Lithium associated autoimmune thyroiditis

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Abstract
A case of autoimmune thyroiditis after long term treatment with lithium is described in a 29 year old Japanese woman with manic depression. Positive serum antithyroglobulin and antimicrosomal antibodies, diffuse goitre, and microscopic chronic thyroiditis, as well as the clinical history of long term lithium treatment were suggestive of lithium associated autoimmune thyroiditis. Microscopically, there was a mild degree of interstitial fibrosis and a moderate degree of lymphocytic infiltration. Some areas showed a moderate degree of stromal fibrosis and atrophic thyroid follicles. Lymphoid follicles with germinal centres, disrupted thyroid follicles with lymphocytic infiltration, and Hürthle cells were also observed. The differential diagnosis in patients presenting with these histological features includes painless (silent) thyroiditis, autoimmune thyroiditis and lithium associated autoimmune thyroiditis. A detailed clinical history is essential if the correct diagnosis is to be reached.

Keywords: thyroid; lithium; autoimmune thyroiditis.

Lithium has been used in the treatment of manic and hypomanic depressive disorders for many years. Long term treatment with lithium is associated with hypothyroidism, euthyroid goitre, and hyperthyroidism. The aetiology of the first two conditions can be explained by the effect of lithium on the thyroid; however, that of hyperthyroidism has not been explained adequately. Other cases of lithium related thyroid disease have been reported but...
the histological findings have not. We describe a case highlighting the histological findings of lithium associated autoimmune thyroiditis.

**Case report**

In August 1993, a 29 year old Japanese woman was admitted hospital for resection of a diffuse goitre because she wanted to have a baby. The patient's illness dated back to July 1988. She had been treated for manic depression with lithium carbonate (600 mg/day) for 27 months. Goitre was not noted and serum thyroid autoantibody was not measured at her initial presentation. In October 1990, the patient complained of palpitations, irritation and weight loss, and was diagnosed with Graves' disease. Immediately after this diagnosis, she was treated with methimazole (15 mg/day) until August 1993. The patient also continued to be treated with lithium. In April 1992, the results of her thyroid function tests were as follows: thyroxine, 233 nmol/l (normal range 58–155 nmol/l); triiodothyronine, 3.6 nmol/l (1.2–3.1 nmol/l); thyroid stimulating hormone (TSH), <0.05 µIU/ml (0.03–5.00 µIU/ml); and TSH binding inhibitor immunoglobulin (TBII), 22.9% (<15%), which were suggestive of a diagnosis of Graves’ disease. However, on admission in 1993, the patient had become euthyroid, and diffuse goitre (right lobe 6.5 × 2.3 × 1.7 cm; left lobe 6.5 × 2.0 × 1.5 cm) was observed. Both serum antithyroglobulin and antimicrosomal antibodies were positive at that time. The patient underwent subtotal thyroidectomy for the diffuse goitre.

**Pathology**

Grossly, the resected thyroid was covered with scattered white spots, but no mass was noted. Microscopically, lobulation of the gland was observed under low power. There was a mild degree of interstitial fibrosis and a moderate degree of lymphocytic infiltration. The thyroid follicles varied in size. Some areas showed a moderate degree of stromal fibrosis and atrophic thyroid follicles. Lymphoid follicles with germinal centres, disrupted thyroid follicles with lymphocytic infiltration, and Hurthle cells were also observed in some areas (figs 1 and 2). In other areas, papillary infoldings projecting into the thyroid follicles and scalloping of the colloid were present.

**Discussion**

The development of hypothyroidism or goitre is a well known complication of long term lithium treatment.\(^1\)\(^-\)\(^4\) There have, however, only been sporadic cases of hyperthyroidism among patients treated with lithium.\(^2\)\(^,\)\(^3\) Other lithium related or associated thyroid diseases have rarely been described in the literature, and only three cases of lithium associated thyroiditis and three cases of lithium associated autoimmune thyroiditis have been reported.\(^5\)\(^,\)\(^6\) In the cases of lithium associated thyroiditis, thyroid antibody levels were not measured. Histologically, in the two cases reported by LiVolpi,\(^1\) lymphocytic infiltration, focal follicular atrophy and mild stromal fibrosis were observed. It was also pointed out that the histopathological appearance was consistent with that found in autoimmune thyroiditis. In the case reported by Kontozoglou and Mambo,\(^7\) prominent fibroblastic activity and numerous lymphoid follicles lacking typical Hurthle cells were observed. Our patient showed lymphocytic infiltration with lymphoid follicles and interstitial fibrosis with focal follicular atrophy, as well as disrupted thyroid follicles and Hurthle cells. In addition, our patient presented with positive serum antithyroid antibodies and diffuse goitre, and a clinical history of long term lithium treatment, all of which are suggestive of lithium associated autoimmune thyroiditis. Lithium may also notably increase the titre of thyroid microsomal antibodies and convert latent subclinical autoimmune disease into clinically overt illness.\(^7\)

In practice, however, it is difficult to arrive at the correct diagnosis without knowledge of the patient's clinical history. In our patient, we considered that the lymphocytic infiltration and lymphoid follicles with germinal centres were too noticeable to be those typically found in Graves' disease, and chronic thyroiditis was clearly observed histologically. Furthermore,
the findings of interstitial fibrosis, disrupted thyroid follicles, and Hürthle cells were not consistent with euthyroid Graves' disease, medically treated Graves' disease, or Hashitoxicosis, because of the lack of classic ophthalmopathy, the replacement of normal thyroid follicular epithelium by hyperplastic epithelium in less than 50% of the specimen, and the euthyroid state in this patient. Painless thyroiditis, also known as silent thyroiditis, is another possibility; this is characterised by a painless thyroid gland, raised serum concentrations of thyroid hormone, low radioactive iodine uptake, and spontaneously resolving hyperthyroidism. Histologically, painless thyroiditis resembles autoimmune thyroiditis, but according to Mizukami et al stromal fibrosis and Hürthle cells are rare in the former. After contacting the patient's clinician, we found that she had been receiving long term lithium treatment (over five years) for her psychiatric condition, and we were then able to arrive at the diagnosis of lithium associated autoimmune thyroiditis. However, without knowledge of the patient's clinical history, it probably would have been difficult for us to differentiate between painless thyroiditis and lithium associated autoimmune thyroiditis. Treatment with methimazole may have partly affected the change from a hyperthyroid to a euthyroid state in this patient.


Atypical manifestations in a patient with systemic lupus erythematosus

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Abstract

Systemic lupus erythematosus (SLE) is a chronic systemic inflammatory disease associated with the production of various autoantibodies and involvement of multiple organs. Necropsy findings in a 65 year old woman with SLE who had multiple aortic aneurysms and dissections, as well as other unusual manifestations, are described. The case illustrates the occurrence of and the difficulties encountered in the diagnosis of several diseases, namely aortic aneurysm, aortic dissection, acute pancreatitis, and Penicillium marneffei infection.

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Keywords: systemic lupus erythematosus; aneurysm; dissection.

Systemic lupus erythematosus (SLE) is a chronic systemic inflammatory disease associated with the production of various autoantibodies and involvement of multiple organs. We report the necropsy findings in a patient with
Lithium associated autoimmune thyroiditis.

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