

CASE REPORT

Hypothyroid Hashimoto's thyroiditis with scintigraphic and echo-color Doppler features mimicking autonomous adenoma

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ABSTRACT. We investigated a 48-yr-old woman on L-T₄ therapy (100 µg/d) for primary autoimmune hypothyroidism, diagnosed 15 yr earlier, presenting a firm oval lump in the right thyroid lobe and symptoms of mild thyrotoxicosis. Free T₄, free T₃, TSH, anti-thyroperoxidase, anti-TG and anti-thyroid microsomal antibodies were determined. Thyroid US and color flow Doppler sonography (CFDS), ^{99m}Technetium (^{99m}Tc), radioiodine scintiscan and US guided fine needle aspiration cytology (FNAC) were performed. On L-T₄ therapy, thyroid function tests showed subclinical hyperthyroidism with high anti-thyroid antibody titers. Thyroid US and CFDS revealed a voluminous hypoechoic hypervascularized nodule with increased peak systolic velocity (type III pattern) in the right lobe; the extranodular tissue volume was markedly reduced and hypoechoic. The presence of an autonomous functioning nodule associated to Hashimoto's thy-

roiditis (HT) was suspected, L-T₄ therapy was temporary withdrawn, and the patient re-evaluated 2 months later. Off L-T₄ therapy, thyroid function tests revealed marked primary hypothyroidism, while thyroid US and CFDS were unchanged. ^{99m}Tc thyroid scan showed a focal increased uptake corresponding to the nodule in the right lobe with nearly absent uptake in the remaining thyroid tissue. Only a faint, patchy thyroid distribution of ¹³¹I was detected by radioiodine scan, and RAIU was very low. Cytological examination by FNAC revealed normal follicular cells and several lymphocytes. The final diagnosis was therefore hypothyroid HT with pseudo-nodular thyroid tissue of the right lobe. To our knowledge, this is the first report of HT mimicking both scintigraphic and CFDS features of an autonomous functioning nodule. (J. Endocrinol. Invest. 25: 469-472, 2002)

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INTRODUCTION

Hashimoto's thyroiditis (HT) may show different clinical presentations including diffuse or nodular firm goiter associated to hypothyroidism, euthyroidism and rarely hyperthyroidism. Other presentations include atrophic gland of primary idiopathic myxedema and asymmetrical thyroid involvement simulating single nodule (1-5). Thyroid scintiscan in HT generally reveals a non-homogeneous, patchy radionuclide up-

take: however, cases of unilateral thyroid uptake mimicking autonomous functioning nodule have been occasionally observed (2, 6-10). In the present report, we describe the case of a patient with hypothyroid HT simulating a "hot" single nodule at ^{99m}Technetium (^{99m}Tc)-pertechnetate thyroid scan in whom echo-color flow Doppler sonography (CFDS) also showed features of autonomous functioning nodule independently from serum TSH concentration.

CASE REPORT

Case history

A 48-yr-old woman was referred to our outpatient service for a control of thyroid function in July 2000. The patient was on long-term therapy with fixed dose (100 µg/day) of L-T₄ for primary hypothyroidism. This diagnosis was made in a different Institution in 1985

Key-words: Autonomous thyroid nodule, thyroid scan, thyroid color flow Doppler sonography, hypothyroidism, Hashimoto's thyroiditis.

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on the basis of increased serum TSH concentration (10.0 mU/l) associated with high titer (1/102,400 by passive hemagglutination) of anti-TG (TGAb) and anti-thyroid microsomal (MAb) antibodies. Thyroid ^{99m}Tc scan already revealed a preferential thyroid uptake in the right lobe, but the possibility of a functioning adenoma was ruled out by the increased serum TSH level. Over the following years, the patient performed sporadic controls of thyroid function, showing suppressed serum TSH and normal serum free T_4 (FT_4) and free T_3 (FT_3). Over the last months the patient noticed symptoms suggestive of mild thyrotoxicosis (palpitations, nervousness and slight weight loss, about 1.5 kg during the last 6 months; her body weight was 58 kg), and a bone densitometry showed marked osteoporosis. Physical examination did not show any abnormality, with the exception of slight tachycardia (85 beats/min); thyroid palpation revealed a firm oval lump in the right thyroid lobe, while the entire left lobe was non-palpable.

