

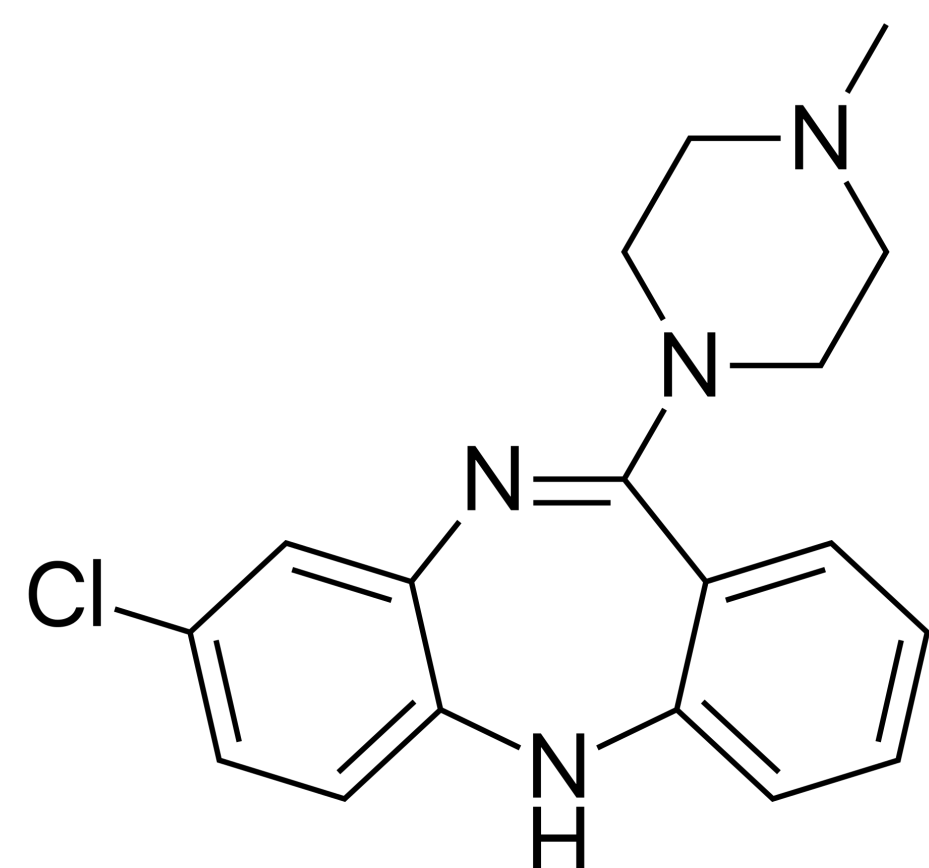
Electroconvulsive Therapy For Malignant Catatonia Due To Clozapine Withdrawal — A Case Series

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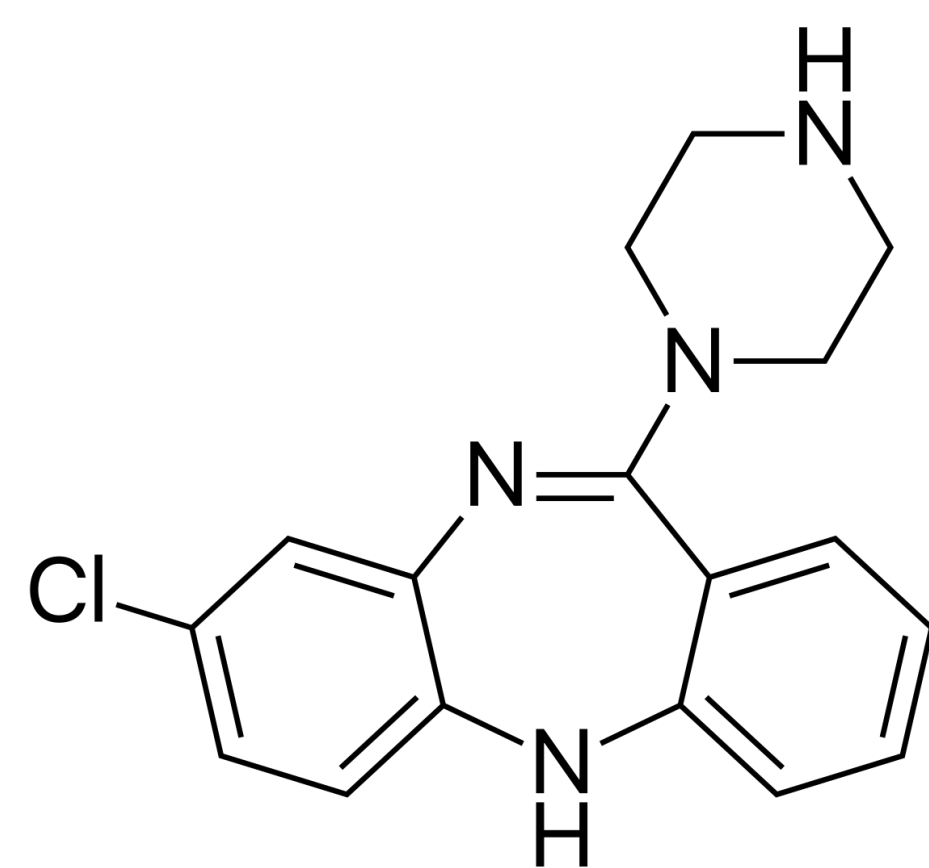
Background

