Figure 2 Endometrial curettage revealing the bone tissue and a fragment of an endometrial gland (arrow head) with neutrophilic infiltration.

ing cause of endometrial ossification is endometritis, especially chronic endometritis, as ossification may develop in the old, healing inflammatory tissue.⁷ Prolonged oestrogenic stimulation is thought to be related to the pathogenesis of endometrial ossification,⁶ however, this is unlikely in this patient.

Bone formation in the endometrium is rare, but may be observed in malignant mixed müllerian tumour and teratoma,⁸ which should be considered as a differential diagnosis,⁹ especially in older women.¹⁰

In summary, endometrial ossification in postmenopausal women is very rare; most women presenting with this condition are between 20 and 40 years of age. Therefore, clinicians should consider the possibility of endometrial ossification as a differential diagnosis of intrauterine foreign body on ultrasound, even in older patients. In addition, pathologists should be aware of this rare entity to avoid a misdiagnosis of malignant mixed müllerian tumour in the endometrial curettage specimen, which may result in unnecessary hysterectomy.

- 1 Qi L, Qunli S, Yanhua S, Xiaojuan Y. Pregnancy achieved after treatment in a case of endometrial ossification. A case report and literature review. *Chin Med J* 1995;108:793-5.
- 2 Acharya U, Pinion SB, Parkin DE, Hamilton MPR. Osseous metaplasia of the endometrium treated by hysteroscopic resection. *Br J Obstet Gynaecol* 1993;100:391-2.
- 3 Rodriguez BD, Adamson GD. Hysteroscopic treatment of ectopic intrauterine bone. A case report. *J Reprod Med* 1993;38:515-20.
- 4 Taylor PJ, Hamou J, Mencaglia L. Hysteroscopic detection of heterotopic intrauterine bone formation. *J Reprod Med* 1988;33:337-9.
- 5 Bhatia NN, Hoshiko MG. Uterine osseous metaplasia. *Obstet Gynecol* 1982;60:256-9.
- 6 Ceccacci L, Clancy G. Endometrial ossification: report of an additional case. *Am J Obstet Gynecol* 1981;141:103-4.
- 7 Waxman M, Moussouris HF. Endometrial ossification following an abortion. *Am J Obstet Gynecol* 1978;130:587-8.
- 8 Wetzels LCG, Essed GGM, de Haan J, van de Kar AJF, Willebrand D. Endometrial ossification: unilateral manifestation in a septate uterus. *Gynecol Obstet Invest* 1982;14:47-55.
- 9 Ombelet W. Endometrial ossification, an unusual finding in an infertility clinic. A case report. *J Reprod Med* 1989;34:303-6.
- 10 Barwick KW, LiVolsi VA. Malignant mixed müllerian tumors of the uterus. *Am J Surg Pathol* 1979;3:125-35.

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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.

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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.¹⁻⁶ The aetiology of the first two conditions can be explained by the effect of lithium on the thyroid; however, that of hyperthyroidism has been not been explained adequately. Other cases of lithium related thyroid disease have been reported but

Figure 1 Thyroid follicles of varying sizes, lymphocytic infiltration and a lymphoid follicle with a germinal centre can be seen.

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); triiodo-thyronine, 3.6 nmol/l (1.2–3.1 nmol/l); thyroid stimulating hormone (TSH), <0.05 μ IU/ml (0.03–5.00 μ IU/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 $6.5 \times 2.3 \times 1.7$ cm; left lobe $6.5 \times 2.0 \times 1.5$ 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 Hürthle 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.^{1–5} 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.^{7–9} In the cases of lithium associated thyroiditis, thyroid antibody levels were not measured. Histologically, in the two cases reported by LiVolsi,⁷ 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,⁸ prominent fibroblastic activity and numerous lymphoid follicles lacking typical Hürthle 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 Hürthle 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.⁹

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,

Figure 2 Hürthle cells (centre) and disrupted thyroid follicles (right) are evident.

the findings of interstitial fibrosis, disrupted thyroid follicles, and Hürthle cells were not consistent with euthyroid Graves' disease, medically treated Graves' disease, or Hashimoto's disease, 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.⁷⁻¹⁰ 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.¹⁰ Histologically, painless thyroiditis resembles autoimmune thyroiditis, but according to Mizukami *et al*¹⁰ 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.

- 1 Jefferson JW. Lithium carbonate-induced hypothyroidism. Its many faces. *JAMA* 1979;242:271-2.
- 2 McDermott MT, Burman KD, Hofeldt FD, Kidd GS. Lithium-associated thyrotoxicosis. *Am J Med* 1986;80:1245-8.
- 3 Mizukami Y, Michigishi T, Nonomura A, Nakamura S, Noguchi M, Takazakura E. Histological features of the thyroid gland in a patient with lithium induced thyrotoxicosis. *J Clin Pathol* 1995;48:582-4.
- 4 Bocchetta A, Bernardi F, Pedditzi M, Loviselli A, Velluzzi F, Martino E, *et al*. Thyroid abnormalities during lithium treatment. *Acta Psychiatr Scand* 1991;83:193-8.
- 5 Lee S, Chow CC, Wing YK, Shek CC. Thyroid abnormalities during chronic lithium treatment in Hong Kong Chinese: a controlled study. *J Affect Disord* 1992;26:173-8.
- 6 Gittoes NJL, Franklyn JA. Drug-induced thyroid disorders. *Drug Saf* 1995;13:46-55.
- 7 LiVolsi VA. Lymphocytes in the thyroid. In: *Surgical pathology of the thyroid*. Philadelphia: WB Saunders, 1990:68-97.
- 8 Kontzoglou T, Mambo N. The histopathologic features of lithium-associated thyroiditis. *Hum Pathol* 1983;14:737-9.
- 9 Calabrese JR, Gullledge AD, Hahn K, Skwerer R, Kotz M, Schumacher OP, *et al*. Autoimmune thyroiditis in manic depressive patients treated with lithium. *Am J Psychiatry* 1985;142:1318-21.
- 10 Mizukami Y, Michigishi T, Nonomura A, Nakamura S, Ishizaki T. Pathology of chronic thyroiditis: A new clinically relevant classification. *Pathol Annu* 1994;29:135-58.

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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

Figure 1 Axial contrast enhanced CT scan of distal thoracic aorta at level of the left ventricle. Presence of an intimal flap (arrowhead) across the aortic lumen at this section would have suggested aortic dissection. This was, however, found to be the undermined edge of a saccular aneurysm. The smaller compartment proved to be the true aortic lumen and the larger one to be the lumen of the saccular aneurysm at necropsy.

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