

Lithium-Related Neurotoxicity During Acute Illness in a Patient on Concurrent Diuretic Therapy: A Case Report

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ABSTRACT

Lithium is an effective mood stabilizer with a narrow therapeutic window and is primarily cleared by the kidneys. Conditions such as acute illness, fluid volume depletion, disturbances in sodium levels, and concurrent drug use can elevate the risk of lithium-induced neurotoxicity. A 57-year-old man with bipolar disorder, type 2 diabetes, hypertension, and ischemic heart disease was admitted due to vomiting, reduced oral intake, and diabetic ketoacidosis. He had been taking lithium carbonate 400 mg twice daily for about four months, along with torsemide and spironolactone. During hospitalization, he exhibited mild slurred speech, tremors, and drowsiness. His serum lithium level was 1.43 mmol/L. Although kidney function remained relatively stable, blood urea nitrogen was elevated, and mild hyponatremia was present. Lithium was discontinued, leading to marked improvement in neurological symptoms within approximately 24 hr. The medication was later resumed at a lower dose of 300 mg twice daily. This case underscores that lithium-related neurotoxicity can occur even when serum levels are below the typical toxicity threshold, especially during acute medical conditions and in the presence of factors affecting fluid and sodium balance. Thorough clinical evaluation, medication review, and therapeutic drug monitoring are crucial for patients on lithium therapy.

Keywords: Adverse Drug Reaction, Bipolar Disorder, Diuretics, Lithium, Neurotoxicity, Therapeutic Drug Monitoring.

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INTRODUCTION

Lithium continues to play a key role in managing bipolar disorder, but its narrow therapeutic range and reliance on renal excretion make it sensitive to changes in kidney function, hydration status, sodium levels, and other medications (Decker *et al.*, 2015).

Neurotoxic effects of lithium may include tremor, drowsiness, speech difficulties, ataxia, confusion, and neuromuscular dysfunction. Notably, clinical signs of toxicity do not always align precisely with serum lithium levels, particularly in individuals on long-term treatment (Gitlin, 2020).

We describe a patient on chronic lithium therapy who developed neurological symptoms during an episode of acute illness involving vomiting, poor intake, diabetic ketoacidosis, and concurrent diuretic use-despite a serum lithium concentration of 1.43 mmol/L.

CASE REPORT

A 57-year-old male with a history of bipolar disorder, type 2 diabetes, hypertension, and ischemic heart disease (with prior PTCA in 2012 and 2014) presented with intermittent chest pain, right-sided headache radiating to the neck, repeated vomiting, low-grade fever, and decreased oral intake.

He had been on lithium carbonate 400 mg twice daily (800 mg/day) for around four months for bipolar disorder. His cardiovascular regimen included torsemide 20 mg and spironolactone 25 mg daily.

Upon admission, he was diagnosed with diabetic ketoacidosis, evidenced by a blood glucose of 261 mg/dL, serum bicarbonate of 18 mmol/L, and blood ketones of 3.5 mmol/L. Treatment with intravenous regular insulin followed by an insulin infusion led to resolution of ketosis.

Echocardiography revealed moderate left ventricular systolic dysfunction (ejection fraction 42%) and a well-defined apical thrombus measuring 2.1×1.5 cm. Antithrombotic therapy was initiated per cardiology guidance.

During his inpatient stay, he began showing mild dysarthria, tremors, and lethargy. Given his ongoing lithium use, lithium-associated neurotoxicity was suspected. Serum lithium was measured at 1.43 mmol/L. Renal function



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remained relatively stable with creatinine between 1.0-1.2 mg/dL, though blood urea nitrogen was elevated at 66 mg/dL, and serum sodium ranged from 133-135 mmol/L (Table 1).

Recurrent vomiting and poor oral intake suggested possible volume depletion and altered sodium homeostasis-both known to reduce lithium clearance. Additionally, concomitant use of diuretics, which affect renal handling of sodium and water, was considered a contributing factor.