Clozapine

- A second-generation antipsychotic, and the only medication approved by the FDA for managing treatment resistant schizophrenia.¹
- Abrupt cessation has been shown to increase the risk of clinical deterioration in a patient.^{2,3}
- Withdrawal has been linked to worsening psychosis, autonomic instability, cholinergic rebound, gastrointestinal symptoms, and in some cases frank catatonia.^{2,3}



Chemical Structure of clozapine



Chemical Structure of n-desmethylozapine (a major clozapine metabolite)

Catatonia

- Malignant catatonia is a life-threatening neuropsychiatric condition, estimated to occur in 0.07% of psychiatric admissions or annually in 0.0004% of community adults.⁴
- The mortality rates exceeded 75% in the pre-antipsychotic era, remained at 60% between 1960 and 1985, and have declined to 10% in cases reported between 1986 and 2020.⁵
- Two recent (2018 & 2019) review articles identified 26 reported cases of catatonia triggered by clozapine withdrawal, of which 13 cases met criteria for malignant catatonia.^{6,7}
- Of these cases, 7 patients were offered Electroconvulsive Therapy (ECT), with 4 patients responding well, 1 with a partial response, and 2 with no response to ECT.^{6,7}
- We present three cases of malignant catatonia secondary to clozapine discontinuation that were successfully treated with ECT, offering additional support that ECT can successfully treat malignant catatonia triggered by clozapine withdrawal.

Citations

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Case:	A	B	C
Age, Sex, Diagnosis	31, Male, Schizophrenia	31, Male, Schizophrenia	35, Male, Schizophrenia
Medications prior to Clozapine Discontinuation	Clozapine 400mg Haloperidol 7.5mg Stable for 7 years	Clozapine 200mg Haloperidol 5mg BID Haloperidol Decanoate 75mg Stable for 2 weeks	Clozapine 500mg Stable for 15 years
Medical Comorbidities and Lab Abnormalities	AKI Pneumonia Upper Extremity DVT Elevated CK (peak of 27,102) Elevated AST (166) Elevated ALT (349)	CK (peak of 19,166)	UTI
Autonomic Irregularities	Fever (T-max 101.4°F) Tachycardia Diaphoresis Tachypnea	Fever (T-max 102.2 °F) Tachycardia	Fever (T-max 105 °F) Tachycardia Hyper/Hypotension Urinary Retention
BFCRS Score	18	11	21
Medications used prior to ECT	Lorazepam Phenobarbital Bromocriptine Valproic Acid	Lorazepam Dantrolene Ketamine Dexmedetomidine Norepinephrine Fentanyl	Lorazepam Bromocriptine Dantrolene
Number of Bitemporal ECT sessions	9	11	25
Medications upon discharge	Clozapine 500mg Lorazepam 3mg QID	Olanzapine 10mg Lorazepam 2mg TID	Clozapine 150mg

ECT Technique and Anesthesia

- All cases were initially treated with Bitemporal placement with a pulse width of 1 millisecond.
- The stimulus charge at the first treatment was determined by “half-age method.”⁸
- The parameters were subsequently adjusted based on the quality of the seizure.
- Flumazenil (0.5 – 1 mg) was used as pre-anesthesia medication to reverse the benzodiazepine effect.
- The induction agents frequently required adjustment based on seizure quality and varied from methohexital, ketamine, etomidate, and remifentanyl to fentanyl drip (intubated patient).
- In all three cases a non-depolarizing muscle relaxant, rocuronium, was used (later reversed by sugammadex).

Somatics Thymatron
 Electroconvulsive Therapy
 Instrument



Discussion

- All the three cases of malignant catatonia were unique and among the most difficult cases that our ECT team had encountered.
- All three cases presented with recent nonadherence of clozapine and catatonic symptoms.
- All of them required Bitemporal ECT treatments and all of them initially required daily ECTs (“en-bloc”).
- Two of the above three cases had been stable on clozapine for at least 7 years with discontinuation resulting from insurance issues, reflecting the challenges of our health care system.
- The psychiatry team considered the differential diagnosis of malignant catatonia vs NMS.
- Some posit that NMS is a subset of malignant catatonia induced by antipsychotic use, while others argue that they are separate entities, near impossible to distinguish through laboratory or clinical assessment alone.⁵

Conclusion

- ECT is a useful treatment for malignant catatonia induced by clozapine withdrawal.
- Given the increased morbidity/mortality of malignant catatonia, early diagnosis and treatment is paramount.
- Clinicians should consider the risk of rapid advancement to malignant catatonia in patients who have recently discontinued clozapine and begin to manifest catatonic symptoms.
- Further studies are needed to understand the pathophysiology of malignant catatonia as well as the mechanism of ECT’s effectiveness.