LITHIUM AND THE SOLITARY THYROID NODULE — A CASE REPORT

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SYNOPSIS

A psychiatric patient on lithium for four and a-half years developed a thyroid nodule within two weeks of starting therapy which persisted even after cessation of lithium for twenty months. She was clinically euthyroid throughout. Thyroid antibodies were absent. Thyroid scan showed a "cold" nodule which proved to be a benign adenoma with multiple areas of cystic and haemorrhagic degeneration. A partial thyroidectomy was performed and she is well. The relationship between lithium and the thyroid nodule is discussed.

INTRODUCTION

The antithyroid effect of lithium was firsted noted in 1968 when an increased prevalence of goitre was found in patients on lithium therapy for affective disorders. These goitres tended to decrease in size or disappear when the lithium was discontinued (1). More recently, there have been reports of patients developing hypothyroidism during long-term lithium therapy (2-5) and paradoxically also thyrotoxicosis (5-7) and ophthalmic Graves' disease (8-10).

We report a case of a solitary "cold" thyroid nodule associated with the exhibition of lithium therapy for over four years.

CASE REPORT

A 22 year-old Chinese female working as a salesgirl in an Emporium was first seen at a psychiatric hospital in October 1973 for being unwell for four months with auditory and visual hallucinations and passivity feelings. She suffered from insomnia and was fearful on admission. She showed cataplexy and was diagnosed to be suffering from catatonic schizophrenia. She was treated with chlorpromazine 300 mg, haloperidol 9 mg and benzhexol 6 mg daily. She remained disturbed and was severely depressed. Despite several courses of electro-convulsive therapy, she made no improvement. Her aggressive, disturbed and irrational behaviour continued. So in August 1975, after serious consideration, she was given oral lithium carbonate 900 mg daily, as she showed no response to all other medication. Two weeks later her neck girth was noted to have increased from 34 cm to 37 cm and after a further two weeks, to have decreased to 35 cm. She responded satisfactoriy when on lithium with blood levels 12 hours after the last dose being in the range of 0.2 to 0.5 mEq/L (measured by flame photometry).

In July 1978 and February 1980, she relapsed while still on lithium which was therefore discontinued. She remained on chlorpromazine and benzhexol. She was clinically euthyroid throughout and the goitre remained unchanged. Nine months after lithium was stopped, she was

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referred to the internist for an evaluation of her goitre.

Clinically she appeared well, in control of herself and able to give a good history. There were no symptoms or signs to suggest hypo- or hyper-thyroidism. A 2.5 cm nodule was palpable in the right lobe of her thyroid gland. It was firm and not tender with no associated cervical lymphadenopathy. Exophthalmos was absent and there was no pretibial myxoedema. Other systems were normal.

Tests of thyroid function revealed a normal T_3 resin uptake of 107% (normal 72-118%), a raised thyroxine level of 13.5 ug/dl (normal 5.6-11.5 ug/dl) and a free thyroxine index (calculated as the arithmetric product of the total serum thyroxine and T_3 resin uptake ratio results) of 14.5 (normal 4.0-13.5). Thyroglobulin antibodies (using Wellcotest) and microsomal antibodies (using undiluted serum on thyroid tissue sections) were negative. A thyroid scan using ^{131}I showed an uptake at 24 hours of 35-38% (normal 16-62%; hyperthyroid range 48-89%), the left lobe of the gland was normal while a "cold" nodule was noted in the lower half of the right lobe. (A "cold" nodule is one showing decreased concentration of the isotope in comparison with surrounding tissue.)

After five months of observation (fourteen months after stopping lithium), the thyroid nodule was the same size although a repeat free thyroxine index was now normal at 12.1. She was euthyroid, still taking chlorpromazine and benzhexol. Antibody studies remained negative.

She consented to surgery for the "cold" nodule and in November 1981 (one year and nine months after cessation of lithium intake), a partial right hemithyroidectomy was performed. Frozen section of the nodule showed it was well circumscribed and encapsulated with shiny colloid within the follicular spaces. Light microscopy showed a benign adenoma with multiple areas of cystic and haemorrhagic degeneration.

To date she remains well and is on regular psychiatric follow-up, showing no active psychotic symptoms.

DISCUSSION

The antithyroid effect of lithium has been shown to be due to the inhibition of thyroid-stimulating hormone (TSH) mediated release of thyroid hormone and colloid droplet formation (11), the inhibition of thyroid hormone release in both thyrotoxic and euthyroid patients (12) and the reduction of the intra-thyroidal iodothyronine-iodotyrosine ratio (13). These lead to a decrease in circulating thyroid hormone and as a compensatory mechanism via raised TSH, to an increase in uptake of iodine by the thyroid gland. Lithium is also concentrated in the thyroid to attain a thyroid to serum ratio of 5 to 1 (14). When goitres result, these are apparently due to the increased secretion of TSH since they regress with the administration of thyroid hormone (14) and all cases of lithium-induced hypothroidism showed elevated levels of serum thyrotropin (5).

