OVARIAN GOITER AS A RARE CAUSE OF HYPERTHYROIDISM

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Introduction. Thyroid tissue ectopically located in the ovary can be reported accidentally after adnexectomy, but as a primary cause of hyperthyroidism this diagnosis is rare. The clinical search for a functional ectopic thyroid tissue requires intense clinical focus and a multidisciplinary approach.

Case Description. This case report demonstrates a patient with a history of Graves' disease who had undergone thyroidectomy combined with postoperative ¹³¹I radioablation. Despite the previous treatment, she developed an outburst of hyperthyroidism ten years later. Only very close follow-up enabled us to disclose the right condition. The ovarian source of thyroid hormone production was removed by laparoscopic adnexectomy and a right sided benign ovarian struma was confirmed.

Conclusion. Most patients treated by thyroidectomy and radioiodine do not require extended periods of follow-up or postoperative investigations, but when the clinical or laboratory signs change, clinicians should be prepared to perform the necessary re-evaluation in order to provide the best care.

Key words: ovarian goiter, thyroidectomy, hyperthyroidism, *struma ovarii*.

INTRODUCTION

Ovarian goiter also named as *struma ovarii* has been rarely presented as a clinical curiosity (1). By definition *struma ovarii* is a mature teratoma composed either exclusively or predominantly of thyroid tissue, mostly diagnosed between the ages 40 and 60 years. The common clinical features are pelvic pain, palpable abdominal tumor mass, and ascites. Clinical and biochemical features of hyperthyroidism are uncommon (<10%), however, thyroglobulin (TGB) can be elevated. For a well-educated clinician aware

of this diagnosis, ultrasonography and radionuclide imaging represent a method of choice to confirm this diagnosis.

CASE REPORT

Patient with no previous pregnancies without declared health problems until the age of 21. At this age, one year before her first pregnancy, she revealed typical clinical signs and symptoms of hyperthyroidism. Laboratory tests mirrored all parameters common to Graves' disease including elevation of anti-rTSH Ab(56.2 U/l). She had no evidence of Graves's orbitopathy at this point. After the first delivery she took 15mg of carbimazol/day for 4 years.

She was seen at our outpatient clinic for the first time at the age of 25 after she became pregnant for the second time and developed slight signs of orbitopathy (clinical activity score - CAS 1). She was immediately switched on 200 mg of propylthiouracil/day and 10 mg/day of prednisone, delivered successfully at term and stopped breast feeding after a fortnight because of a milk shortage. At the age of 27 she finally agreed to total thyroidectomy refused several times before, however, this surgery was recommended to achieve better disease control; including progression of her orbitopathy. The operation was complicated with a slight and temporary post-operative hypoparathyroidism. A steep rise of TSH levels was observed after a four weeks post-operative wash-out period (Table 1). To eliminate remains of thyroid tissue she was administered 1 GBq of ¹³¹I and eventually stabilized on 175 µg of levothyroxin daily. Afterwards the glucocorticosteroid treatment was gradually tapered and stopped finally, her eye disease completely vanished and remained stable (CAS 0).

The following years were medically uneventful, however, nine years after total thyroidectomy a drop in

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Table 1. Evolution of thyroid markers during evolution

	Initial time	After thyroidectomy		2 nd flare-up of thyrotoxicosis		Adnexectomy	
Year	1999	2001	2009	2011	2012	2014	2014
TSH (mU/L)	0.026	33.621	0.252	0.006	0.004	0.004	54.823
fT4 (pmol/L)	24.6	11.5	18.0	21.1	20.6	15.1	11.6
fT3 (pmol/L)	8.5					2.14	3.15
anti-TPO (kU/L)	57.5		22.0	6.7		31.3	14.7
anti-hTG (kU/L)	27.2					237.7	72.7
anti-rTSH (IU/L)	56.2	32.7	0.2	1.2	1.3	1.5	2.2
TGB (µg/L)	27.2					1686	<0.04

TSH (thyroid stimulating hormone) 0.350 – 4.940 mIU/L, fT4 (free thyroxin) 9.1 – 19.1 pmol/L, fT3 (free triiodothyronine) 2.62 – 5.7 pmol/L, anti-TPO (antibodies against human thyreoperoxidase) > 5.6 kU/L, anti-hTG (antibodies against human thyreoglobulin) >4.1 kU/L, anti-rTSH (TRAB, antibodies against thyroid stimulating hormone receptors) 1 – 5 IU/L, TGB (thyroglobulin) 3.5 – 77 µg/L.

Figure 1. Whole-Body Scan (^{99m}Tc). Physiologic uptake in all salivary glands, mouth, stomach and in both side renal pelvis, urine accumulation in the bladder, urine contamination out of the bladder. Pathologic lesion can be found in the right hypogastrium.

