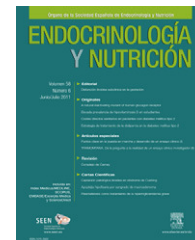




ENDOCRINOLOGÍA Y NUTRICIÓN

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SCIENTIFIC LETTERS

Incidental finding of struma ovarii[☆]

Hallazgo incidental de estruma ovárico

The most common functional ovarian tumors are strumal and sexual cord tumors. Depending on the histological variant, these may secrete various hormones, including estrogens, androgens, human chorionic gonadotropin (hCG), and thyroid hormones. The ovary has a complex embryological development, and tumors of a very diverse histology may therefore arise in it.¹ Mature cystic teratoma of the ovary or benign dermoid cyst is the most common benign ovarian tumor and derives from germ cells.² It may consist of a wide variety of mature tissues, and from the hormonal viewpoint it may behave as a carcinoid tumor or as a neoplasm secreting thyroid hormones, the so-called struma ovarii. Struma ovarii accounts for 3% of all benign teratomas and may lead to a true thyrotoxicosis in up to 8% of cases.³ It is usually benign in nature. Struma ovarii occurs most commonly between the fifth and sixth decades of life, and is rare before puberty. A unilateral adnexal tumor mass corresponding to the ovarian tumor may sometimes be palpated.⁴

The case of a patient in whom struma ovarii was incidentally found during follow-up for a follicular thyroid carcinoma is reported below. This was a 32-year-old female who attended the endocrinology clinic for goiter. The patient reported a mass in the anterior side of the neck appearing two months before, but with no local or general clinical signs or symptoms suggesting thyroid dysfunction. She reported no toxic habits or routine use of medication. She also had no family history of goiter. At a physical examination, a left thyroid nodule approximately 3 cm in diameter and of medium consistency which rose upon swallowing was palpated, as well as a slightly enlarged right thyroid lobe. No adenopathies were palpated.

Laboratory tests showed no changes in complete blood count and chemistry tests, thyrotropin (TSH) 1.3 mIU/mL (normal range (NR), 0.2–3.5), free thyroxine (fT4) 14 ng/dL (NR, 0.8–2.1), and negative anti-thyroid and anti-thyroglobulin antibodies (Ab). A thyroid scan revealed a normally located, enlarged thyroid gland with a low global uptake of irregular distribution, showing a low uptake area in the left lobe coinciding with the palpable

nodule. A neck ultrasound showed a left thyroid lobe 25 mm × 32 mm × 58 mm in size with preserved echogenicity, while the middle and lower thirds were occupied by a single hypoechoic nodule 24 mm × 26 mm × 30 mm in size and with mixed vascularization. The isthmus had an anteroposterior diameter of 22 mm and showed no parenchymal lesions. The right thyroid lobe measured 24 mm × 28 mm × 49 mm and had a preserved echo structure. No pathological adenopathies were seen in the neck. Based on these findings, fine needle aspiration of the nodule was requested. The cytological diagnosis was follicular tumor.

Left hemithyroidectomy and isthmectomy were performed. The pathological laboratory reported a 3 cm follicular carcinoma with focal oncocyctic features in the base of the left lobe. Right thyroidectomy was therefore performed at repeat surgery. No pathological changes were reported in the right side of the thyroid gland.

A pT2N0 Mx follicular thyroid carcinoma was diagnosed, and the patient was subsequently administered an ablation dose of 100 millicuries (mCi) of ¹³¹I as supplemental treatment. The results of laboratory test performed before ¹³¹I administration included TSH 58 mIU/mL, fT4 0.1 ng/dL, thyroglobulin (Tg) 46 ng/mL (NR, 2–16), and negative anti-thyroglobulin Ab. A whole body scan showed uptake at neck level and another active area in the lesser pelvis, slightly displaced to the right, suggesting ovarian uptake (Fig. 1).

The patient was referred to the gynecology department for evaluation. A gynecological ultrasound revealed a uterus of normal size with a 25-mm myoma in the posterior and lateral aspect, a right ovary with scant stroma and abundant follicles (polycystic), and a left ovary with predominant follicular tissue. The patient underwent right laparoscopic oophorectomy. The surgical specimen, 3 cm in size, consisted of the ovary, with two small gaps. The pathological diagnosis was an ovary with very abundant follicles and a fragment of thyroid tissue (2 mm) with no remarkable changes (struma ovarii) (Fig. 2).

The results of laboratory tests performed four months after the ¹³¹I ablation dose were as follows: TSH 0.22 mIU/mL, fT4 1.34 ng/dL, Tg < 0.2 ng/mL, and negative anti-thyroglobulin Ab.

