Electroconvulsive Therapy in Drug Resistant Neuroleptic Malignant Syndrome

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Abstract
We report a case of a 20 years female referred to us with a history of a brief psychotic episode for which she was given inj. Haloperidol. The patient presented in an unconscious state with high grade fever. The diagnosis was kept as neuroleptic malignant syndrome after ruling out other possibilities. The patient did not respond to Bromocriptine and Dantrolene. With the recent evidence of electroconvulsive therapy being useful in these patients, we went ahead with the same. We present this case to share our experience of the excellent response of neuroleptic malignant syndrome to electroconvulsive therapy. ©

Introduction
Neuroleptic malignant syndrome is a rare but potentially life threatening idiosyncratic reaction to neuroleptic medications with no satisfactory treatment available at present. The underlying aetiopathogenesis is thought to be a hypodopaminergic state of the brain secondary to central D2 receptor blockade or dopamine depletion in the hypothalamus and nigrostriatum. Electroconvulsive therapy has been anecdotally reported to be effective in refractory neuroleptic malignant syndrome. We report a case of a 20 years female patient with neuroleptic malignant syndrome who failed to respond to the pharmacological therapy but improved dramatically after electroconvulsive therapy. To the best of our knowledge, no case of drug resistant neuroleptic malignant syndrome responding to electroconvulsive therapy has been reported from India till date.

Case Report
A 20 years unmarried female, referred from civil hospital Thane, was brought to our casualty in an unconscious state with high grade fever and bladder incontinence of 12-16 hours duration. Prior to this, she was admitted at the civil hospital for an acute psychotic episode which, as per her relatives started after a breakup with her boyfriend. She was treated there with intramuscular injection of haloperidol. There was no history of psychiatric illness in the past. There was no history suggestive of seizures, headaches or vomiting.

On examination her temperature was 39°C, heart rate was 110 per minute and her blood pressure was 110/70 mm Hg. The patient was diaphoretic. There was no cyanosis, icterus or rash on the body. On CNS examination she was unconscious, not responding to verbal commands or painful stimuli. Pupils were bilaterally normal in size and reacting to light. She had neck stiffness, lead pipe rigidity in all four limbs and plantar response was flexor. Rest of the systemic examination was normal.

In this clinical setting with a background history of antipsychotic medication we made a provisional diagnosis of neuroleptic malignant syndrome (NMS). Differential diagnoses were acute meningitis, encephalitis, cerebral malaria and nonconvulsive status.

Patient’s neuroimaging (CT and MRI brain), CSF studies (gram stain, microscopy, culture), CBC were normal and peripheral smear was negative for malarial parasites. EEG did not show any epileptic focus. Patient’s serum creatine phosphokinase (CPK) level was 3670 U/L (24 – 170 U/L).

Patient was started on Tab. Bromocriptine 5 mg four times daily, Tab. Dantrolene sodium 50 mg thrice daily and supportive care. Her fever subsided with this treatment; however there was no improvement in the sensorium and rigidity even after 4 weeks.

In view of refractoriness to the above pharmacological therapy, a decision to administer ECT was taken. Our patient was given a total of nine ECT cycles with a frequency of three cycles per week. During each cycle
patient was intubated, ventilated with 100% oxygen and succinylcholine was administered as a muscle relaxant. Bilateral ECT with a current strength of four volts for one second was given. Her EEG, ECG and blood pressure were monitored. An adequate response was considered when patient had a seizure activity on EEG lasting for at least 30 to 40 seconds. Patient showed dramatic improvement after the third cycle of ECT in the form of spontaneous eye opening and decrease in muscular rigidity to some extent. Subsequently, after fifth ECT cycle she was able to sit on her own, take oral feeds and was able to communicate. At the end of ninth cycle, patient’s muscular rigidity had completely resolved and she was ambulatory. She was discharged without any residual deficit.

**DISCUSSION**

NMS is an idiosyncratic reaction to neuroleptic drugs and is characterized by fever, muscular rigidity, altered mental status, autonomic dysfunction, elevated serum CPK and leucocytosis.

Many cases of NMS were reported after it was first described by Delay et al in 1960. Based on case series and reviews from western countries the incidence of NMS averages 0.2% in patients treated with neuroleptics. Chopra et al reported an incidence of 1.4/1000 cases treated with neuroleptics in India.

Blockade of dopamine type 2 receptors in the striatum and hypothalamus is thought to be the underlying mechanism causing NMS. It has been described with typical as well as atypical antipsychotic medications. Atypical antipsychotics differ from the typical ones in that they have weak dopamine type 2 receptor blocking action and they produce few extrapyramidal symptoms. Newer antipsychotic medications like clozapine, risperidone and olanzapine have all been found to cause NMS.

NMS has been conventionally treated with dopaminergic drugs like bromocriptine, amantadine and dantrolene sodium. These medications are effective during the first few days of treatment and are unlikely to show delayed response. In contrast, ECT remains effective even late in the course, often after other interventions have failed. Our patient did not show any response to bromocriptine and dantrolene sodium even after 4 weeks except for subsidence of fever; however she responded well to ECT.

Hermesh et al in 1987 first described a case of NMS that responded to ECT. Subsequently Scheftnet et al in 1992 and Trollor et al in 1999 described ECT to be an effective modality of treatment when drug therapy had failed.

While Scheftnet et al reported clinical response within 72 hours of first ECT cycle; Trollor et al found that improvement is usually apparent after a few ECT sessions generally up to six. Our patient started showing improvement after third ECT session.

Scheftnet et al has further suggested a treatment sequence for NMS which includes medications for first 48 hours and in the absence of clinical response ECT to be initiated.

ECT is relatively safe in the treatment of NMS, although the risk of cardiovascular complications should be considered. Malignant hyperthermia due to the anesthesia associated with ECT has not been reported in patients with NMS and succinylcholine has been used safely in these patients. Our patient did not develop malignant hyperthermia following ECT therapy with succinylcholine nor did she develop any cardiac arrhythmia.

Finally, the mechanism by which ECT cures NMS has not been established. The efficacy is probably related to its facilitatory effect upon dopamine activity in CNS.

**CONCLUSION**

Though NMS is a rare disorder, considering its life threatening nature, ECT should be offered to patients with severe drug resistant NMS, not only because it is safe but it is also effective as evident from the ample amount of data available from the western studies. However more studies from the Indian population will be needed as to its efficacy and adverse effects before it is routinely recommended in the treatment of drug resistant NMS for Indian patients.

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