Parkinsonism is a red herring:
Broad differential diagnoses in a case of catatonia secondary to clozapine withdrawal

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Background

- Catatonia is a complex neuropsychiatric syndrome that may be caused by clozapine withdrawal. Although the underlying mechanisms are not clear, the effects of clozapine on GABA interneurons may be implicated (1).
- Clozapine withdrawal catatonia often responds poorly to lorazepam only; studies show an effective response by the reintroduction of clozapine (1-2).

The Case

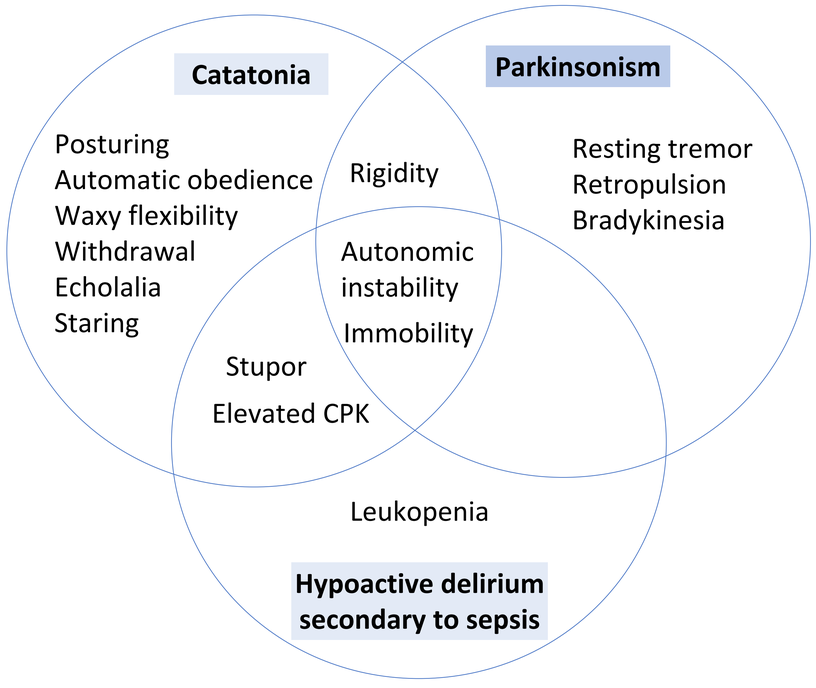
Patient profile: 56-year-old woman with schizophrenia recently discharged from state psychiatric hospitalization.

Home medications:
1. Haloperidol decanoate 150mg intramuscularly monthly (last given 2 weeks prior to admission)
2. Valproic acid (VPA) 1250mg orally daily
3. Clozapine 200mg orally bedtime

ED Course:
The patient presented to the emergency room with significant resting tremors in the extremities. Collateral reported patient had discontinued clozapine, believing it was causing tremors. Patient also noted to be staring, hypoactive, and rigid, with a Bush Francis Catatonia Rating Scale (BFCRS) score of 13. Patient showed no improvement after two doses of IM lorazepam 2mg but tremors improved after IM benztropine 2mg. Patient was then started on intravenous (IV) lorazepam 2mg BID for catatonia and IV benztropine 1mg BID for Parkinsonian symptoms of unclear etiology, including retropulsion and bradykinesia.

Relevant Diagnostic Work-up:
1. Lab tests: elevated ammonia (72), VPA (109.9), CK (643)
2. Urinalysis: Positive leukocyte esterase
3. Head CT, brain MRI, lumbar puncture, and EEG were noncontributory.

CL Course → Day 1 to 5:
Upon admission to Medicine, her symptoms worsened to a BFCRS score of 17. Ceftriaxone was started to treat urinary tract infection. VPA was held for hyperammonemia. Benztropine was stopped due to concern for anticholinergic side effects (urinary retention). Lorazepam was gradually titrated to 3mg IV four times per day.



CL Course → Day 5 to 7:
The patient showed no significant response to lorazepam and instead exhibited worsening immobility and withdrawal, eventually necessitating nasogastric tube placement. Additionally, the patient developed a febrile episode to 101.3°F and intermittent tachycardia despite treatment of UTI with ceftriaxone, raising concern for development of malignant catatonia.

CL Course → Day 7 to 19:
Given lack of response to lorazepam, clozapine was restarted at 25mg at bedtime once NG tube was placed and increased by 25mg every two days to 150mg a day.

Four days after clozapine was reintroduced, she began to show improvements in voluntary movements. A week later, her catatonia resolved and her vitals stabilized.

Discussion

- This case presents a complex clinical scenario in which no single diagnosis fully accounted for the presenting symptoms.
- Differential diagnoses included delirium, idiopathic Parkinsonism, medication-induced Parkinsonism, neuroleptic malignant syndrome, stroke, and seizures.
- The case underscores the importance of recognizing clozapine withdrawal catatonia and managing it appropriately with clozapine reintroduction, as case report data has suggested that benzodiazepines alone may not be sufficient for management (1).

Conclusions

- **In a complex clinical scenario, competing differentials must sometimes be treated simultaneously before they can be ruled out.**
- **Re-initiation of clozapine should be considered when clozapine withdrawal is a suspected etiology of catatonia.**

Clozapine withdrawal catatonia[1]	
Duration of clozapine treatment	Long term
Response rate to BZDs	Low
Most effective treatments	Clozapine, ECT
Time to response	Days to weeks

References

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2. Boazak M, Cotes RO, Potvin H, Decker AM, Schwartz AC. Catatonia Due to Clozapine Withdrawal: A Case Report and Literature Review. Psychosomatics. 2019 Jul-Aug;60(4):421-427. doi: 10.1016/j.psym.2018.07.010. Epub 2018 Jul 29. PMID: 30268340.

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