Asymptomatic Graves' disease during lithium therapy

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Summary: Lithium salts are widely recognized to cause biochemical hypothyroidism and have been used to treat thyrotoxicosis. We present a case of Graves' disease which developed during lithium therapy. The patient was asymptomatic until the lithium was discontinued; she subsequently developed florid symptoms of thyrotoxicosis.

Introduction

The incidence of biochemical hypothyroidism has been estimated to be as high as 30% in patients taking lithium (Lazarus *et al.*, 1981). There are several different mechanisms involved. Lithium has been shown to block release of thyroxine from the thyroid gland (Spaulding *et al.*, 1972) and probably also directly inhibits thyrotrophin-stimulated adenyl cyclase in the thyroid gland. Lazarus *et al.* (1981) showed that 24% of patients on lithium had thyroid antibodies compared with 10%–14% of a normal population studied by Tunbridge *et al.* (1977). Weetman *et al.* (1981) demonstrated a rise in thyroid antibodies in patients treated with lithium and showed that lithium increased immunoglobulin synthesis. Furthermore, Hassman & Lazarus (1984) showed that lithium increased the severity of autoimmune thyroid disease by modification of the autoimmune process. Lithium thus not only inhibits the action of thyrotrophin and the release of thyroxine, but also interferes with the autoimmune process.

Rosser (1976) and Rons *et al.* (1979) have reported cases of thyrotoxicosis occurring during lithium therapy though none showed convincing evidence of autoimmune disease as the aetiological factor. Schoenberg *et al.* (1979) reported Graves' disease manifesting after cessation of maintenance lithium. We report a case of a patient with Graves' disease occurring during lithium therapy but who remained free from symptoms until lithium was withdrawn. We would suggest that the antithyroid actions of lithium caused suppression of the symptoms of thyrotoxicosis, and propose that lithium might have initiated the autoimmune disease in our patient.

Case report

A 47 year old woman was referred to surgical out-patients in December, 1983 with a two month history of thyroid swelling. She had been on lithium carbonate for manic depressive psychosis for 12 years but had never previously been noted to have a goitre. Serum free thyroxine earlier in 1983 had been normal at 18 nmol/l (normal 9–24 nmol/l) when routinely checked at psychiatric out-patients. There was no family history of autoimmune disease. She was considered to be clinically euthyroid but was noted to have bilateral exophthalmos and a smoothly enlarged thyroid gland. Serum thyroxine was 165 nmol/l (normal 60–150), free thyroxine index 156 (normal 50–160) and serum triiodothyronine 4.7 nmol/l (normal 1.2–3.0). Thyroid microsomal antibodies were present in a dilution of > 1/1600 and ^{99m}technetium scan showed an enlarged right lobe of the thyroid with a 20 min uptake of 4.2%, in the equivocal range. As she was asymptomatic, no therapy was judged necessary.

In June, 1984 the patient was referred to the endocrine clinic with marked clinical thyrotoxicosis and active ophthalmopathy, having discontinued lithium seven weeks previously. Serum thyroxine was 224 nmol/l (normal 63–135), free thyroxine index 75.9 (normal 20–38) and serum triiodothyronine 5.4 nmol/l. Treatment was initiated with antithyroid drugs and the patient is at present clinically and biochemically euthyroid on carbimazole 45 mg and thyroxine 150 µg daily. The ophthalmopathy has been successfully treated with oral prednisolone.

Discussion

The case reported by Rosser (1976) developed thyrotoxicosis during lithium therapy, but exacerba-

tion of symptoms was experienced when lithium was discontinued. In the report by Schoenberg *et al.* (1979) the patient developed Graves' disease after cessation of lithium. As lithium has been used as an antithyroid drug (Lazarus *et al.*, 1974) it is hardly surprising that cessation of this drug led to worsening symptoms in our case and previous cases reported. We would therefore recommend that if lithium is discontinued in cases of suspected thyrotoxicosis, then the patient should be covered with beta-adrenergic blockade until thyroid function can be re-assessed. Propranolol reduces the peripheral conversion of thyroxine to triiodothyronine, leading to elevation in serum thyroxine levels and a fall in triiodothyronine levels and this should be considered when the results of subsequent thyroid function tests are interpreted.

Graves' disease is not an uncommon condition and it is therefore inevitable that a proportion of lithium-treated patients will develop the disease coincidental to their lithium therapy. The high proportion of patients on lithium who have thyroid antibodies in their serum (Lazarus *et al.*, 1981) and the demonstra-

tion of a rise in thyroglobulin antibodies in patients treated with lithium (Weetman *et al.*, 1981), however, point to lithium having a role in the initiation of autoimmune thyroid disease. We therefore propose that lithium may have acted to stimulate the production of thyroid antibodies in our patient, though the patient was protected from the manifestations of thyrotoxicosis by the separate antithyroid effects of lithium. Further work is necessary, however, to explore the role of lithium in thyrotoxicosis.

Finally, we would reiterate the advice of other authors that thyroid function tests and thyroid antibodies should be measured before commencing lithium therapy, regularly monitored during the course of therapy, and also evaluated after cessation of treatment.

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