Thyroid dysfunction and lithium

Case report[1]

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A patient with prelithium TSH and microsomal antibody abnormalities showed diminished thyroid function during lithium treatment but subsequently responded to thyroid supplements while still receiving lithium. This case demonstrates the necessity of routine screening for thyroid microsomal antibody titres before and during lithium treatment. In addition, it suggests that manic depressives with laboratory evidence of hypothyroidism prior to lithium treatment can be safely treated with lithium and thyroid supplements.

Index terms: Depression • Thyroid, hypothyroidism • Lithium
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Lithium carbonate therapy results in frank hypothyroidism in approximately 5% of manic-depressives treated and in benign, diffuse, nontoxic goiter in 3%.[1–3] Of those with frank hypothyroidism, 30% show elevated thyroid-stimulating hormone (TSH) levels during the first year of treatment.[4] Furthermore, subclinical hypothyroidism may have multiple psychiatric presentations.[5,6] Lithium affects thyroid metabolism by inhibition of iodine uptake into the thyroid, iodination of tyrosine, release of T_3 and T_4 from the thyroid, and peripheral degradation of thyroid hormones.[7–9] Lithium also blocks the thyroid-stimulating effects of TSH by interfering with TSH-sensitive adenyl cyclase, much in the same manner that antidiuretic hormone is inhibited by lithium to produce diabetes insipidus.[10]

Current studies of the incidence of Hashimoto's thyroiditis in lithium-treated manic depressives at the Cleveland Clinic (unpublished data) indicate that there are at least three patterns of thyroid disease in lithium-treated manic depressives.

1. Positive thyroid microsomal antibody titres and elevated TSH levels before treatment with lithium show a worsening of the two factors during treatment.
2. Negative antibody titres with solitary elevations in TSH levels without antibody or T_4 abnormality during lithium treatment.
3. Negative antibody titres were converted to positive microsomal antibody titres without TSH or T_4 abnormality during lithium treatment in one case.

Case report

A 35-year-old white man was referred for prophylaxis for bipolar affective disease. One year before being seen at the Cleveland Clinic, he had had one trial of lithium therapy that lasted only four days because of poor compliance.

He described a six-year history of recurrent depression during winter and fall and recurrent mania during spring and summer. His depressions were stereotyped, occurring about twice a year, lasting 1–3 months. Those cycles were accompanied by gradual onset of anorexia with weight loss of 5–6 kg and crying spells. He denied suicidal ideation. He reported initial, middle, and terminal insomnia. His episodes of mania occurred about twice a year and lasted 1–2 months. These manic episodes usually were precipitated by alcohol ingestion and were accompanied by racing thought, rapid speech with loose associations, inability to sleep for 2 to 3 days at a time, spending sprees, and feelings of grandiosity.

The patient's father is an alcoholic. He has three brothers and one sister. Two brothers, 38 and 25 years of age, are both described as "alcoholics with mood swings identical" to the patient's. His 36-year-old brother is described as an "alcoholic with recurrent depression."

During a psychiatric admission 18 months previously, the patient had an unremarkable physical examination without signs of thyroid disease. At that time his free thyroxine index

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was 0.92 ng/dl (normal, 0.8–1.04 ng/dl). TSH and microsomal antibody determinations had not been done. Eighteen months later, at the time lithium therapy was started, physical examination again revealed no signs of thyroid disease and he denied symptoms. SMA-18 was normal and electrocardiogram was normal. His T_4 was 6.4 μg/dl (normal, 5.2–11.3 μg/dl); TSH, 27.9 μU/ml (normal, <7 μU/ml); and thyroid microsomal antibody titres were 1:1600 (normal, negative). Thyrotropin-releasing hormone (TRH) stimulation test was not done.

He was thought to have subclinical Hashimoto's thyroiditis in addition to bipolar affective disease. He was not given thyroid supplements initially, but was given lithium carbonate, 300 mg three times a day. After 14 days his lithium level was 0.55 mEq/L. The dose was increased to 300 mg, four times a day with peripheral levels rising to 0.7 mEq/L. Thereafter, because of complaints of persistent fatigue and blunted affect not accompanied by crying spells or anorexia, it was thought an initial trial of antidepressants was indicated for treatment of an atypical depression. He was given imipramine with the dose gradually increased to 200 mg/day. After two months of imipramine therapy, complaints of persistent fatigue and "just not feeling right" persisted. It was thought that these complaints might have been due to his otherwise subclinical hypothyroidism. After four months, repeat T_4 was 5.5 μg/dl; TSH, 96.5 μU/ml; and microsomal antibody titres, 1:6400. At this time he denied dry skin, constipation, shortness of breath, intolerance to cold, hair loss, and weight gain. He instead reported a worsening of persistent fatigue and weakness. He continued to deny vegetative signs of endogenous depression such as anorexia, insomnia, crying spells, and feelings of hopelessness. He was given a trial of levothyroxine sodium (Synthroid), 0.15 mg daily. Imipramine was continued. After 30 days he reported he was back to "normal," his feeling of "not being just right" had gone away, and he felt his improvement was dramatic. Repeat T_4 was 6.7 mg/dl; TSH, 34.6 μU/ml; and microsomal antibody titres, 1:1600. Despite thyroid supplements for nine months, his current TSH is 21.8 μU/ml; and antibodies, 1:6400.

Discussion

This case is one of a series in a current study of the incidence of Hashimoto's thyroiditis in lithium-treated manic depressives. It is hypothesized that lithium therapy may cause asymptomatic subclinical thyroid disease of the Hashimoto type to become symptomatic. It is suspected that this patient's subclinical thyroid disease was exacerbated by the antithyroid effects of lithium. The worsening thyroid function observed after lithium treatment had begun was reversed after levothyroxine was started, although thyroid functions never completely returned to normal. We believe this was due to the continued antithyroid effects of lithium. Since the latency period prior to clinical response with imipramine is thought to require only 3–6 weeks, it is believed he was given an adequate trial of imipramine. We believe the patient's improvement was due to the addition of levothyroxine and to the combination of imipramine, lithium carbonate, and levothyroxine.

Since its first description in 1912, Hashimoto's thyroiditis has been increasingly recognized and is now considered the most common disorder of the thyroid gland.[10] A chronic, progressive disease, it is presumed to result from an autoimmune process, which can eventually produce frank hypothyroidism in a majority of patients. In this case the patient did not mention thyroid disease in any relatives, but did report bipolar affective disorders, recurrent unipolar affective disorders, and alcoholism.

We hypothesize that even with the finding of a strong family history of mood disorders and an absence of thyroid problems, the clinician still should be alert for an increased risk of hypothyroidism in a person with a lithium-treated mood disorder. If subclinical Hashimoto's thyroiditis is established at the onset of lithium treatment by thyroid microsomal antibody titres, an exacerbation of this disorder can be seen as early as four months after lithium treatment and can be safely and effectively treated with thyroid supplement.

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