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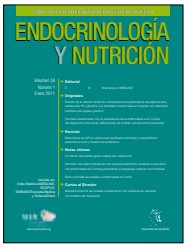

SCIENTIFIC LETTER

Struma ovarii with malignant histology: a case of papillary thyroid carcinoma

Struma ovarii con histología maligna: un caso con carcinoma papilar de tiroides

To the Editor:

Struma ovarii is an uncommon germ cell, monodermal, specialized ovarian tumor characterized by the total or partial presence of thyroid tissue. The first reports of this tumor were published by Boettlin in 1889 and Pick in 1901[1]. These tumors may have a malignant potential either because of its histological characteristics or its dissemination outside the ovary[2].

We report a case of papillary thyroid carcinoma arising from struma ovarii.

A 76-year-old female patient with an unremarkable clinical history consulted for abdominal pain and dizziness. Palpation revealed tenderness in left iliac fossa and hypochondrium. Blood and urine laboratory test results, electrocardiogram, and plain chest X-rays were normal. Plain abdominal X-rays showed a pelvic calcification, and a subsequent computed tomography (CT) scan of the abdomen and pelvis revealed a heteroechoic periovarian mass 42 x 47 mm in size. A CT scan without contrast showed a heterogeneous left suprauterine mass with a predominance of fat and calcifications in its most posterior and cranial part. Tumor markers (CEA, CA 19.9, CA 125, b-HCG, a-fetoprotein) were negative. A laparotomy found a 6-7 cm solid ovarian tumor with a cystic component, mobile, not adhering to the surrounding structures. Pathological examination revealed a mature cystic teratoma with a central nodular formation 0.7 cm in size consisting of many complex papillae, with diagnosis being consistent with papillary thyroid carcinoma (Fig. 1A). The previously established histological and immunohistochemical criteria were used: expression of thyroid transcription factor (TTF-1) in extrathyroid locations (Fig. 1B)[3,4]. No malignant cells were found in peritoneal lavage.

After surgery, neck palpation found a multinodular goiter. A subsequent ultrasound examination showed a dominant 0.9 cm nodule in the right thyroid lobe and no locoregional adenopathies. Cytological study of fine needle aspiration revealed a colloid goiter. Thyroid function was normal. No metastases were found in total body CT or bone scan. After surgery, tumor was classified as stage IA (limited to one ovary, with an intact capsule, and with no tumor evidence on its surface), and watchful waiting was decided. Eighteen months since diagnosis, the patient is doing well and shows no evidence of tumor persistence or recurrence.

Seven percent of ovarian teratomas contain thyroid tissue. It is commonly accepted that the term "struma ovarii" is used when thyroid tissue accounts for more than 50% of total teratoma volume[5], which occurs in only 2% of ovarian teratomas[6]. The former does not apply to cases where thyroid tissue in an ovarian teratoma shows unequivocal malignant characteristics. The tumor is then called a "malignant struma ovarii", accounting for 5%-10% of all tumors of this type[7]. Ectopic thyroid tissue may or may not be functioning. Hyperthyroidism secondary to struma ovarii has been reported in 5%-10% of the cases[8].

Malignant struma ovarii may be classified in the same histological types as described for the thyroid gland[9]. Roth reviewed 101 cases of various histological types published from 1924 to 2007 and reported four additional cases[9]. The largest series to that date, not included by Roth, had been reported by Devaney[3] and consisted of 11 papillary and 2 follicular carcinomas from malignant struma ovarii. Robboy[10] recently reviewed 18 papillary carcinomas derived from struma ovarii, four of which were considered to be of the follicular variant. The largest series (10 cases) of the follicular variant had already been reported by Boutross-Tadross in 2007[11]. To date (considering the cases reported by these and other authors, including our own case), 73 papillary carcinomas (52.5%), 36 follicular carcinomas (26%), 28 papillary carcinomas of the follicular variant (20%), one anaplastic carcinoma (0.75%), and one insular carcinoma (0.75%) have been reported.

