Neuroleptic malignant syndrome associated with the use of injection zuclopenthixol acetate

Zuclopenthixol is usually used in parental form to manage acute agitation and psychosis. It has high affinity for dopamine D1 and D2 receptors. There are very few reports of Neuroleptic Malignant Syndrome (NMS) with use of zuclopenthixol monotherapy. In this case report, we present a 35 year old male with alcohol dependence, presented to the emergency with altered sensorium, fever and stiffness of limbs. He had history of consuming alcohol for the last 10 years in a dependence pattern characterized by craving, tolerance, and withdrawal. Just prior to the presentation, he was consuming about 750 mL of Indian-made foreign liquor per day.

Ten days prior to the presentation, while the patient was lifting a heavy object at his home, he developed severe backache and remained bedbound. In view of the severe pain, he was not able to go out to take alcohol. After about 72 h of the last intake of alcohol, the patient developed withdrawal symptoms in the form of irritability, visual and auditory hallucinations, agitation, sweating, palpitations, misrecognition, and disturbed sleep with a reversal of sleep–wake cycle.

These symptoms would often fluctuate over 24 h with evening worsening of symptoms. Over the period of 1 week and tablet bromocriptine was tapered off, after 1 week of being asymptomatic.

A 35-year-old male presented to the emergency department with altered sensorium, fever, and stiffness of limbs. Exploration of the history revealed that he has been consuming alcohol for the last 10 years in a dependence pattern characterized by craving, tolerance, and withdrawal. Just prior to the presentation, he was consuming about 750 mL of Indian-made foreign liquor per day.

Ten days prior to the presentation, while the patient was lifting a heavy object at his home, he developed severe backache and remained bedbound. In view of the severe pain, he was not able to go out to take alcohol. After about 72 h of the last intake of alcohol, the patient developed withdrawal symptoms in the form of irritability, visual and auditory hallucinations, agitation, sweating, palpitations, misrecognition, and disturbed sleep with a reversal of sleep–wake cycle. These symptoms would often fluctuate over 24 h with evening worsening of symptoms. Over the period of 1 week and tablet bromocriptine was tapered off, after 1 week of being asymptomatic.

Keywords: Neuroleptic malignant syndrome, side effects, zuclopenthixol

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next 3–4 days, the symptoms kept on increasing and his agitation increased markedly, leading to a consultation with a local practitioner. In view of the marked agitation, he was given injection zuclopenthixol acetate 200 mg thrice on the same day. Within 12–14 h of the last injection, the patient developed fever, stiffness in the limbs, profuse sweating, increase in the symptoms of intermittent agitation, and altered sensorium. In view of these symptoms, he was referred to a tertiary care hospital for further management.

Detailed exploration of history did not reveal evidence any other substance use and any other psychotic symptoms, seizures, head injury, hematemesis, melena, and depressive features.

On examination, the patient had profuse sweating, and his pulse rate was 130/min, temperature was 102°F, and blood pressure was 80/50 mmHg, with marked fluctuation in the vital over time. He had features of dehydration. Neurological examination revealed marked lead pipe-like rigidity, diminished reflexes, flexor planter response, normal-sized pupils, and normal bowel sounds. On mental status examination, he was mute. However, there were no other signs of catatonia and evidence of hepatic damage.

On investigation, he was found to have raised serum creatinine phosphokinase levels (839.9 U/L; reference laboratory value: 26–308 U/L) and leukocytosis. Other investigations in the form of renal function test, liver function test, serum electrolytes, blood glucose levels, blood and urine culture, magnetic resonance imaging of brain, and cerebrospinal fluid analysis did not reveal any abnormalities.

In view of a temporal correlation of the onset of symptoms after the use of zuclopenthixol, a diagnosis of NMS was considered. An additional diagnosis of alcohol dependence syndrome, currently in withdrawal, was also considered. The patient was started on supportive management to address the dehydration and was given thiamine 500 mg thrice daily. In addition, he was started on tablet bromocriptine 5 mg thrice daily and lorazepam 2 mg/day. With this intervention, his symptoms improved over a period of 1 week and tablet bromocriptine was tapered off, after 1 week of being asymptomatic. He was psychoeducated about alcohol dependence and relapse prevention counseling was started. He was also attached to the orthopedic services for evaluation of his backache.

zuclopenthixol in seven cases. Out of the seven cases, in three cases, NMS was associated with zuclopenthixol decanoate[2,4,5] and in other three cases, NMS was associated with zuclopenthixol acetate.[6] NMS was also associated with the use of oral zuclopenthixol hydrochloride in one case, who had previously developed NMS with haloperidol.[7] However, in all the previously reported cases of NMS associated with zuclopenthixol acetate, the patients were receiving additional antipsychotic medication. However, in the index case, zuclopenthixol acetate was used as monotherapy. In three out of the seven reported cases, the patients were managed with bromocriptine and in three cases, management was limited to the use of benzodiazepines. In the index case, we used both as the patient was exhibiting symptoms of NMS, in the background of alcohol withdrawal state. Previous reports have shown that NMS can develop after 1–11 days of use of zuclopenthixol acetate. In the index case, NMS developed after 1 day. This was possibly due to the use of higher doses administered over a short span of time in the index case. Existing literature clearly suggests an association of higher doses and rapid increase in the dose of antipsychotics with NMS.[7,8]

Few case reports suggest that NMS can mimic alcohol-withdrawal delirium.[9] Further, only one case report in the existing literature suggest the development of NMS after intravenous administration of haloperidol in a patient with alcohol-withdrawal delirium, much like the index patient, and the authors concluded that even a small dose of neuroleptic drugs can precipitate NMS in an already-exhausted patient.[10] Similar incident has been reported during benzodiazepine withdrawal.[11] The index case possibly developed alcohol-withdrawal delirium to start with, which was misinterpreted as psychosis in view of the psychotic symptoms and marked agitation. This possibly led to the administration of higher doses of zuclopenthixol over a short span of time. Alcohol withdrawal and agitation contributed to the development of dehydration and exhaustion, which are known risk factors for NMS.[8,9] These factors possibly contributed to the development of delirium.

Accordingly, it can be said that clinicians should properly evaluate patients presenting with psychotic symptoms for delirium, associated with alcohol withdrawal, and cautiously use antipsychotics for the management of alcohol-withdrawal delirium.

DISCUSSION

There is limited literature on the association of NMS with zuclopenthixol. In our literature search, we could find only five reports, reporting the association of NMS with zuclopenthixol in seven cases. Out of the seven cases, in three cases, NMS was associated with zuclopenthixol decanoate[2,4,5] and in other three cases, NMS was associated with zuclopenthixol acetate.[6] NMS was also associated with the use of oral zuclopenthixol hydrochloride in one case, who had previously developed NMS with haloperidol.[7] However, in all the previously reported cases of NMS associated with zuclopenthixol acetate, the patients were receiving additional antipsychotic medication. However, in the index case, zuclopenthixol acetate was used as monotherapy. In three out of the seven reported cases, the patients were managed with bromocriptine and in three cases, management was limited to the use of benzodiazepines. In the index case, we used both as the patient was exhibiting symptoms of NMS, in the background of alcohol withdrawal state. Previous reports have shown that NMS can develop after 1–11 days of use of zuclopenthixol acetate.[8] In the index case, NMS developed after 1 day. This was possibly due to the use of higher doses administered over a short span of time in the index case. Existing literature clearly suggests an association of higher doses and rapid increase in the dose of antipsychotics with NMS.[7-9]

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Declaration of patient consent

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

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Conflicts of interest
There are no conflicts of interest.

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