Malignant Struma Ovarii: Case Report and a Review of the Literature.

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Abstract
Struma ovarii is a rare tumor. Malignant change in this tumour is even rarer. While clinical presentation is protean, a preoperative diagnosis is equally difficult. Diagnosis is confirmed by histology. Treatment of malignant struma ovarii is by surgical resection of the tumor or total abdominal hysterectomy and bilateral salpingo-oophorectomy. A total thyroidectomy allows radioactive iodine ablation and the use of thyroglobulin as marker to monitor recurrence. However due to rarity of the disease, standard treatment is still controversial. We present a case of malignant struma ovarii, followed up for five years after treatment, and a review of the literature on the disease. *The patient was treated with surgery and radiation. She is still free of disease after 5 years.*
Key Words: Malignant Struma Ovarii, Ovarian Teratoma, Papillary Thyroid Carcinoma

Introduction
Struma ovarii is a rare tumor, accounting for approximately 1% of all ovarian tumors [1]. It is a monodermal variant of ovarian teratomas in which thyroid tissue is the major constituent (>50%) [2, 3]. Struma ovarii constitutes only 2.7 % of mature cystic teratomas[4]. Malignant struma ovarii is even much rarer, being seen in just about or less than 5% of struma ovarii [5,6].

Clinical Case
We present a 44year old Para $2+^{0}$ female who was first seen at an Indian hospital about June 2005 when she presented with a history of worsening lower abdominal pains. The pain was not relieved by analgesics. There was no known precipitating or aggravating factor. There was no unusual vaginal bleeding or discharge. Her last confinement was 26 years prior to presentation. There was no past or current use of intrauterine contraceptive devices. Her menstrual cycle had been fairly regular. She was not a known peptic ulcer patient.

Ultrasonography of the abdomen showed a left adnexal mass measuring 37mm x 35mm in the transverse plane. The mass was anechoic and had posterior acoustic enhancement. The uterus and contralateral ovary were essentially normal but minimal fluid was seen in the pouch of Douglas. An impression of a functional left ovarian cyst was made with a request for clinical correlation.

Progression of patient's symptoms led to a laparatomy. Operative findings showed normal sized right ovary with small cysts which contained serous fluid. The left ovary was enlarged, had multilocular cysts containing sebaceous materials, hair and serous fluid. The uterus was grossly unremarkable.

A total abdominal hysterectomy (TAH) with bilateral salpingo-oophorectomy (BSO) was carried out. The histopathology revealed that the left ovary had features of mature cystic teratoma with malignant transformation in thyroid tissue consistent with papillary thyroid carcinoma. Post operatively, serum alpha fetoprotein level was 7ng/ml, CA-125 was 2U/ml, â HCG was <0.05mIU/ml.

CT scan of the abdomen scan as well as thyroid ultrasound scan done two months post operatively were normal. A base line thyroid function test showed T3 (1.7µg/dl), T4 (9.5µg/dl), TSH (5.3µIU/ml). This was followed by a pertechnetate (TcO4) thyroid uptake test, which showed uniform uptake in both thyroid lobes. No abnormal extra-thyroidal uptake was seen. A near total thyroidectomy (NTT) was

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carried out in November 2005. Histology of the thyroid specimen showed no evidence of malignancy in the sections examined and patient was discharged on thyroxin replacement and referred for remnant ablation.

In July 2006, an ablative dose of 100 mCi ^{131}I was administered. Post therapy scan showed only remnant uptake in the thyroid bed and patient was discharged on thyroxine replacement. A stimulated diagnostic ^{131}I scan was done later and it confirmed the success of the ablation. She is being followed up with yearly clinical reviews including physical examinations, thyroid function tests, thyroglobulin (Tg) and anti thyroglobulin antibody (ATA) assays and has so far been disease free. Her last thyroid function tests (done in March 2010) recorded undetectable thyroglobulin levels and TSH was 2.0µIU/l.

Discussion

Struma ovarii was described by Von Kalden in 1895, and Gottschalk and Mayer in 1903. (7, 8) The incidence of malignant struma ovarii is said to be only 5% of all struma ovarii cases. Thyroid element can be noted in almost 20% of ovarian teratomas, however, the term 'struma' is used when the thyroid tissue constitutes more than 50% of the tumor (5, 6). Even though it is a neoplasm consisting of thyroid tissue, only 8% of patients with struma ovarii present with clinical hyperthyroidism (9). This low incidence is reflected in this patient who showed no clinical or laboratory features of hyperthyroidism.

Clinical symptoms that may manifest due to the presence of struma ovarii are lower abdominal pains, palpable lower abdominal mass, abnormal vaginal bleeding, ascites, hydrothorax and rarely, thyroid tumors (10, 11). In a series Yoo and co-workers (12) found 14 out of 34 patients had no symptoms at all.