TSH level was observed. The dose of levothyroxin was gradually lowered, but the levels of TSH stayed low, therefore we stopped the treatment and reevaluated the thyroidectomised patient for a new attack of hyperthyroidism.

^{99m}Tc scintigraphy confirmed minor activity on the right side of the neck, but we considered this focus too small to cause such an overt hyperthyroidism. The whole body ^{99m}Tc scintigraphy, added immediately afterwards, disclosed a clear activity deep at the bottom of the patient's right groin and SPECT/CT revealed hyperactivity situated at the rim of the enlarged right ovary (53×40×76 mm, Figs 1, 2). Non-contrast CT confirmed a nonhomogeneous structure of the ovary with hypo-densities and calcifications. Our patient underwent laparoscopic adnexectomy. Ovarian

Figure 2. SPECT/low dose CT (^{99m}Tc). Fusion SPECT/CT (transversal slice) with pathologic lesion localized at the margin of the right ovary.

cell type, so called monophasic, represented usually by *struma ovarii* or less frequently carcinoid tumors. Nomenclature can be confusing, but approximately 20 % of any ovarian teratomas contain thyroid tissue; <5% of teratomas are *struma ovarii*, by definition the thyroid tissue represents half or more of the tumor (2), histopathologically composed of normal thyroid-type tissue with follicles filled by colloid resembling eutopic thyroid tissue (3). This tissue rarely produces sufficient amounts of thyroid hormones to cause clinical signs of hyperthyroidism (4). Similarly to the thyroid gland the ectopic thyroid tissue may function autonomously (5). Malignant *struma ovarii* represents 0.01 % of all ovarian tumors and 5-10% of all *struma ovarii* (mostly papilocarcinomas) with prevalent good prognosis (3, 6). In general, it is the most common sporadic histopathological finding revealed by the resection of the tumor masses during adnexectomy.

Reviewing the previously published data we found only a report of one patient having clinical signs and symptoms of hyperthyroidism 23 years after thyroidectomy with radioiodine ablation (7). One

Figure 3. Residual ovarian tissue and struma ovarii (He x100).

of the largest series of ovarian goiter submitted to surgery is that of Wee *et al.* who published a total of 68 patients undergoing surgical removal of ovarian cyst or mass (24 cystectomy, 20 salpingo-oophorectomy and 24 total hysterectomy and bilateral salpingo-oophorectomy) during 11 years (8). Rare case reports describe *struma ovarii* corresponding to autoimmune thyroiditis (9) or even typical thyroid carcinomas (6, 10). In a recent and exhaustive report of Anastasilakis *et al.* data of 15 case reports, published between 1970 – 2013, are summarized. We find important to point out the difficulties in diagnosing the ovarian goiter, since the time to confirm the diagnosis, ranged from 6 months to 26 years, 7.75 years on average (1).

Our young patient with a past history of active Graves' disease, thyroidectomised with consecutive elimination with ^{131}I , was stable on thyroid hormone supplementation for many years. Up to 10 years after complete remission, laboratory evidence of functional thyroid tissue was discernible (Table 1). TGB steeply increased, fortunately neither change in anti-rTSH nor in CAS were observed. $^{99\text{m}}\text{Tc}$ scintigraphy was crucial for re-establishing the diagnosis. It localized ectopic source of thyroid hormones to the right ovary region (Figs 1, 2).

There is a substantial evidence that TSH promotes tissue growth, but in our patient during the 9-year follow-up in between the thyroidectomy and the hyperthyroidism outburst the TSH level remained in normal range; consequently, we do not suspect TSH to be the relevant growth factor in our patient. It is also presumed that, in patients with Graves' disease long lasting anti-rTSH antibody stimulatory effect on the thyroid tissue in the ovary, might result in gradual growth and increase the thyroid hormone production;

Figure 4. Struma ovarii, hyperplastic area with vacuoles filled with colloid (He x 200).

our patient was regularly followed by an endocrinologist and the anti-rTSH antibody level remained low (1). It can be only speculated about the long-term effect of activating anti-rTSH antibodies even in low titers on the ectopic ovary thyroidal cells and its later tumor development. Unfortunately, at the time of diagnosis discrimination of activating anti-rTSH antibodies was not available for our clinical routine.

In conclusion, most thyroidectomised patients with radioiodine elimination do not require extended follow-up periods or postoperative investigations. But in case of clinical or laboratory signs of deterioration, clinicians should be prepared to re-evaluate the patient and to consider even rare diagnosis as a possible cause of the patients problems in order to provide the best care for our patients.

Conflict of interest

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review.

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