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A Rare Case Of Lithium Toxicity With Obstructive Uropathy: A Case Report

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Abstract
Lithium is an indispensable medication in the management of bipolar disorder. Despite its clinical effectiveness, lithium has a narrow therapeutic index which increases the risk of toxicity, requiring a close monitoring of lithium levels. We present a case of chronic lithium toxicity in a patient diagnosed with bipolar disorder, and concomitant renal calculus which an unqualified healthcare provider erroneously treated. An accurate clinical diagnosis followed by a timely intervention prevented fatal outcomes in this case.

Keywords: *Lithium, Lithium Toxicity, obstructive uropathy, bipolar disorder, tribal healthcare disparities,*

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I. Introduction

Lithium plays a major role in the treatment of bipolar disorder and is indicated as the first-line therapy either as a monotherapy or in combination with other atypical antipsychotics such as Quetiapine.[1–3]

Lithium was first approved for treating bipolar disorder (BD) in France in 1961, followed by approvals in the United Kingdom in 1966, Germany in 1967, and Italy and the United States in 1970. In 1974, its use was further expanded to include the prevention of manic-depressive illness.[4]

Despite its therapeutic efficacy, the long-term use of lithium is associated with significant adverse effects, most notably nephrotoxicity and thyroid dysfunction. Chronic lithium therapy can lead to nephrogenic diabetes insipidus (NDI), chronic tubulointerstitial nephritis, and a measurable decline in renal function over time.[5] [6]

Patients with bipolar disorder often present with medical comorbidities, which can complicate pharmacological management and exacerbate the risk of adverse events. These comorbidities are frequently underdiagnosed, overlooked, or inadequately managed, underscoring the psychiatrist's role in recognising and addressing these challenges.

This case report describes a 35-year-old male from a remote tribal region of Telangana, India, who presented to the emergency department with clinical signs indicative of chronic lithium toxicity. Despite resource constraints, the diagnosis was made based on clinical judgment, and timely, appropriate intervention was administered, effectively saving the patient's life.

This case explores the intricacies of management with lithium in a patient with bipolar disorder, emphasising the challenges of balancing therapeutic efficacy with long-term adverse effects while effectively monitoring the levels for toxicity given a narrow therapeutic index. By presenting this case, we aim to contribute to the understanding of lithium's risk-benefit profile and provide insights into optimal management strategies for patients at risk of or experiencing lithium toxicity, especially in patients with comorbidities.

II. Case Presentation

A 35-year-old male was brought to our rural emergency department with complaints of generalized weakness, decreased urine output, and constipation persisting for one week. The primary survey was unremarkable revealing a patent airway, unlaboured breathing, and adequate circulation. However, the Glasgow coma scale (GCS) was noted as E3V2M6. The patient exhibited muscle fasciculations and myoclonic jerks, hindering effective verbal communication. ECG demonstrated QT and PR interval prolongation. Detailed history obtained from the patient's attendant revealed a recent diagnosis of bipolar disorder by a local unlicensed healthcare provider who initiated Lithium carbonate 600mg twice a day and Quetiapine 300mg once a day. Further inquiry into the patient's history disclosed that the patient had been revisiting the same provider for the past three months with complaints of abdomen and flank pain. During this period, the patient was prescribed analgesics, corticosteroids, and antibiotics of unknown class and doses. The patient's socio-economic

status, lack of medical records, and the limited literacy level of the attendant further hindered the accurate elicitation of medical history.