Thyroid evaluation on L-T₄ therapy (April 2000)

Thyroid function tests at the first evaluation performed on 100 $\mu\text{g/d}$ of L-T₄ (Table 1) showed subclinical hyperthyroidism and high anti-thyroid autoantibody titers. Thyroid US was performed using an Acuson 128 XP 10 color Doppler system with a 7.5 MHz linear electronic transducer (Acuson Co, Mountain View, U.S.A.). Apparently the right lobe was almost entirely substituted by a solid hypoechoic nodule with the largest diameter of 40 mm with a peripheral rim (halo). The remaining thyroid tissue was atrophic and markedly hypoechoic (left lobe volume estimated 2.5 ml). The right nodule showed at CFDS a type III pattern (peripheral and intranodular hypervascularization), with increased (45 cm/s) intranodular arteriolar peak systolic velocity (PSV) (Fig. 1A). No significant blood flow was detected in the other areas of the gland. US-guided fine needle aspiration cytology (FNAC) performed on the right nodule showed normal shaped follicular cells and several lymphocytes. Since the in-

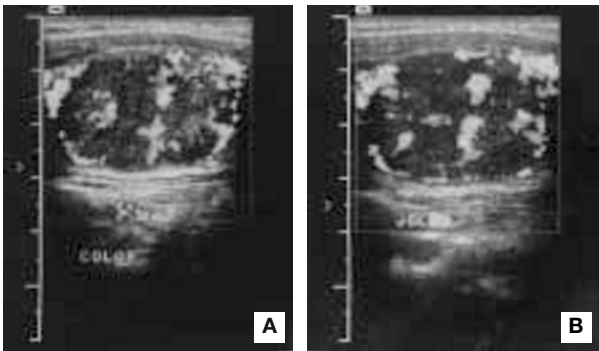


Fig. 1 - Color flow Doppler sonography of right thyroid nodule, performed on L-T₄ therapy (A) displayed increased blood flow in peripheral and intranodular tissue (type III pattern). Features observed off L-T₄ therapy (B) showing a pattern indistinguishable from that shown in Figure 1A.

creased blood flow observed in the context of the lesion in the right lobe could not be explained by TSH stimulation, the presence of an autonomously functioning thyroid adenoma associated to HT was suspected. To ascertain this hypothesis, at the end of October 2000 L-T₄ therapy was temporary suspended and the patient was re-evaluated 2 months later.

Thyroid evaluation off L-T₄ therapy (December 2000)

Thyroid function tests 2 months after withdrawal of L-T₄ therapy (Table 1) revealed marked primary hypothyroidism, while thyroid autoantibody titers were even higher than that observed on L-T₄. Thyroid conventional US and CFDS results were very similar to that observed on L-T₄ therapy: in particular, CFDS displayed a hypervascularized nodule in the right lobe and no significant blood flow in the remaining glandular tissue (Fig. 1B). Thyroid scintigraphy was then performed by means of a computerized gamma camera equipped with a pinhole collimator (Elscent, SP4; Haifa, Israel). ^{99m}Tc thyroid scintiscan was performed 30 min after injection, while ^{131}I scintiscan was performed 24 h after ^{131}I intake. Four days elapsed between the first (^{99m}Tc) and the second (^{131}I) scintiscans and the patient denied the intake of any substance able to interfere with ^{131}I uptake in this time. ^{99m}Tc thyroid scan (Fig. 2A) revealed a focal increased uptake localized in the right lobe and corresponding to the nodule detected by palpation and US, with nearly absent uptake in the left lobe. To achieve a better functional characterization of this apparent "hot" nodule, RAIU and a ^{131}I thyroid scan were also performed. The RAIU was 9% at 3 h and 3% at 24 h; differing from the ^{99m}Tc scan, faint patchy distribution of ^{131}I with no evidence of focal uptake

Table 1 - Serum thyroid hormones, TSH and thyroid autoantibodies on and off L-T₄ therapy.

Assay	On L-T ₄	Off L-T ₄	Normal range
FT ₄ (pg/ml)	15.5	1.2	6.6-16
FT ₃ (pg/ml)	2.9	0.1	2.8-5.6
TSH (mU/l)	0.003	95	0.2-3.0
Anti-TG (titer)	1/25600	1/102400	Negative
Anti-M (titer)	1/25600	1/102400	Negative
Anti-TPO (UI/ml)	378	1243	<20

Anti-M: anti-thyroid microsomal; Anti-TPO: anti-thyroid peroxidase; TSH: serum thyrotropin.