Age of our patient (76 years) was outside the range seen in papillary carcinomas of this type reported to date (21-68 years)[9]. On the other hand, 80% of cases with histopathological findings similar to our patient are also unilateral, and approximately 30% have a similar size of 6 cm[10].

Biological malignancy has also been assessed. The term "biological malignancy" refers to tumor dissemination to or beyond ovarian surface, including "strumosis" (or peritoneal dissemination of benign tissue) and recurrence[10]. Biological malignancy was not found in our patient, in whom extraovarian dissemination was not shown.

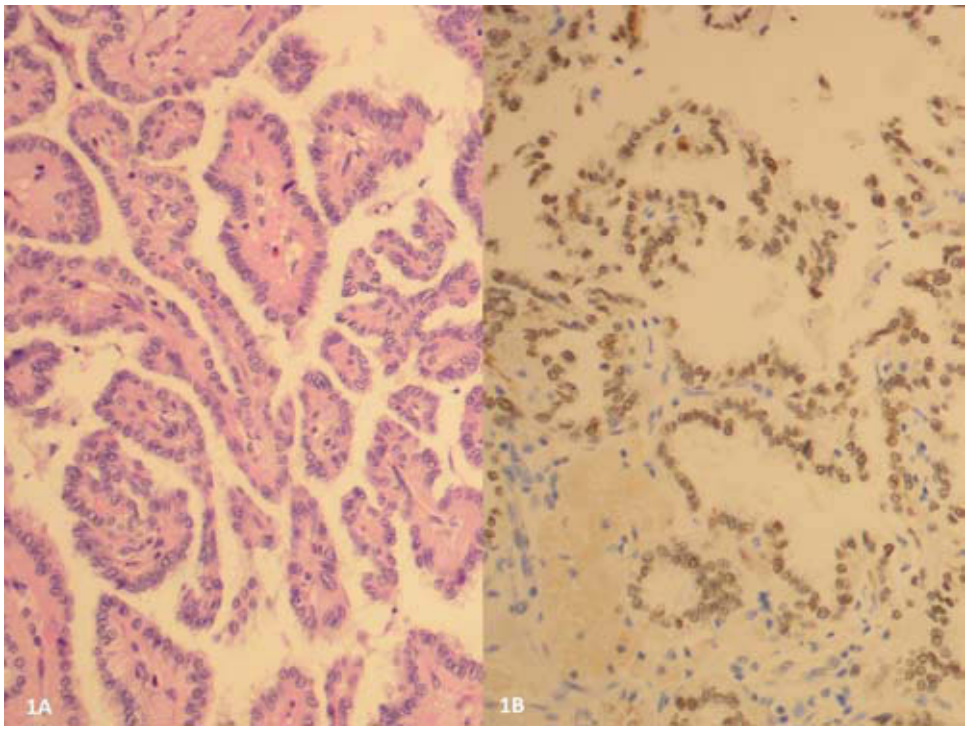

Figure 1 A) Multiple complex papillae with a fibrovascular axis lined with cuboidal cells with optically empty nuclei, nuclear clefts, and pseudoinclusions. B) Focal nuclear positivity for the thyroid transcription factor (TTF-1).

Metastases occur more commonly in follicular than in papillary carcinomas[9,10].

If histological malignancy criteria are only considered[9], 7% of papillary carcinomas had a fatal outcome from 2 weeks to 21 years after diagnosis, with a mean 8-year survival. In cases with biological malignancy, mean survival rates were 89% at 10 years and 84% at 25 years.

To sum up, the rarity of this condition makes it difficult to establish the most adequate management approach. Treatment should therefore be individualized, and long-term follow-up of these patients is indispensable.

The same criteria are used for clinical staging of these tumors as for other germ cell tumors of the ovary. In the reported case, the TNM system was used.

There is no consensus on optimal therapeutic management of malignant struma ovarii, but the most widely accepted therapeutic option in cases with extraovarian dissemination[12] consists of total thyroidectomy and subsequent ablation therapy with ^{131}I. In the reported case, a more conservative management was decided based on the usually indolent course of the disease and the lack of evidence of extraovarian dissemination.