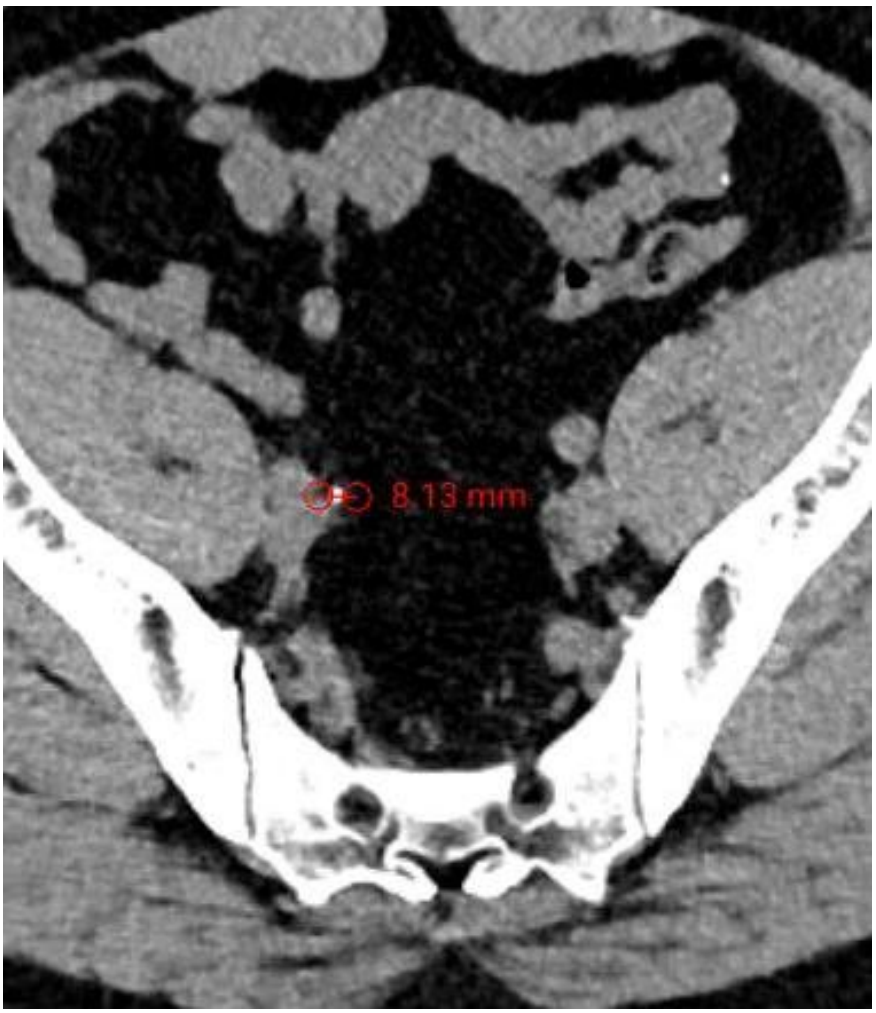

Figure 1: CT KUB; Sagittal CT showing 8mm Right Distal Ureteric Calculus

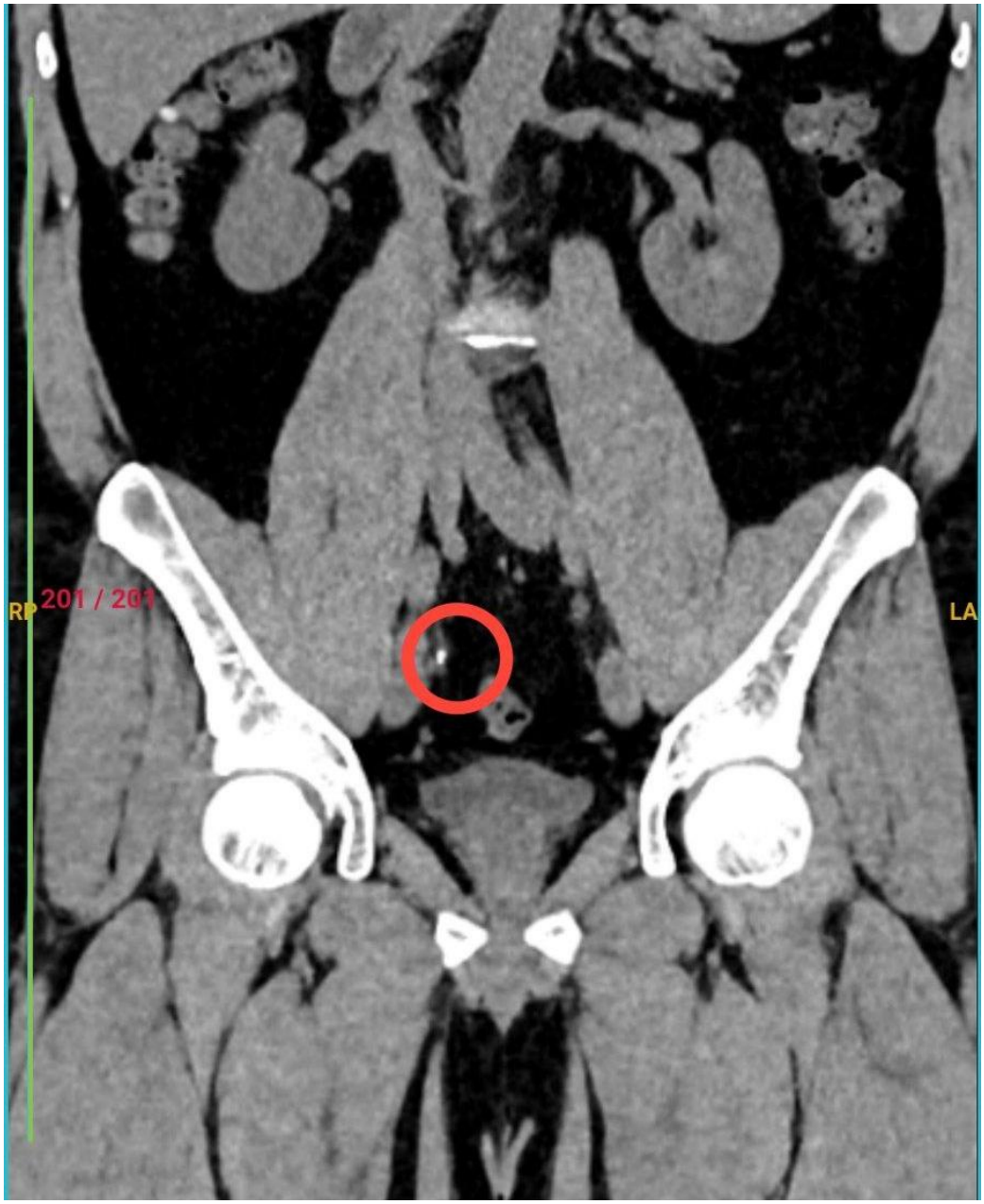

Figure : CT KUB; Coronal CT showing 8mm Right Distal Ureteric Calculus

Parameter	**Patient Values**	**Reference range**
pH	7.2	7.35 – 7.45
pCO_2	60 mmHg	35 – 45 mmHg
Bicarbonate (HCO_3)	13 mEq/L	21 – 28 mEq/L
lactate	15mmol/L	0 – 2 mmol/L
Initial Serum Creatinine	4 mg/dl	0.62 – 1.10 mg/dL
Initial Serum Lithium Level	2.9 mEq/l	0.6–1.2 meq/l

Repeat Serum Lithium Level	0.3 mEq/l	0.6–1.2 meq/l

Table 1 Laboratory Investigations

Over the past week, the patient observed significantly reduced urine output, recurrent episodes of seizure-like episodes without loss of consciousness, and persistent myoclonic jerks involving the neck, shoulder, and thoracic muscles which compelled him to seek medical attention from the Emergency department. [Table 1] On preliminary Arterial blood gas analysis, the patient was found to have mixed metabolic (lactic acidosis) and respiratory acidosis with pH of 7.2, bicarbonate of 13mEq/l, lactate of 15mmol/l and pCO_2 of 60mmHg. Abdominal CT [Figures 1-2] showed grade two renal parenchymal changes, and right distal ureteric calculus measuring 8 mm. Laboratory investigations revealed a serum creatinine level of 4 mg/dl, indicative of Acute kidney injury. It was hypothesised that the calculus likely led to obstructive uropathy and post-renal AKI.

Given that lithium is predominantly eliminated by the renal system, it was postulated that the obstructive uropathy impaired lithium clearance, contributing to the toxicity. [7] Due to the lack of adequate diagnostic testing resources in the Emergency Department for real-time serum lithium measurement, a provisional diagnosis of Lithium toxicity was made based on clinical presentation and clinical instincts. Blood samples for serum lithium level assessment were sent to the nearest diagnostic laboratory. The patient was promptly initiated on Intravenous crystalloid fluids, non–invasive ventilation support, and emergent haemodialysis. The patient showed significant improvement after the first haemodialysis session, with a reduced frequency of myoclonic jerks, improved breath-holding test and oriented speech. The patient was slowly weaned off the NIV after 24 hours and two additional sessions of haemodialysis were continued in the subsequent days.

