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CASE REPORT

Severe Hypercalcemia and Acute Kidney Injury in a Patient on Chronic Lithium Therapy: A Case Report and Brief Review of the Literature

Nabil HMAIDOUCH, Loubna BENAMAR, Naima OUZEDDOUN, Tarik BOUATTAR

ABSTRACT

Background: Lithium remains a cornerstone treatment in the long-term management of bipolar disorder. However, its chronic use is associated with various adverse effects, particularly affecting renal function and calcium metabolism. **Case Presentation:** We report the case of a 41-year-old man with no significant medical history who was followed for bipolar disorder and treated with lithium carbonate for over ten years. He was referred to the nephrology department due to acute confusion occurring in the context of renal failure and hypercalcemia, accompanied by elevated parathyroid hormone (PTH) levels, in the absence of other obvious causes. Clinical, biological, and radiological investigations, supported by the Naranjo Adverse Drug Reaction Probability Scale, identified lithium as the probable causal factor for these abnormalities. Following lithium discontinuation and symptomatic management, significant clinical and biological improvement was observed. According to the literature, lithium-induced hypercalcemia is most often secondary to hyperparathyroidism. The main associated renal complications include nephrogenic diabetes insipidus and chronic tubulointerstitial nephropathy. Psychiatric comorbidities can delay the recognition of these adverse effects. Regular monitoring of renal function, serum calcium levels, and lithium concentrations is essential for early diagnosis and optimal management. **Conclusion:** This case highlights the importance of rigorous clinical and biological monitoring in patients receiving lithium therapy to detect renal and metabolic complications early. Discontinuation or adjustment of lithium treatment, combined with appropriate management, often leads to significant improvement, reinforcing the need for close collaboration between psychiatrists and nephrologists to ensure therapeutic safety.

Keywords: bipolar disorder, hypercalcemia, lithium, nephrology, pharmacovigilance, renal failure, side effects, tubulointerstitial nephropathy.

Ibn Sina Hospital, Rabat - Morocco

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Correspondance to: Nabil HMAIDOUCH
E-mail : Hmaidouchn@gmail.com

1. INTRODUCTION

Lithium (Li) has been widely used for nearly a century in the treatment of bipolar disorder, including manic and depressive episodes, as well as for maintenance therapy. It also exerts a proven anti-suicidal effect, as demonstrated in several meta-analyses. Despite its efficacy, lithium has a narrow therapeutic index and is associated with numerous adverse effects, including hypercalcemia—often secondary to lithium-induced hyperparathyroidism [3]. We report a clinical case of hypercalcemia and renal failure related to chronic lithium therapy.

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2. CASE REPORT

We report the case of a 41-year-old male diagnosed with bipolar disorder, under psychiatric treatment since 2007. His regimen included lithium carbonate (Téralithe® 250 mg, 4 tablets/day), chlorpromazine (Largactil® 100 mg, 2 tablets/day), trihexyphenidyl (Artane® 5 mg/day), olanzapine (Ranozyp® 10 mg, 2 tablets/day), quetiapine (Quetiaphi® 300 mg, 2 tablets/day), amisulpride (Amiprim® 200 mg, 2 tablets/day), and sodium valproate (Depakine® 500 mg/day). The patient demonstrated poor compliance, with irregular dosing and no consistent psychiatric follow-up. He presented to the emergency department of Ibn Sina Hospital with acute confusion and was subsequently transferred to nephrology for further assessment and management of renal failure.

On examination, the patient weighed 65 kg. He was obnubilated with a Glasgow Coma Scale score of 12 (E4 V3 M5), apyretic, and hemodynamically stable (BP: 130/70 mmHg). Signs of dehydration were present, including reduced skin turgor and tachycardia (107 bpm). The remainder of the physical examination was unremarkable.

Laboratory investigations revealed severe hypercalcemia (serum calcium 3.56 mmol/L) with normal albumin (41 g/L), full serum electrolytes within normal limits except for mild hypernatremia (Na^+ 140 mmol/L) and normal potassium (K^+ 4.5 mmol/L), elevated creatinine (194.6 µmol/L; eGFR 34.9 mL/min), urea 6.6 mmol/L, phosphorus 0.93 mmol/L, magnesium 0.88 mmol/L, marked vitamin D deficiency (5 ng/mL), and a supratherapeutic lithium level (1.16 mmol/L; therapeutic range 0.5–0.8 mmol/L). Urinary studies showed a reversed Na^+/K^+ ratio (38/45 mEq/L), with a urinary calcium of 9.2 mmol/24 h (elevated; normal 2.5–7.5 mmol/24 h) and a urinary phosphate of 10 mmol/24 h (low–normal), findings consistent with functional acute kidney injury. Thyroid function was normal, and an electrocardiogram revealed no hypercalcemia-related abnormalities. Therapeutic management included discontinuation of lithium without introducing any other mood-stabilizing medication and daily intravenous rehydration with isotonic saline (0.9% NaCl, total 3 L/day), combined with sodium bicarbonate (14%, 500 mL to 1 L) to correct metabolic acidosis and enhance renal calcium excretion. The volume and composition of fluids were selected to safely restore intravascular volume, promote urinary calcium clearance, and prevent further lithium accumulation. Furosemide was avoided due to dehydration and the risk of worsening prerenal injury. Calcitonin was not used because the hypercalcemia was not life-threatening, and bisphosphonates were avoided given the reduced eGFR and their potential nephrotoxicity.

