



An unusual case of struma ovarii

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Abstract

Introduction: Struma ovarii is a teratoma of the ovaries predominantly composed of thyroid tissue. Hyperthyroidism associated with struma ovarii is rare, occurring in approximately 8% of cases. Due to the rarity of struma ovarii, available data are limited to case reports and small case series.

Methods and results: We report on a 61-year-old female patient with known Hashimoto's thyroiditis on levothyroxine replacement therapy for years with transition to clinical and biochemical hyperthyroidism despite antithyroid medication with carbimazole (10 mg/day), new diagnosis of urothelial carcinoma and an adnexal mass suspicious of ovarian cancer. The patient underwent resection of the adnexal mass and histopathology revealed a mature teratoma predominantly composed of thyroid tissue showing high levels of sodium iodide symporter protein expression. Following struma ovarii resection and disappearance of autonomous production of thyroid hormones, the patient developed hypothyroidism with severely decreased thyroid hormone levels fT4 and fT3 (fT4 0.4 ng/dL, reference interval 0.9–1.7 and fT3 < 1.0 pg/mL, reference interval 2.0–4.4). This has previously been masked by continued thyroid-stimulating hormone suppression due to long-term hyperthyroidism pre-surgery indicating secondary hypothyroidism, in addition to primary hypothyroidism based on the known co-existing chronic lymphocytic thyroiditis of the orthotopic thyroid gland. Levothyroxine administration was started immediately restoring euthyroidism.

Conclusion: This case illustrates possible diagnostic pitfalls in a patient with two concurrent causes of abnormal thyroid function.

Learning points:

- Struma ovarii is an ovarian tumor containing either entirely or predominantly thyroid tissue and accounts for approximately 5% of all ovarian teratomas.
- In rare cases, both benign and malignant struma ovarii can secrete thyroid hormones, causing clinical and biochemical features of hyperthyroidism.
- Biochemical features of patients with struma ovarii and hyperthyroidism are similar to those of patients with primary hyperthyroidism. In such cases, thyroid scintigraphy should reveal low or absent radioiodine uptake in the thyroid gland, but the presence of radioiodine uptake in the pelvis in a whole body radioiodine scintigraphy.
- We give advice on possible diagnostic pitfalls in a case with two simultaneous causes of abnormal thyroid function due to the co-existence of struma ovarii.

Background

Struma ovarii is an ovarian tumor containing either entirely or predominantly thyroid tissue (> 50%) and accounts for approximately 5% of all ovarian teratomas (1, 2, 3). Traditionally, struma ovarii does not secrete thyroid hormones, however, in 8% of cases clinical and biochemical features of hyperthyroidism have been described (4). Around 40% of cases are asymptomatic and are accidentally discovered by routine ultrasound (5). In symptomatic cases of struma ovarii, common symptoms include palpable abdominal mass, abdominal pain or vaginal bleeding as well as tachycardia and ascites (5). Biochemical features of patients with struma ovarii and hyperthyroidism are similar to those of patients with hyperthyroidism of the orthotopic thyroid gland, showing low thyroid-stimulating hormone (TSH) and elevated peripheral thyroid hormones. In such cases, thyroid scintigraphy should reveal low or absent radioiodine uptake in the orthotopic thyroid gland, but whole body ^{123}I scintigraphy should confirm the presence of functional thyroid tissue within the ovarian mass.

The treatment of benign struma ovarii is unilateral surgical resection of the ovarian tumor. In case of malignant transformation, the decision on performing total thyroidectomy followed by radioiodine therapy should be made based upon the risk of recurrence and the presence of metastatic disease (6, 7). Furthermore, molecular genetic analysis of tumor tissue may assist in managing difficult cases (8, 9, 10).

We present an extraordinary case of a woman with two simultaneous causes of abnormal thyroid function, that transitioned from Hashimoto's thyroiditis-induced hypothyroidism to struma ovarii-induced hyperthyroidism and, after unilateral adnexectomy, back to hypothyroidism with persistent TSH suppression.

Case presentation

A 61-year-old female patient was admitted to the urology department because of urothelial carcinoma of the bladder. In the diagnostic work up an adnexal mass suspicious of ovarian cancer was detected by MRI (Fig. 1). Radical cystectomy and ileal neobladder reconstruction was performed as well as resection of the adnexal mass.