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A fifty-one year old woman with raised testosterone concentration

Mujer de 51 años con concentración sérica de testosterona elevada

Testosterone is the hormone responsible for secondary sexual characteristics in men, in whom the serum concentration is 10 times higher than in women. A raised testosterone concentration in women may be due to various diseases, such as polycystic ovary syndrome, congenital adrenal hyperplasia, and adrenal or ovarian tumors, among other ovarian or adrenal disorders.

In the absence of clinical symptoms, a testosterone concentration above the reference interval may be due to interference in the immunoassay[1-4].

Case report

A 51-year-old woman who started her menopause a year previously, in good general health and not on any medication, had goiter as the only medical history of interest, for which periodical thyroid hormone monitoring was performed. In december 2008, her testosterone concentration was studied fortuitously, with a value of 5.47 ng/mL (table 1) (reference interval 0.2-0.8 ng/mL). The testosterone level was measured in an UniCel DxI 800 autoanalyzer (Beckman Coulter®, CA USA), an automated chemiluminescence immunoassay system. To confirm this value, the analysis was repeated and the same result was obtained. A new sample was requested, which was processed in the same autoanalyzer. A testosterone concentration of 5.76 ng/mL was found (table 1). The concentration of other androgens and hypophyseal hormones was studied for a possible subclinical disorder. The results obtained were as follows: androstenedione 1.1 ng/mL (0.4-4.5); dehydroepiandrosterone sulfate (DHEA-S) 900 ng/mL (700-3,900); sex hormone binding globulin 40 nmol/L (11-124); 17OH-progesterone 0.67 ng/mL (<4); cortisol 13.4 µg/dL (8-25); thyroid stimulating hormone 2.4 µU/mL (0.3-4.8); FSH 61.9 mU/mL (42-126); luteinizing hormone 31.9 mU/mL (11-50); prolactin 4.7 ng/mL (6.0-29.9).

To rule out possible interferences in the immunoassay, serial dilutions[5] were performed with the Access Testosterone Calibrator 0, at 1:1; 1:2; 1:4 and 1:8, with the following results: 5.62 ng/mL; 4.97 ng/mL; 4.96 ng/mL and 4 ng/mL respectively (table 1).

To rule out any possible artefacts in the chemiluminescence system, various parameters (TSH, FT4, AFP, CEA, cortisol and testosterone) were determined in the same autoanalyzer. All the results, except those for testosterone, fell within the reference interval.

Alternatively, the sample was processed in the Modular E170 (Roche® Diagnostics GmbH, Mannheim), an automated electrochemiluminescence immunoassay system. A testosterone concentration of 0.30 ng/mL was found (reference interval 0.06-0.82 ng/mL) (table 1). The sample was also processed by radioimmunoassay in the solid phase, Coat-A-Count Testosterone Total (Siemens®, CA USA), and a concentration of 0.26 ng/mL was found (0.04 -0.62) (table 1).

Finally, extraction with diethyl ether was performed, prior to immunoassay[2], and the testosterone concentration was measured in the same autoanalyzer. A result of 0.28 ng/mL (table 1) was found.

In view of the absence of clinical symptoms compatible with hyperandrogenism, a raised testosterone concentration in a woman when other androgen concentrations are normal suggests interference in the immunoassay used[6,7].

Table 1 Testosterone concentration (ng/mL) found in distinct samples and with different methods

Method used	First sample	Second sample
Chemiluminescence Immunoassay		
UniCef DxI 800 *(Beckman Coulter)*		
Direct	5.47	5.76 (1)
½ Dilution		4.97
¼ Dilution		4.96
1/8 Dilution		4.0
Extraction*		0.28
Electrochemiluminescence Immunoassay (Roche)		0.30 (2)
Radioimmunoassay (Coat-A-Count Testosterone)		0.26 (3)

Reference values (1): 0.2-0.8; (2): 0.06-0.82; (3): 0.04-0.62 ng/mL.
*Previous extraction using ethyl ether.