Lithium was stopped. There were no seizures, loss of consciousness, or severe neurological decline, and extracorporeal removal was not needed. Symptoms improved significantly within about 24 hr of discontinuation. Lithium was later restarted at a reduced dose of 300 mg twice daily. The patient remained stable and was discharged with follow-up instructions.

DISCUSSION

This case highlights the importance of interpreting lithium levels in conjunction with clinical presentation. Although the patient's serum lithium concentration (1.43 mmol/L) was below the commonly referenced threshold of 1.5 mmol/L for increased toxicity risk, he displayed clear neurological signs consistent with lithium neurotoxicity. Prior reports have shown similar neurotoxic effects even when levels are within or near the therapeutic range (Gitlin, 2020).

Table 1: Clinical and laboratory findings relevant to suspected lithium-associated neurotoxicity.

Parameter	Finding
Age	57 years
Lithium dose	400 mg twice daily
Duration of lithium therapy	~4 months
Serum lithium	1.43 mmol/L
Torsemide	20 mg
Spironolactone	25 mg
BUN	66 mg/dL
Creatinine	1.0-1.2 mg/dL
Sodium	133-135 mmol/L
Glucose during DKA	261 mg/dL
Ketones	3.5 mmol/L
Bicarbonate	18 mmol/L
Neurological manifestations	Tremor, dysarthria, lethargy
Intervention	Lithium withheld
Clinical response	Substantial improvement within ~24 hr
Subsequent lithium dose	300 mg twice daily

Several factors likely contributed to his vulnerability. First, persistent vomiting and inadequate oral intake may have led to volume contraction and sodium imbalance conditions known to enhance renal reabsorption of lithium and promote accumulation. Second, the use of torsemide and spironolactone could have influenced lithium kinetics. While thiazide diuretics are most strongly linked to lithium interactions, loop and potassium-sparing diuretics may also alter lithium clearance and require careful monitoring (Decker *et al.*, 2015). The combination of such agents during acute illness increases the potential for toxicity. Third, the presence of diabetic ketoacidosis-along with associated vomiting and metabolic disruptions-may have heightened susceptibility, although DKA itself is not a direct cause of neurotoxicity. Notably, significant renal impairment was absent. Creatinine levels remained stable, but the elevated BUN (66 mg/dL) in the context of poor intake and vomiting suggests altered intravascular volume despite preserved glomerular filtration. The rapid improvement following lithium discontinuation supports a likely causal relationship, though definitive causality cannot be established due to lack of baseline and post-withdrawal lithium levels. Other elements such as comorbid conditions and polypharmacy must also be considered.

Management of lithium toxicity depends on symptom severity, lab values, kidney function, and overall clinical status. In severe cases, extracorporeal treatment may be necessary, especially when neurological deterioration is pronounced or elimination is impaired (Grandjean & Aubry, 2009). Here, symptoms resolved quickly without such intervention.

CONCLUSION

This case also emphasizes the value of clinical pharmacy services and medication reconciliation. Patients on lithium require routine monitoring of lithium levels, kidney function, and electrolytes. They should also be advised to seek medical care during episodes of dehydration, gastrointestinal losses, or acute illness, and before starting drugs that may interfere with lithium excretion (Grover *et al.*, 2022; Decker *et al.*, 2015). The decision to reduce the lithium dose from 400 mg to 300 mg twice daily after the event reflects the need for reassessment following suspected toxicity. Close monitoring of lithium levels and renal and electrolyte parameters is warranted after restarting therapy.

ABBREVIATIONS

BUN: Blood Urea Nitrogen; **DKA:** Diabetic Ketoacidosis; **EF:** Ejection Fraction; **PTCA:** Percutaneous Transluminal Coronary Angioplasty; **mmol/L:** Millimoles per Liter; **mg/dL:** Milligrams per Deciliter; **mg/day:** Milligrams per Day.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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