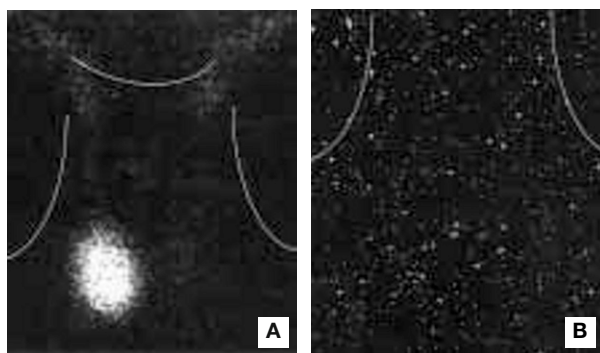


Fig. 2 - Technetium^{99m} (^{99m}Tc) (A) and ¹³¹I (B) thyroid scintiscan performed off L-T₄ therapy. ^{99m}Tc thyroid scan revealed a focal increased uptake in the right lobe ("hot" nodule) with nearly absent uptake in the remaining thyroid tissue. ¹³¹I thyroid scan show faint patchy distribution, without evidence of focal uptake.

in the right lobe was detected by radioiodine scan (Fig. 2B).

The final diagnosis was therefore hypothyroid HT mimicking autonomous thyroid nodule with subclinical iatrogenic hyperthyroidism; L-T₄ substitution therapy was re-started at a dose of 75 µg/d.

DISCUSSION

We report here a case of hypothyroid HT mimicking scintigraphic (^{99m}Tc scan) and CFDS features of autonomously functioning thyroid nodule. The patient was first seen at our Institution on long-term L-T₄ therapy, and displayed symptoms and hormonal findings of subclinical hyperthyroidism. The complete absence of autonomous thyroid function was demonstrated by the severe hypothyroidism documented 2 months after withdrawal of L-T₄.

Cases of HT mimicking "hot" nodules at the scintiscan (mostly performed with radioiodine) have occasionally been reported for a long time (2, 6-9). This feature has been generally interpreted as the consequence of residual thyroid function limited to localized residual tissue, often presenting as a pseudo-nodule, stimulated by TSH in hypothyroid HT patients. In our case, a clear scintigraphic image of "hot" nodule was only seen with ^{99m}Tc, while RAIU was low and the scan with radioiodine displayed only a very faint uptake on the thyroid. Although rare, this pattern has been reported for a long time and it was estimated that at least one of 30 unselected thyroid nodules can be "hot" with ^{99m}Tc and "cold" with ¹³¹I (11-14). Such discrepancy is generally believed to be the consequence of the maintenance by the nodular tissue of the trapping mechanism even in the absence

of all the later steps involved in thyroid hormone synthesis (12). Thus, the positive ^{99m}Tc and the negative ¹³¹I scan observed in our case are probably due to trapping of pertechnetate in the residual tissue having still intact transport process, but almost devoid of organification capacity (11-17).

Autonomous hyperfunctioning thyroid nodules (toxic and pre-toxic adenomas) have also been more recently characterized by US associated to CFDS (18-21), which shows typical solid iso-hypoechoic nodules with internal hypervascularization (type III pattern) and increased PSV at intranodular arteriolar level. Increased thyroid vascularization by CFDS is present in hyperthyroid Graves' disease (5, 18, 20-23), but it has also been detected in hypothyroid goitrous HT. The latter phenomenon has been attributed to elevated serum TSH and is generally unevenly distributed throughout the gland (5, 20). In our case, the pseudo-nodular thyroid residue of the right lobe displayed a typical type III hypervascularized CFDS pattern: this phenomenon may easily be explained by increased serum TSH only in the hypothyroid state after L-T₄ withdrawal; although no systematic studies are available on the effects of L-T₄ therapy on CFDS pattern in hypothyroid HT, the observation that increased vascular action at CFDS is found in hypothyroid but not in euthyroid goitrous HT (5-20), strongly suggests the TSH-dependency of this phenomenon. Thus other mechanisms (cytokines?, angiogenetic factors? TSH receptor antibodies-TRAb?) could be involved to explain the same CFDS pattern observed on L-T₄ doses able to fully suppress serum TSH. Regarding TRAb, it is clearly established that high levels of thyroid stimulating antibodies (TSAb) are able to strongly enhance thyroid vascularization in Graves' disease (5, 20-23). As far as we know, no data are available on the effect on thyroid vascularization of blocking type TRAb, which may be present in hypothyroid HT (24). Unfortunately, we did not measure either TRAb or TSAb and the relevance of TSH receptor antibodies in our case remains speculative. The final diagnosis was supported by US [markedly hypoechoic thyroid tissue (4, 25-31)] and cytological criteria of classic HT (32-33). In conclusion, this is to our knowledge, the first report of HT mimicking both scintigraphic (^{99m}Tc) and CFDS features of an autonomous functioning thyroid nodule. This case further stresses the need to use caution in the interpretation of imaging results in the presence of biochemical and serological evidence of HT.

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