examination was done and broad spectrum antibiotics and diazepam (5 mg I/V slowly qid) were started. On psychiatric consultation, the author (RCS) kept a strong possibility of NMS with aspiration pneumonia and started bromocriptine 10 mg bid first day then 10 mg tid orally and swapped diazepam with lorazepam 8 mg/day I/V dividedly.

Patient’s ECG, CT-head, CSF examination, urinalysis, blood and urine culture were within normal limits but chest X-ray was suggestive of aspiration pneumonia. Complete blood count (CBC) showed marked leukocytosis (WBC—23,300/cmm) with a shift to left (neutrophil count—90%). Abnormal laboratory parameters included aspartate aminotransferase 501 IU (normal 10-43) and alanine aminotransferase S21 IU (normal 10-30), blood urea nitrogen—77 mg/dl (normal 20-40), serum creat nine—1.7/dl (normal 0.5-1.5) and total CPK-1997 IU/l (normal 24-195). The patient’s temperature normalized after 1 week but other parameters kept fluctuating; pulse rate 80 to 126 beats/minute, blood pressure 100/60 to 130/90 mm Hg and respiratory rate 18 to 24 breaths/minute.

Just after 2 days, patient’s sensorium improved, rigidity decreased and he started responding to verbal commands. He cooperated for chest physiotherapy also and over the next 5 days, he became more alert and afebrile and his vital signs stabilized. He showed marked improvement after 15 days and was shifted to psychiatry ward. He started taking orally; bromocriptine and lorazepam were gradually tapered off over next 15 days (total duration 30 days) without any recurrence of psychotic symptoms. The patient was discharged on 4 mg trihexyphenidyl/day after 3 weeks of hospital stay and was maintaining well 1 month after discharge.

DISCUSSION

Different types of diagnostic criteria have been proposed for diagnosing NMS; however, due to its variable presentation, no single set of criteria is used universally. Levenson’s criteria have been widely cited. It includes three major criteria; fever, rigidity and raised CPK levels and six minor criteria; altered consciousness, diaphoresis, tachypnea, tachycardia, abnormal blood pressure and leukocytosis. For the diagnosis of NMS, presence of all the three major or two major and four minor criteria need to be satisfied. On the basis of history of exposure to neuroleptics, clinical examination and positive Levenson’s criteria, a final diagnosis of NMS with aspiration pneumonia was made in our case. Possibility of meningocencephalitis was already ruled out by a negative CSF report.

All the three neuroleptics taken by this patient, i.e. haloperidol, clozapine and fluphenazine are known to cause NMS and furthermore, propensity for NMS rises with neuroleptic polypharmacy. Therefore, this may be a possible reason for developing NMS in the present case. However, as NMS is most often seen with the high potency and depot neuroleptics, such as haloperidol and fluphenazine, it is more likely that these two drugs must have lead to the development of NMS in this case. In our patient, in addition to dehydration, administration of another depot injection of fluphenazine just after 7 days of the first, might have contributed more or compounded the risk for NMS with haloperidol by way of massive dopaminergic receptor antagonism because, NMS is known to result from deficient compensatory mechanisms following blockade of dopaminergic regulation of muscle tone and autonomic function.

Bromocriptine (2.5-5 mg 8 hourly per orally or by nasogastric tube) has been listed under 1st line intervention for the treatment of moderate to severe NMS spectrum-related symptoms. It has been recommended that bromocriptine should be instituted with a starting dose of 2.5 mg 2 to 3 times a day, which can be increased to a total daily dose of 45 mg if needed. In view of the severity of NMS on the very first day, we had started with bromocriptine 10 mg bid which is a relatively higher than recommended starting dose for bromocriptine and increased it to 10 mg tid on the 2nd day. Bromocriptine can worsen psychosis and hypotension and may precipitate vomiting, and thus should be avoided in patients with risk of aspiration. Premature discontinuation of bromocriptine should be avoided as it can result in rebound symptoms in some cases.

Rapid development of NMS symptoms, quick response and full recovery with bromocriptine which enhanced dopamine transmission and lorazepam which reduced muscle rigidity is noteworthy and is in line with similar reports.

Neuroleptic malignant syndrome is a potentially lethal side effect of neuroleptic drugs regardless of their duration or dose. The mortality and morbidity associated with NMS can be decreased significantly if the offending agents are stopped immediately; drugs like bromocriptine and lorazepam are instituted early and in high tolerable doses along with careful screening and management of complications by a multidisciplinary team.

REFERENCES