Further investigation into the hypercalcemia revealed markedly elevated PTH (261 ng/L; normal: 11–62), normal TSH (2.3 UI/mL), cervical ultrasound showing benign thyroid nodules (EU-TIRADS 2 and 3) without parathyroid adenoma, unremarkable parathyroid scintigraphy and CT scans (neck, chest, abdomen), and no history of vitamin D or calcium supplementation. Given these findings, and based on the Naranjo algorithm (score: 10) [4], lithium was deemed the probable cause of the hypercalcemia and renal dysfunction. Following treatment, serum calcium normalized, creatinine levels progressively improved, and PTH decreased significantly without requiring surgical intervention such as parathyroidectomy. The full day-to-day evolution of these parameters is presented in **Figure 1.** The patient was discharged and continued follow-up in psychiatric consultations. Medium-term follow-up showed stabilization of renal function without progression to chronic kidney disease.

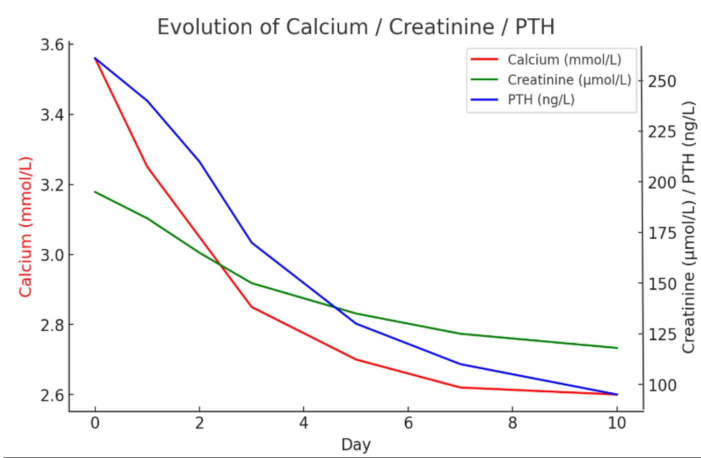

Figure 1. Dynamics of Calcium, Creatinine, and PTH during Follow-up.

3. DISCUSSION

Lithium is a well-established mood stabilizer for bipolar disorder, but its narrow therapeutic window predisposes patients to adverse effects, particularly involving the parathyroid glands and kidneys [4,5]. Lithium-induced hyperparathyroidism affects approximately 15% of long-term users and is caused by lithium's antagonistic action on calcium-sensing receptors in the parathyroid glands, which disrupts normal negative feedback and leads to inappropriate secretion of parathyroid hormone (PTH) despite hypercalcemia [6–9]. This results in persistent hypercalcemia and hypocalciuria, usually after prolonged exposure beyond two years [10]. Clinical manifestations are often nonspecific, including gastrointestinal and neuropsychiatric symptoms, which may be confounded by bipolar disorder or lithium toxicity, delaying diagnosis [11].

Management primarily involves lithium discontinuation and supportive measures such as intravenous hydration, with surgical intervention reserved for autonomous adenoma formation [12-14]. In this case, the patient was receiving multiple psychotropic agents concurrently, including lithium, three antipsychotics, an anticholinergic, and valproate. This degree of polypharmacy likely contributed to the complexity of the clinical picture by blunting early manifestations of lithium toxicity, complicating adherence, and influencing overall pharmacokinetics. Although none of the associated medications directly explained the hypercalcemia or renal failure, the cumulative burden of multiple psychotropics highlights the importance of regular medication review and the potential need for dose adjustment or deprescribing.

Our case illustrates these mechanisms, with both hypercalcemia and renal impairment clearly linked to chronic lithium exposure and showing substantial improvement after lithium discontinuation and supportive management. Furthermore, previous studies show that long-term lithium therapy is associated with nephrotoxicity, manifesting as tubulointerstitial nephritis and progressive chronic kidney disease (CKD), particularly in patients with prolonged treatment duration or elevated serum lithium levels [15–19]. Regular monitoring of renal function and lithium serum concentrations every 3 to 6 months is essential to detect early signs of toxicity and mitigate progression to irreversible renal damage [17], and close interdisciplinary collaboration between psychiatry and nephrology is vital to balance the psychiatric benefits of lithium with its potential systemic toxicities.

4. CONCLUSION

Lithium is an effective treatment for bipolar disorder, but long-term use in high doses can induce side effects, particularly at the renal and parathyroid level. Psychiatric illness may mask or delay diagnosis of these complications. However, regular monitoring of blood calcium levels, renal function, and serum lithium levels is essential for early detection and management of these complications. Therefore, collaboration between the nephrologist and the psychiatrist is required, as the risks of psychiatric decompensation or non-response to other treatments are very real.

Ethical Considerations: Written informed consent for publication of this case report and any accompanying data was obtained from the patient. All identifying information has been removed to ensure full anonymity.

Competing interests: The authors declare that they have no competing interest.

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