Our patient was clinically euthyroid throughout the period she was on lithium. The initial increase in size of the thyroid gland was noted after two weeks on lithium therapy, regressing slightly after a further two weeks, and remained the same size thereafter even after cessation of lithium. These changes could be the result of TSH upsurge initially followed by a fall to plateau levels as the acute fall in serum thyroid hormone levels has been noted to be most marked in the first two weeks of starting lithium (15, 16). The goitres induced by lithium were usually soft and diffuse, sometimes asymmetrical (1). Two patients have been reported as having new thyroid nodules while on lithium which were active nodules on thyroid scan and which subsided with supplemental thyroxine (8). The scan in our patient showed a normal ^{131}I uptake despie the elevated free thyroxine index with the "cold" nodule corresponding to the clinically palpable thyroid lump. No thyroxine was given to try to decrease the goitre.

Goitre frequency was increased among lithium-treated patients and discontinuane of lithium led to shrinkage or disappearance of the goitres within a few months (1). As the "cold" nodule persisted, and there is an incidence of 16% malignancy among solitary "cold" nodules in the local population (17), she consented to surgery. The multiple areas of degeneration within the benign adenoma was the reason for the nodule being "cold" and no malignancy was detected.

Lithium-induced hypothyroidism was found to be 20% among women and about two-thirds of them had thyroid antibodies (5). Our patient had no thyroid antibodies, no family history of thyroid disease and remained euthyroid clinically.

We postulate that our patient probably had an impalpable thyroid nodule to begin with. On lithium therapy, the TSH rose in response to the lithium-induced fall in thyroid hormones and this TSH drive helped the nodule to grow and become detectable clinically. Its slight subsidence could be attributed to a lower level of TSH after the initial upsurge. That this "cold" nodule failed to completely subside after a 21-month observation period on neuroleptic drugs alone prompted us to advise surgery.

REFERENCES

1. Schou M, Amdisen A, Jensen SE, Olsen T: Occurrence of goitre during lithium treatment. Brit Med J 1968; 3: 710-3.
2. Rogers MP, Whybrow PC: Clinical hypothyroidism occurring during lithium treatment. Two case histories and a review of thyroid function in 19 patients. Amer J Psychiat 1971; 128: 158-63.
3. Growe MJ, Lloyd GG, Bloch S, Rosser RM: Hypothyroidism in patients treated with lithium; a review and two case reports. Pyschological Medicine 1973; 5: 337-42.
4. Brownlie BEW, Chambers ST, Sadler WA, Donald RA: Lithium-associated thyroid disease. A report of 14 cases of hypothyroidism and 4 cases of thyrotoxicosis. Aust NZ J Med 1976; 6: 223-9.
5. Lindstedt G, Nilsson L, Walinder J, Skott A, Ohman R: On the prevalence, diagnosis and management of lithium-induced hypothyroidism in psychiatric patients. Brit J Psychiat 1977; 130: 452-8.
6. Franklin LM: Thyrotoxicosis developing during lithium. A case report. New Zealand Med J 1974; 79: 782.
7. Rosser R: Thyrotoxicosis and lithium. Brit J Psychiat 1976; 127: 61-6.
8. Segal RL, Rosenblatt S, Eliasoph I: Endocrine exophthalmos during lithium therapy of manic-depressive disease. N Engl J Med 1973; 289: 136-8.
9. Chaudhri MA, Bebbington PE: Lithium therapy and ophthalmic Graves' disease. Brit J Psychiat 1977; 130: 420.
10. Schoenberg M, Ts'o TOT, Mersel AN: Graves' disease manifesting after maintenance lithium. J Nervous Mental Dis 1979; 167: 575-7.
11. Wiliams JA, Berens SC, Wolff J: Thyroid secretion in vitro: Inhibition of TSH and cyclic AMP stimulated ^{131}I release by Li^+. Endocrinology 1971; 88: 1385-8.
12. Spawlding SW, Burrow GN, Bermudez F, Himmelhoch JM: The inhibitory effect of lithium on thyroid hormone release in both euthyroid and thyrotoxic patients. J Clin Endocr 1972; 35: 905-11.
13. Berens SC, Bernstein RS, Robbins J, Wolff J: Antithyroid effects of lithium. J Clin Invest 1970; 47: 1357-67.
14. Burrow GN, Burke WR, Himmelhoch JM, Spencer RP, Hershman JM: Effect of lithium on thyroid function. J Clin Endocr 1971; 32: 647-52.
15. Cooper TB, Simpson GM: Preliminary report of a longitudinal study on the effects of iodine metabolism. Curr Ther Res 1969; 11: 603-8.
16. Sedvall G Jonsson B, Petterson U: Evidence of an altered thyroid function in man during treatment with lithium carbonate. Acta psychiat Scand 1969; Supp 207; 59-67.
17. Tan BC, Chang CH, Sethi VK: Thyroid scanning and the significance of the solitary cold nodule. Ann Acad Med Sing 1981; 10: 293-7.