

## Lithium-Induced Transient Euthyroid Hyperthyroxinemia: A Case Report

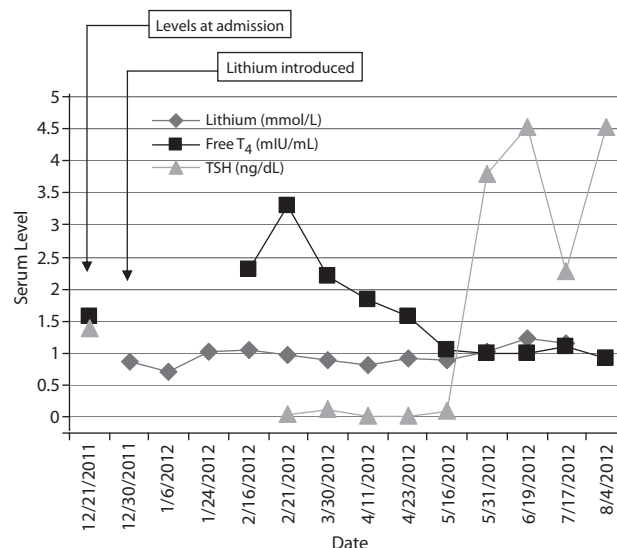
**To the Editor:** Sixty years after its introduction, lithium remains a first-line medication in the treatment of bipolar disorder.<sup>1</sup> While lithium treatment has been associated with a wide range of adverse effects,<sup>2,3</sup> thyroid-related abnormalities, especially hypothyroidism, are the most commonly reported ones.<sup>4,5</sup> Lithium-associated hyperthyroidism, however, is quite rare, and only a few sporadic case reports of thyrotoxicosis that developed after several years of lithium therapy or after stopping lithium<sup>3,6</sup> are described in the literature. Lithium-induced euthyroid hyperthyroxinemia, described as an elevation in serum thyroid hormone levels without clinical manifestations of thyrotoxicosis,<sup>7</sup> has not been reported to our knowledge. Stratakis and Chrousos<sup>8</sup> described a case of transient euthyroid hyperthyroxinemia associated with discontinuation of chronic lithium treatment. We report a patient who developed transient euthyroid hyperthyroxinemia within a few weeks of initiation of lithium therapy.

**Case report.** Ms A, a 24-year-old African American woman with a 4-year history of schizoaffective disorder, bipolar type (*DSM-IV-TR*), was admitted to our hospital in December 2011 with signs and symptoms consistent with mania with psychosis. At admission, she presented with a labile mood with aggressive and violent behavior, insomnia, poor concentration, pressured speech with racing thoughts, and increased psychomotor activity. She was also very paranoid, reported auditory hallucinations, and was often found responding to internal stimuli. She had no acute medical findings, except for past history of gastroesophageal reflux/dyspepsia symptoms and urinary urgency. She had never been pregnant, and her family history was negative for thyroid abnormalities. Her admission laboratory workup, including thyroid function, was unremarkable except for elevated serum total creatine kinase level of 574 U/L (normal range, 26–140 U/L), which subsequently normalized. She was started on lithium carbonate titrated to 900 mg daily, risperidone, and clonazepam. Under this regimen, her mood and psychotic symptoms started to improve. Serum lithium, free T<sub>4</sub>, and thyroid-stimulating hormone (TSH) levels were serially monitored over the course of her hospitalization (Figure 1).

About 2.5 months after treatment initiation, we noticed an elevation in her free T<sub>4</sub> levels with a slight decrease in TSH levels. During this period, she remained clinically euthyroid with no evidence of thyrotoxicosis. A full hyperthyroidism workup revealed the following: an elevated serum total thyroglobulin level over 180 ng/mL (normal range, 1.2–35 ng/mL), thyroid antibody levels within normal limits, no evidence of a thyroid nodule on ultrasonogram, a 0.9% I<sup>123</sup> uptake at 4 hours (normal, 5%–15%) and a 0.3% uptake at 24 hours (normal, 5%–15%) on a thyroid uptake scan, and no evidence suggestive of an ectopic thyroid tissue. Lithium therapy was continued with careful monitoring for evidence of thyrotoxicosis. Elevation of free T<sub>4</sub> and associated drop in TSH levels persisted for the next 2 months (Figure 1). During the fourth month of treatment, free T<sub>4</sub> levels returned to within normal limits.

The incidence of transient euthyroid hyperthyroxinemia in acute psychiatric inpatients at admission has been reported to be at 9%–18%.<sup>7</sup> The subject in the present report had normal TSH and T<sub>4</sub> levels at admission. To our knowledge, this is the first reported case of lithium-induced transient euthyroid hyperthyroxinemia. Although the role of lithium in thyroid hormone synthesis and release has been extensively investigated and reviewed,<sup>9</sup> how it may induce euthyroid hyperthyroxinemia is unclear. From a

**Figure 1. Serial Serum Levels of Lithium, TSH, and Free T<sub>4</sub> in a Patient Treated With Lithium**



\*The therapeutic range for lithium is 0.50–1.20 mmol/L. The reference ranges for TSH and free T<sub>4</sub> are 0.270–4.200 mIU/mL and 0.91–1.70 ng/dL, respectively.

Abbreviation: TSH = thyroid-stimulating hormone.

clinical perspective, if a clinician finds elevated thyroxine levels in the absence of overt thyrotoxicosis in a patient started on lithium therapy, it would seem prudent to carefully monitor clinically for development of thyrotoxic symptoms without immediately resorting to an extensive and expensive diagnostic workup.

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