A Case of Lithium-Induced Symptomatic Hypercalcemia

To the Editor: Hypercalcemia has been associated with long-term lithium carbonate treatment, yet is often unrecognized.[1] Symptoms of hypercalcemia can progress insidiously and can mimic psychiatric disturbances, eg, delirium and symptoms resembling mood disturbances.[2,3] We report on a unique case of a lithium-treated patient presenting with depression-like symptoms secondary to hypercalcemia requiring lithium discontinuation.

Case report. Ms A, a 53-year-old woman, presented to the hospital in 2009 complaining of abdominal pain, nausea, constipation, and weakness of 1 week's duration. Prescribed lithium carbonate 300 mg tid daily for 10 years for *DSM-IV-TR* bipolar disorder, she complained of fatigue, decreased concentration, decreased appetite, and muscle weakness for several weeks, prompting concerns of an exacerbation of depression. Admission laboratory studies revealed a marginally elevated serum lithium level at 1.27 mEq/L and hypercalcemia (13.5 mg/dL; normal range, 8.4–10.2 mg/dL). Serum phosphate was 3.2 mg/dL (normal range, 2.7–4.5 mg/dL), and magnesium was 1.35 mg/dL (normal range, 1.69–2.73 mg/dL).

Hypercalcemia workup revealed a parathyroid hormone (PTH) level of 24.4 pg/mL (normal range, 15–65 pg/mL) and a 25-hydroxy vitamin D level of 36.8 ng/mL (normal 32–100 ng/mL), both within normal limits. Blood urea nitrogen and creatinine levels were 9 mg/100 mL (normal range, 6–20 mg/100 mL) and 0.5 mg/dL (normal range, 0.5–0.1 mg/dL), respectively. A skeletal series and chest x-ray failed to identify malignancy or sarcoid as potential etiologies.

Intravenous fluids and furosemide were initiated to decrease serum calcium; Ms A was asymptomatic once levels reached 11.3 mg/dL. Lithium was discontinued and substituted with lamotrigine. Serum calcium levels normalized within 4 weeks following lithium discontinuation.

Rates of lithium-induced hypercalcemia are estimated to be 5%–40%.[3] Symptoms can consist of anorexia, nausea, constipation, mood disturbances, and, in severe cases, delirium, stupor, and coma. In the present case, the gastrointestinal symptoms and weakness prompted evaluation of medical etiologies, unearthing an underlying hypercalcemia ascribable to long-term lithium use. Other potential causes, eg, primary or secondary hyperparathyroidism, malignancy, sarcoid, and vitamin D toxicity, were eliminated by history and laboratory investigations.

Lithium may induce increased calcium reabsorbtion within the loop of Henle. Concurrently, lithium can alter feedback mechanisms within the parathyroid gland, impeding the suppression of PTH normally produced by hypercalcemia.[1]

Evidence of asymptomatic hypercalcemia can be monitored with continued lithium use. Traditionally, symptomatic cases may be managed with discontinuation of lithium along with use of diuretics and hydration, resulting in prompt symptom resolution. Recently, use of calciuric agents, eg, cinacalcet, has been advocated, allowing resolution of hypercalcemia without necessitating lithium discontinuation.[4] Refractory cases, unresponsive to the above measures, may warrant parathyroidectomy.

Although the interval has not been established, clinicians should periodically monitor lithium-treated patients for hypercalcemia. Exacerbation of mood symptoms may be the initial sign of emerging hypercalcemia.

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