Papillary thyroid cancer in struma ovarii: case series

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Abstract
Struma ovarii is a mature ovarian teratoma composed exclusively or predominantly of thyroid tissue. Histopathological diagnosis of malignant struma ovarii is difficult and controversial due to the rarity of the disease, lack of uniform diagnostic criteria and similarities with ovarian tumors such as granulose cell tumour or carcinoid. We present two cases of papillary thyroid cancer in struma ovarii and discuss the current thinking and issues involved in the diagnosis, treatment and prognosis of this rare malignancy.

Key words: case series, in struma ovarii, papillary thyroid cancer

Introduction

Struma ovarii is a mature ovarian teratoma composed exclusively or predominantly of thyroid tissue. Malignant transformation seems to vary from 5 to 37% of cases [1]. It is usually diagnosed postoperatively based on histological findings. The majority of these cases represented examples of papillary thyroid carcinoma. Preoperatively, patients present most commonly with a pelvic mass. They may have associated abdominal or pelvic symptoms. Approximately 5-8% of patients have clinical hyperthyroidism. Imaging studies usually reveal an ovarian mass and surgical intervention is administered. We present two cases of papillary thyroid cancer in struma ovarii.

Patients

Case report 1

This case was sent for a second opinion. A 39 year-old woman with a story of abdominal pain and a left sided pelvic mass (diameter 5 cm) underwent laparoscopic unilateral annessiectomy in July 2013.

Histology showed a struma ovarii with papillary thyroid carcinoma of 1 cm diameter. Immunohistochemistry performed at our centre by the pathologist providing a second opinion confirmed a struma ovarii with thyroid tissue showing neoplastic transformation into papillary thyroid carcinoma, tall cell variant type. Immunohistochemical markers were strongly positive for thyroglobulin and TTF1, PAX8.

The patient had no prior history of thyroid disease and ultrasound evaluation revealed absence of pathologic involvement of thyroid. Ca 125 and FT3, FT4, TSH were within normal range.

Pelvic ultrasonography demonstrated an anteverted uterus with inhomogeneous structure because of the presence of an intramural myoma (32 × 25 mm). Endometrium was regular. Right ovary appeared multifollicular and enlarged (47 × 23 mm). Positron emission tomography/computed tomoraphy (PET/CT) did not reveal suspected focal hypercaptant lesions.

The patient was staged as FIGO (International Federation of Gynecology and Obstetrics) stage Ia malignant struma ovarii and no other adjuvant treatment was given. It was decided to keep her on follow up.

Case report 2

V.G., a 34-year-old caucasian woman, presented with an incidental finding of a large left ovarian mass during her gynaecologic exam in 2013. She did not have any medical comorbidity. She had no signs or symptoms of hyperthyroidism. The pelvic magnetic resonance imaging (MRI) with contrast demonstrated a semisolid enhancing lesion within the left abdomen and pelvis measuring 8 × 10 × 11 cm. This lesion arose from the left adnexa and was confirmed as a primary ovarian tumour. The patient underwent video laparoscopic left salpingo oophorectomy in May 2013. On gross pathological examination, there was a left ovarian mass measuring 10 cm. The capsule was not intact.

Microscopically the tumour was composed of solid and

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microfollicular areas, which were seen as either distinct or nodular aggregates. The tumour cells exhibited nuclear pleomorphism with occasional mitoses.
Immunohistochemical stain for thyroglobulin was positive within the epithelium of the follicular structure as well as in the centrally contained colloid. Vascular invasion was identified. Tumour cells were also positive for TTF-1, MNF116, CK7, CK19 and negative for chromogranin A, synaptophysin, calretinin and CD10. There were wide necrotic foci.
With these histologic features, the diagnosis of follicular carcinoma in malignant struma ovarii was made.
A whole body CT scan was performed on 26 June 2013 showing a left adnexal cyst.
Thyroid function was postoperatively evaluated showing a TSH level of 1.65 μIU/mL, a thyroglobulin level of 7.6 ng/mL and a FT4 level of 1.43 ng/mL. Ultrasonography of the neck revealed a hypoechoic nodule. A fine-needle aspiration was performed: the cytological test was negative for tumour cells. A Tc-99m thyroid scan did not reveal any residual intra-abdominal disease. Due to the presence of high risk features (broken capsule, tumour dimension) even in absence of residual disease, subsequent total thyroidectomy and radioactive iodine ablation was performed.