Ultrasound cannot specifically identify struma ovarii; however one must consider this diagnosis especially in solid looking teratomas. Preoperative diagnosis of struma ovarii is only possible in patients with hyperthyroidism by measurement of serum TSH in combination with ^{123}I scintigraphy. (13) Although no preoperative ^{123}I scan was done in this patient, the diagnostic dilemma was worsened because the trans-abdominal ultrasound scan failed to detect the solid component of the cyst. From our experience, barring the limitations from very large ovarian tumors, trans-vaginal scans whenever possible usually provide images with sufficient and better resolution to improve the differential diagnosis of ovarian masses. However, at best ultrasound picture in struma ovarii is not much different from a mature cystic teratoma. (14)

There is no universal therapy for malignant struma ovarii throughout literature. Surgery varies from laparoscopic unilateral oophorectomy to total abdominal hysterectomy with bilateral salpingo- oophorectomy (TAH+ BSO) with omentectomy.

Devany (13) and co-workers have urged the use of the same histological criteria to diagnose malignant struma ovarii as that used for tumors in the thyroid. Others maintain the histologic criteria for malignancy may be different from those of thyroid carcinoma, invasive growth being difficult to appreciate and papillary formations may not be conclusive. The diagnosis may rely on the presence of cellular atypia (15, 16). This however seemed not to be the case in our patient where typical features papillary

Table 1: Comparative Findings in the Literature* versus those seen in the Patient.

Features*		Index Patient
Age distribution in years (n=34)	21-80	44 years
Patients aged 41-50 (n=34)	26.6%	Yes
Palpable abdominal mass (n=34)	23.5%	No
Abdominal Pain (n=34)	20.6%	Yes
Vaginal Bleeding (n=34)	8.8%	No
Increased CA125 (n-13)	30.8%	No
Benign cyst at US scan (n=34)	8.8%	Yes

**Yoo et al [12]*

carcinoma allowed a confident diagnosis.

There was no apparent metastasis in our patient as evidenced by negative extra thyroidal bed uptake after the therapeutic ^{131}I whole body scan (WBS) and undetected thyroglobulin levels till date. Indeed metastatic struma ovarii is rare, and so are aggressive histologic variants like mixed adenocarcinoma, Hurtle cells and anaplastic carcinoma though they have been described (17). Contributory to the absence of metastasis in this patient also include the early diagnosis and aggressive intervention (surgical and radioiodine ablation and a follow up TSH suppression).

Total thyroidectomy following surgical removal of the ovarian lesion allows the exclusion of primary thyroid carcinoma with metastasis to the ovary and in addition, allows radioiodine (^{131}I) for the treatment of micro-metastasis. After total thyroidectomy, thyroglobulin can be used as a tumor marker for follow up (18). The presence of a primary thyroid carcinoma must be excluded. (19)

Management of patients who desire fertility might be challenging. (9) Another challenge sometimes encountered fact is a patient's refusal to accept thyroidectomy, as shown by Yücesoy et al (20). Patients treated without thyroidectomy with survival rates of 12- 180 months have been reported. (21) In struma ovarii, peritoneal fluid levels of thyroglobulin might indicate an intra-abdominal extension or recurrence. Follow up by means of this marker obviates the need for repeated ^{131}I scanning and the unpleasant hypothyroid symptoms inherent to the interruption of thyroid substitution. (22) Except for the diagnostic scan to confirm ablation, we did not have cause to repeat a ^{131}I WBS in the 5 years of following up this patient. The thyroid function tests, serum thyroglobulin and anti thyroglobulin antibody (ATA) assays have so far remained excellent indices to monitor recurrence.

The widely accepted tumor marker of ovarian cancers CA-125 is found to be increased in 80% of epithelial ovarian carcinomas. This marker is also elevated in other tumorous lesions of the endometrium, intestines, breasts, and lungs as well as in non malignant related gynecologic conditions, thus indicating that there is a limit to the clinical application of CA-125 as a tumor marker of ovarian neoplasms. Moreover, it has been postulated that increased levels of CA-125 is not a direct consequence of the presence of malignant tumor, but rather a secondary effect due the presence of ascites. (23)

In the case series by Yoo et al (12), it was observed that CA-125 was increased in 4 among 13 patients with struma ovarii (3 malignant and 10 benign). This comprised of 1 out of the 3 malignant cases and 3 of the 10 benign cases. The elevation in the malignant case was minimal. This, coupled with the presence of elevations in benign struma ovarii cases caused them to propose that serum CA-125 measurements are of little clinical value in struma ovarii patients. In the case we report the patient had no ascites and the CA-125 level was normal.

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