Medical history revealed Hashimoto's thyroiditis for 3 years that was supplemented with levothyroxine (LT4) until the diagnosis of Graves' hyperthyroidism was made 1.5 years ago by her general practitioner based on her history of autoimmune disease despite the lack of TSH



Figure 1

Pelvic MRI. The sagittal T2-weighted image revealed a large high-intensity cystic mass of the right ovary with a diameter of 15 cm.

receptor antibodies. Antithyroid medication (carbimazole) was started 1.5 years ago and titrated to a dose of 10 mg/day at the time of admission.

Investigation

Preoperative thyroid function tests (TFTs) revealed a suppressed TSH of < 0.01 $\mu\text{U}/\text{mL}$ (reference interval: 0.27–4.2), a free thyroxine (fT4) of 0.8 ng/dL (reference interval 0.9–1.7) and free triiodothyronine (fT3) of 3.3 pg/mL (reference interval: 2.0–4.4). Thyroid-specific autoantibody (TSH-receptor-, thyroid peroxidase- and thyroglobulin-antibodies) levels were within the reference range.

The patient was clinically euthyroid and thyroid ultrasound findings were highly suggestive of chronic lymphocytic thyroiditis (Fig. 2). Due to low fT4-levels, carbimazole was reduced to 5 mg/day.

Treatment

Meanwhile, the patient underwent radical cystectomy and ileal neobladder reconstruction as well as unilateral adnexectomy. A giant cystic tumor of 15 × 14 × 7 cm in size was present in the right ovary, suspicious of a benign tumor. Histopathology of the adnexal mass revealed a mature teratoma predominantly composed of thyroid tissue, without signs of malignancy. Due to decreasing fT4-levels, carbimazole was stopped completely post-operatively.

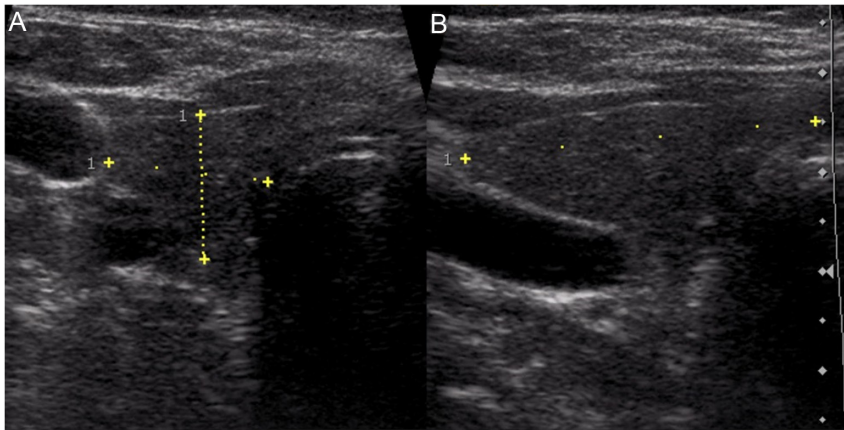


Figure 2

A sonogram of the right lobe of the thyroid ((A) transverse scan view, (B) longitudinal scan view) shows an inhomogeneous echotexture with hypoechoic areas compatible with chronic lymphocytic thyroiditis.

Outcome and follow-up

Three days after withdrawal of carbimazole, TFTs were as follows: low TSH levels of 0.6 μ U/mL in the presence of significantly decreased peripheral thyroid hormone levels of fT4 0.4 ng/dL and fT3 < 1.0 pg/mL. The failure to mount a TSH response post-operatively is consistent with secondary hypothyroidism after long-term thyrotropin-releasing hormone (TRH)/TSH suppression from extra-thyroidal thyroid hormone secretion. Biochemical assessment, including cortisol, corticotropin (ACTH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin as well as an ACTH stimulation test, revealed no additional pituitary hormone deficiencies. Due to post-surgical risk of developing myxedema coma, intravenous LT4 therapy was started immediately with 250 μ g LT4/day for 3 days and switched to oral LT4 treatment with 100 μ g/day. Follow-up of the patient showed TFTs within the normal range; TSH was 1.0 μ U/mL, fT4 was 1.3 ng/mL and fT3 was 2.0 pg/mL.

Immunohistochemical analysis of sodium iodide symporter (NIS) expression of paraffin-embedded tissue sections of the teratoma was performed as described previously (11). Immunohistochemical staining revealed strong basolateral NIS staining in the thyroid follicular cells indicative of overactive thyroid tissue (Fig. 3).