Discussion

Struma ovarii represents approximately 15% of mature cystic teratomas. It is a rare, non-malignant monodermal tumour of ovarian origin containing functional thyroid tissue or consisting of predominantly (>50%) thyroid tissue. Although struma ovarii is most often found within a background of teratoma, it may also occur in the absence of teratoma features [2]. Malignant transformation is reported in 5–37% of struma ovarii cases and can be papillary thyroid carcinoma (most common), follicular thyroid carcinoma [3] or highly differentiated follicular carcinoma of ovarian origin [1].
The average age of a patient with malignant struma ovarii is in the fifth decade of life, although cases occurring before puberty and after menopause have been reported [4]. About 94% of the tumours are unilateral and seem to involve the left ovary more commonly than the right one [5]. Approximately one third of struma ovarii patients can present with ascites or Meigs syndrome (the triad of ovarian tumour with ascites and pleural effusion that resolves after resection of the tumour). The fluid rarely contains tumour cells [6]. Hyperthyroidism appears clinically in about 5–8% of cases [4, 5].
Some authors reported that hypersecretory thyroid cancer is not uncommon, but may occasionally cause thyrotoxicosis and, in this situation, distant metastasis are present in 83% of cases.
The pathophysiology of the hyperthyroidism in patients with malignant struma ovarii is not clear. Some authors suppose that struma ovarii originates from a single germ cell with several chromosomal abnormalities. Struma ovarii-induced hyperthyroidism seems to be mediated by mechanisms different from those of the classical thyroid toxic adenoma [7]. Kung et al. [8] reported that struma ovarii is an autonomous hormone-secreting tumour of ovarian thyroid tissue stimulated by TSH receptor antibody. Thyroglobulin is a glycosylated protein that represents a matrix for thyroid hormone synthesis and storage. It is produced by normal or malignant thyroid tissue as well as struma ovarii. Thyroglobulin may be used as a valuable tumour marker in patients with thyroid carcinoma as well as malignant struma ovarii [2].
As malignant transformation is rare, the histopathological diagnosis of malignancy in struma ovarii is controversial. This is due to lack of uniform diagnostic criteria [8]. All of the known thyroid-type carcinomas have been described in struma ovarii, some of which may cause differential diagnostic difficulties with ovarian tumors such as granulose cell tumour or carcinoid [9].
Initial criteria for pathologic diagnosis were proposed by Geist and Smith in the 1940s [10, 11]. Cellular atypia, vascular invasion and metastases were the crux of the diagnosis. In 1983, Pardo-Mindan et al. supposed that struma ovarii is malignant only if the tumour clearly shows invasiveness and/or metastasis and if there is no evidence of primary carcinoma of the thyroid, and if it presents a follicular and/or papillary histology with positive thyroglobulin [9].
The criteria for diagnosis of malignancy were reviewed in 1993 by Devaney et al. [12] and the features for papillary thyroid carcinoma in struma ovarii are similar to those seen in the thyroid – ground-glass-like overlapping nuclei, nuclear grooves and inclusions, mitotic activity, vascular invasion and papillary architecture. Presence of papillary architecture only or a closely packed follicular pattern only in the absence of typical nuclear characteristics were designated as categories of proliferative struma [12]. Lesions with nuclear features of papillary thyroid carcinoma but lacking papillary architecture represent a follicular variant of papillary thyroid carcinoma.
Immunohistochemical markers such as cytokeratin 19, HBME-1 and galectin 3 have been suggested to help in the distinction between benign thyroid tissue and papillary thyroid carcinoma [13, 14].
Treatment in malignant struma ovarii needs to be individualized, as presently there are no consensus guidelines. The standard treatment of a patient with thyroid carcinoma in struma ovarii is surgery, with a total abdominal hysterectomy, bilateral salpingo oophorectomy and com-

plete surgical staging, including peritoneal washings for cytology, pelvic and para-aortic lymph node sampling, and omentectomy [15, 16].

In women who wish to preserve fertility and with the tumour confined to one ovary, unilateral oophorectomy may be considered.

Metastases from malignant struma ovarii have been documented in the literature but are rare (5–6% of malignant struma ovarii cases) [17, 18]. The tumour can spread via regional lymphatics to pelvic and para-aortic lymph nodes, by direct spread to the omentum, the peritoneal cavity, the contralateral ovary and by haematological dissemination to the bone, lung, liver and brain [19–21].

There is no consensus on the postoperative management of malignant struma ovarii patients. When there is residual malignant disease after surgery, some authors practice total thyroidectomy and recommend radio-ablation therapy with I131 in order to prevent local and distant recurrence [15, 16]. Chemotherapy, external beam RT and thyroid suppression have been used in order to treat recurrent or metastatic disease.

If histology shows a malignant struma ovarii, a risk stratification similar to that used in thyroid carcinoma should be performed. Yassa et al. suggested that small focus of thyroid carcinoma confined to the struma ovarii measuring less than 20 mm with no worrisome histologic features should be considered as low risk [16]. Patients with larger carcinomas, disease extension outside the struma ovarii, or aggressive histological variants are considered as high risk [16]. In such cases, total thyroidectomy and radio-ablation are required [15]. This would allow both serum thyroglobulin monitoring and radioactive iodine treatment of recurrent disease [13].

The prognosis of thyroid carcinoma in struma ovarii is difficult to estimate because of its rarity and lack of treatment guidelines. A review of 88 cases of malignant struma ovarii showed that the tumour is associated with long survival (25-year survival 84%) and that histologic or clinical feature are not accurate predictors of biological malignancy, although fibrous adherences and larger stromal size, especially >12 cm, are suggestive of tumours that will have spread at the time of operation or are likely to recur [22].

Long-term follow up for the detection of metastases or recurrence disease by serial serum thyroglobulin and I131 or PET/CT or a combination of these tests or interventions may be considered in patients with malignant struma ovarii.

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