Initial blood investigations were reported 48 hrs later showing a serum lithium level of 2.9 mEq/l (reference range 0.4–1.2 mEq/l; lower end of the range for maintenance therapy and the elderly, higher end for children)[4] confirming the provisional diagnosis of lithium toxicity. The patient was managed with multi-disciplinary specialist care, including right ureteral DJ stenting to relieve the obstruction. Repeat serum lithium levels showed a decline to 0.3 mEq/l. After five days of hospitalisation, the patient was discharged from the hospital in an ambulatory and hemodynamically stable condition.

III. Discussion

This case calls attention to the critical importance of clinical acumen and the ability to optimize limited resources to save lives in resource-deficient settings, particularly in time-sensitive scenarios like emergency care departments. The patient was diagnosed with bipolar disorder and prescribed a combination of lithium and quetiapine by an unlicensed healthcare provider. Furthermore, the patient's underlying renal calculus were misdiagnosed and erroneously managed with antibiotics and steroids, which contributed to the worsening of the condition.

Bipolar disorder is a complex and debilitating mental illness characterized by episodes of mania or hypomania alternating with depression often interspersed with periods of remission. With an estimated lifetime prevalence of 2.4% globally, it poses significant challenges for affected individuals, including substantial morbidity, mortality, and an elevated risk of suicide. [7]

Bipolar disorder often presents with predominant depression, making it hard to differentiate from unipolar depression or other conditions. Severe cases, like psychotic BD, can resemble schizophrenia, leading to inaccurate diagnosis and treatment.[8] These diagnostic challenges contribute to significant errors in accurate treatment administration. Among available treatments, lithium has remained the keystone for mood stabilization for over five decades, offering protection against both depressive and manic episodes. Notably, it is the only pharmacological intervention that consistently demonstrated reduced suicide risk in bipolar patients.[9] [7]

The exact mechanism of action of lithium in mania remains incompletely understood. However, it is hypothesized to suppress inositol signalling by depleting intracellular inositol and inhibiting glycogen synthase kinase-3 (GSK-3). Lithium also influences neurotransmitter dynamics by decreasing the release of norepinephrine and dopamine while transiently increasing serotonin release.[10] Pharmacologically, lithium is a low-molecular-weight monovalent cation that is neither metabolized nor protein-bound. It initially distributes in extracellular fluid and achieves intracellular equilibrium over 5–10 days.[6,11] Renal excretion is the primary route of elimination, with approximately 80% of the filtered lithium being reabsorbed, primarily in the proximal tubule and the thick ascending limb of the loop of Henle. Lithium has an elimination half-life ranging from 18 to 36 hours. Conditions that impair or delay its elimination, such as the presence of renal calculus observed in this patient, may enhance lithium reabsorption, leading to its accumulation and increasing the risk of chronic toxicity. [7,10]

The toxic effects of lithium, particularly on the principal cells of the collecting duct, are thought to involve the inhibition of GSK-3β-dependent signalling pathways. Its physicochemical properties, including low

molecular weight, minimal protein binding, and lack of metabolism, make lithium highly dialyzable. Given its narrow therapeutic index, routine monitoring of serum lithium levels and renal function is imperative, particularly in patients with chronic kidney disease or those undergoing haemodialysis. [10–12]

This is a rare case presentation of lithium toxicity secondary to obstructive uropathy, emphasizing the critical importance of meticulous monitoring of patients and their comorbid conditions. It underscores the necessity of comprehensive evaluation before initiating high-risk medications such as lithium, given its narrow therapeutic index and potential for severe adverse effects. Moreover, this case highlights the need for stringent regulation to ensure that such medications are prescribed solely by qualified professionals, thereby mitigating the risks associated with inappropriate or unqualified prescribing practices.

IV. Conclusion

In conclusion, lithium toxicity poses a significant risk in the long-term management of bipolar disorder. This case shows the need for enhanced research into diagnostic tools for the early detection and screening of lithium toxicity, particularly in resource-limited settings. Furthermore, it highlights the necessity of ensuring that medications such as lithium are prescribed and monitored by qualified healthcare professionals, with appropriate regulation and oversight, to ensure quality patient care.

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