Discussion

Hyperthyroidism can be caused by a number of conditions, including Graves' disease, hyperfunctioning thyroid nodules and thyroiditis. Struma ovarii is one of the rare causes of hyperthyroidism and diagnosis can be even more difficult in the presence of co-existing thyroid disorders. In such cases, autonomous production of thyroid hormones by struma ovarii causes suppression of the thyroid gland. In 1390 cases of surgically removed ovarian tumors, Duzendorfer *et al.* reported only five cases of struma

ovarii and only one with co-existing hyperthyroidism (1). Another review of 1501 ovarian neoplasms did not detect a single case of hyperthyroidism due to struma ovarii (12). Approximately 8% of patients with struma ovarii develop hyperthyroidism, mostly originating from adenomas, rarely from differentiated thyroid carcinomas (1, 4).

Biochemical features of patients with struma ovarii and hyperthyroidism are similar to those of patients with primary hyperthyroidism. In such cases, thyroid scintigraphy should reveal low or absent radioiodine uptake in the thyroid gland, but the presence of radioiodine uptake in the pelvis in a whole body radioiodine scintigraphy. Histopathological findings of benign struma ovarii are identical to cervical thyroid tissue. Malignant struma ovarii is exceedingly rare and diagnostic criteria are similar to those for differentiated thyroid cancer.

Based on clinical and laboratory findings in our case, transition from hypothyroidism due to Hashimoto's thyroiditis to overt hyperthyroidism 1.5 years before adnexectomy had been caused by autonomously functioning thyroid tissue in the teratoma that was controlled by antithyroid medication. After resection of the teratoma, the patient switched back to hypothyroidism due to known

Tumor

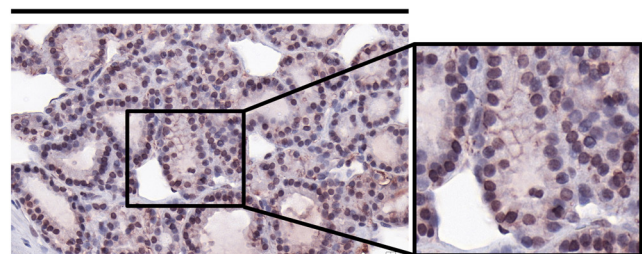


Figure 3

High NIS protein expression in teratoma. NIS-specific immunoreactivity (red) was detected in thyroid follicular cells in the teratoma tissue. The image is shown at $\times 40$ magnification and $\times 60$ magnification..



Hashimoto's thyroiditis of the orthotopic thyroid gland that was initially masked by continued TRH/TSH suppression as a result of long-term insufficiently controlled hyperthyroidism caused by the struma ovarii indicating additional secondary hypothyroidism. Based on the patient's history and clinical and laboratory parameters, hypothyroidism was diagnosed and thyroid hormone replacement therapy was started immediately. After 3 weeks of LT4-replacement therapy, normalization of TFTs was achieved.

Comparing our case to other cases in the literature, Carvalho *et al.* described an almost identical case of a 62-year-old woman with symptoms of hypothyroidism after struma ovarii tumor resection most likely due to Hashimoto's thyroiditis of the orthotopic thyroid gland (13). Amareen *et al.* reported a comparable case of clinical hypothyroidism following a resection of struma ovarii with positive thyroid peroxidase-antibodies in a 41-year-old woman (14). After initiation of LT4-replacement therapy, clinical symptoms and laboratory findings returned to normal. The authors assume that the ovarian tumor probably maintained normal thyroid function until surgical resection. The only difference to our case, which presented with preoperative hyperthyroidism, is that the patient was euthyroid before surgical resection of struma ovarii.

Our case, as one of the very few cases reported so far, illustrates two simultaneous causes of abnormal thyroid function due to the co-existence of struma ovarii causing hyperthyroidism in the presence of an orthotopic thyroid gland with chronic lymphocytic thyroiditis as well as possible diagnostic pitfalls.

Declaration of interest

Viktoria F Koehler has received honoraria for lectures and travel expenses from Novartis and Sanofi. Christine Spitzweg has received honoraria for advisory boards and lectures from Ipsen, Lilly, Bayer, Eisai, Genzyme. Patrick Keller, Elisa Waldmann, Nathalie Schwenk, Carolin Kitzberger, Kathrin A Schmohl, Thomas Knösel, Christian Georg Stief have declared no conflicts of interest.

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Patient consent

Written informed consent was obtained from the patient for publication of the submitted article and accompanying images.

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