Clozapine Toxicity Unveiled: Cerebral Edema as a Rare and Alarming Complication

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Introduction

- Clozapine is an atypical antipsychotic utilized in the treatment of treatment-resistant schizophrenia.
- Clozapine is an antagonist at dopamine receptors (highest at D4) and partial agonist at 5-HT1A.
  - Muscarinic, histamine, and alpha-1 adrenergic-receptor antagonist[1]
- Reserved for treatment-resistant cases due to its variety of known side effects including but not limited to:
  - Agranulocytosis
  - Metabolic syndrome
  - Neuroleptic malignant syndrome
  - Seizures[1]
- Clozapine requires extensive monitoring due to its known adverse effects.[1]
- Advantages of clozapine over other antipsychotics may include:
  - Lowering risk of suicide
  - Lowering risk of tardive dyskinesia[1]
- Clozapine toxicity can be a result of changes in absorption, distribution, or elimination.[1,2,3]
- Some known adverse events associated with clozapine toxicity include hypersalivation, tachycardia, hypotension, sedation, and seizures.[1]
- This case presentation demonstrates a patient with severe clozapine toxicity who developed cerebral edema, an under-recognized complication.

Case Presentation

A 40-year-old female with schizophrenia, hypothyroidism, and hyperlipidemia presented with altered mental status for 2–3 days. She had reduced oral intake, poor hygiene, and incoherent speech and was prescribed clozapine 100 mg twice daily. During hospitalization, she was diagnosed with E. coli bacteremia and acute kidney injury (AKI). She received antibiotics and dialysis, but her mental status remained unchanged. A clozapine serum level of 1788 ng/mL was detected, well above the therapeutic range. MRI showed cerebral edema with posterior fossa fullness and low-lying cerebellar tonsils. Dexamethasone treatment led to marked improvement.

Imaging

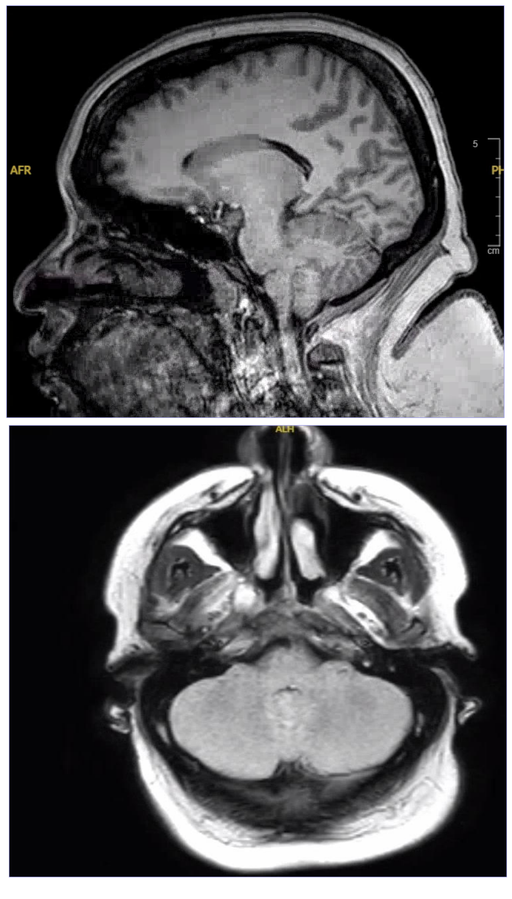

Figure 1: MRI brain without contrast demonstrating posterior fossa fullness and low-lying cerebellar tonsils.

Discussion

- Cerebral edema is not a well-recognized result of clozapine toxicity.
- There is a lack of a clear alternative medical etiology for the cerebral edema seen in this patient.
- Compromised hepatic and/or renal function can contribute to clozapine toxicity.
- Genetic polymorphisms in CYP enzymes can also play a role in clozapine toxicity.[3]
- The elevated clozapine level and renal dysfunction likely contributed to the manifestation of cerebral edema.
- Resolution of neurologic status with dexamethasone suggests that the cerebral edema may be reversible with appropriate intervention.

Conclusion

- This case heightens awareness for rare, but serious complications associated with clozapine toxicity.
- Clinicians should remain vigilant in monitoring clozapine levels, especially in patients with comorbidities such as renal impairment, to prevent toxicity and its sequelae.

References

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