Six months later, a whole body scan performed after the discontinuation of levothyroxine treatment was negative, and laboratory test results included: TSH 38 mIU/mL, fT4 0.1 ng/dL, Tg < 0.2 ng/mL, and negative anti-thyroglobulin Ab. The patient had uncomplicated pregnancies two and four years after this whole body scan. At the next follow-up visits, data continued to suggest complete remission, with

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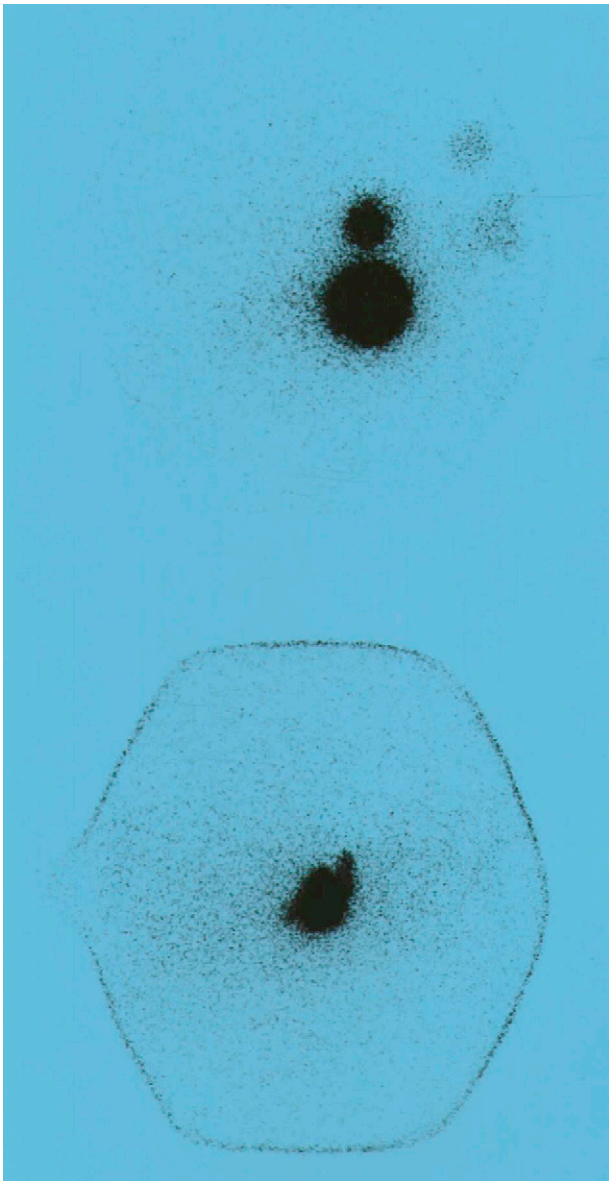


Figure 1 Whole body scan after treatment with ^{131}I .

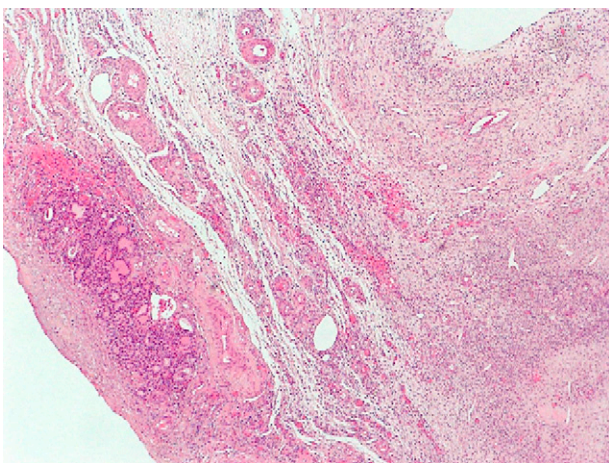


Figure 2 Histological image of struma ovarii in the right ovary.

Tg < 0.2 ng/mL, negative anti-thyroglobulin Ab, and normal neck ultrasound examinations.

The ability to concentrate radioiodine depends on the expression of the NIS iodine symporter in the cell membrane. Such expression may be detected in extrathyroid tissues such as the ovary. When ovarian uptake of ^{131}I is seen, a differential diagnosis should be made between struma ovarii, ovarian metastases of thyroid carcinoma, and thyroid carcinoma arising in struma ovarii.⁵ Ovarian uptake of ^{131}I has rarely been reported in the literature, probably because a whole body scan is reserved for thyroid carcinoma and for hyperthyroidism with prior total thyroidectomy.

A literature review found only a few reported cases where struma ovarii was incidentally found during follow-up for differentiated thyroid carcinoma.^{6–10} In four of these cases, similarly to what occurred in our patient, struma ovarii was detected in a whole body scan following the ^{131}I ablation dose for a differentiated thyroid carcinoma.^{6,8–10}

In the reported case, struma ovarii was an incidental finding during the follow-up of follicular carcinoma. Ovarian metastasis should always be considered in differential diagnosis, especially when no other teratoma elements are identified in the ovarian surgical specimen.¹⁰ Metastases account for less than 10% of malignant ovarian tumors. If metastasis occurs, a primary thyroid tumor is rare. The pathological study will establish whether the condition is benign or malignant. In the reported case, metastasis from a follicular carcinoma was ruled out. After oophorectomy was performed, basal Tg remained undetectable at all times, and subsequent scans were negative.

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Familial hypocalciuric hypercalcemia: An atypical presentation[☆]

Hipercalcemia hipocalciúrica familiar: una presentación atípica

Familial hypocalciuric hypercalcemia (FHH) is a condition of autosomal dominant inheritance due to inactivating mutations in the calcium-sensing receptor (CaSR) gene. It is biochemically characterized by mild to moderate hypercalcemia, relative hypocalciuria, and inappropriately normal or high (by 20%) PTH levels. Clinically, patients usually have few or no symptoms of hypercalcemia, and bone or renal involvement is rare. Adequate differential diagnosis between primary hyperparathyroidism (PHP) and FHH is important, because the latter is a benign condition that does not improve after parathyroidectomy. We report here on the members of a family with FHH showing the biochemical heterogeneity of the disease and the difficulty of differential diagnosis with PHP.

Measurements of intact PTH (normal range, 10–65 pg/mL) were performed by electrochemoluminescence with an ELECSYS analyzer. A Cobas 711 analyzer (Roche Diagnostics) was used to perform measurements of phosphorus (normal range, 2.7–4.5 mg/dL) by spectrophotometry using molybdate; calcium (normal range, 8.6–10.4 mg/dL) using the Schwarzenbach method with o-cresolphthalein complexone; and creatinine (normal range, 0.67–1.17 mg/dL) by the Jaffé method. Urine measurements of calcium (normal range, 100–320 mg/24 h), phosphorus (normal range, 700–1500 mg/24 h), and creatinine (normal ranges, 740–1570 mg/24 h in females and 1040–2350 mg/24 h in males) were performed using the same methods as in serum. 25-hydroxyvitamin D levels were normal in all reported cases (normal range, 30–100 ng/mL). Calcium levels were expressed corrected for albumin [$4 \times \text{albumin (g/dL)} \times 0.8$] + calcium (mg/dL). Magnesium, gastrin, growth hormone, insulin-like growth factor-1, TSH, free T4, ACTH, cortisol, prolactin, LH, FSH, subunit alpha, and calcitonin were measured in all subjects, as well as catecholamines in 24-h urine, with results within the normal range in all cases. Orthopantomography ruled out the presence of

fibro-osseous jaw tumors, and renal ultrasound showed kidneys of normal morphology in all the subjects studied. The genetic study showed no mutations associated with multiple endocrine neoplasia type 1 syndromes in any of the cases.

The index case was a 16-year-old female patient referred in 1996 for hypercalcemia work-up. From that date, nine members of the family have been studied, of whom six are affected. Among the nine family members, six were tested at the hospital. The four family members affected and followed up at our center are reported below (Fig. 1). The remaining three subjects were seen at another center (their data are not available).

The index case reported urinary frequency, polydipsia, and epigastric pain. Laboratory test results were as follows in 1996 and in the last measurement respectively: calcium, 10.6 and 11.1 mg/dL; phosphate, 2.4 and 3.6 mg/dL; and PTH, 40.7 and 62.2 pg/mL. The corresponding results in 24-h urine included: calcium, 127.9 and 179.4 mg/24 h; phosphorus, 680 and 870 mg/24 h; and Ca/CrCl < 0.01 in all measurements. A ^{99m}Tc sestamibi scan showed no pathological uptake. Bone densitometry (BMD) performed at 23 years was normal for age.

The 20-year-old patient's sister was symptom-free and had the following blood test results: calcium, 10.5 and 10.9 mg/dL; phosphorus, 2.9 and 3.4 mg/dL; and PTH, 48.6 and 94.7 pg/mL. The results in 24-h urine included: calcium, 174.4 and 231.4 mg/24 h; phosphorus, 710 and 1320 mg/24 h; and Ca/CrCl < 0.01 in all measurements. BMD measured at 26 years showed osteopenia in lumbar spine, femur, and forearm.

The 70-year-old maternal grandfather was symptom-free and had the following blood test results: calcium 11.4 mg/dL, phosphorus 2.4 mg/dL, and PTH 69.9 pg/mL. His 24-hour urine results included calcium 348.2 mg/24 h, phosphorus 1240 mg/24 h, and Ca/CrCl > 0.01.

The blood test results of the 40-year-old mother, asymptomatic and premenopausal, included: calcium, 10.8 and 11.6 mg/dL; phosphorus, 3 and 3.1 mg/dL; and PTH, 83.4 and 118.3 pg/mL. The results in 24-h urine included: calcium, 228 and 496.8 mg/24 h and phosphorus, 710 and 1004 mg/24 h, Ca/CrCl > 0.01 in all measurements, except for one in which it was lower than 0.01. BMD showed osteopenia in the femur and forearm and osteoporosis in the lumbar spine. Sestamibi revealed hyperplasia in all four parathyroid glands. A molecular study of the CaSR gene was performed in the mother using automatic sequencing of exons 2 (codons 1–62), 3 (codons 62–164), 4 (region

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