Poorly Differentiated Thyroid Carcinoma Arising in Struma Ovarii: Case Report and Review of the Literature

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ABSTRACT

An 81-year-old woman presented with a pelvic mass. The computed tomography scan showed a non-calcified solid cystic mass, 10.4x11.5x6.7 centimeters. She underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy and ascitic fluid for cytology. Histopathology reported poorly differentiated thyroid carcinoma arising in struma ovarii. Currently she has been free of disease for 5 months from the date of diagnosis.

Keywords: Poorly differentiated thyroid carcinoma, struma ovarii

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INTRODUCTION

Struma ovarii was first described by Bottlin in 1888 and later by Pick in 1902[1]. Although thyroid tissue can be detected in approximately 15% of cases of mature teratoma, the latest World Health Organization classification remarks that the struma ovarii must contain at least 50% of thyroid tissue. Therefore, struma ovarii is diagnosed in only 2.7% of ovarian teratomas[2]. Malignant transformation occurs in approximately 5-10% of these tumors with papillary carcinoma and follicular carcinoma being the most common[1]. The diagnosis of thyroid carcinoma arising in struma ovarii should be based on the similar criteria of primary thyroid gland disease. Due to the rare nature of this condition, no consensus exists on the surgical and post-surgical treatment of patients with thyroid carcinoma arising in struma ovarii. We report a rare case of poorly differentiated thyroid carcinoma arising in struma ovarii and review the literature on the general agreement for diagnosis and treatment of these cancers.

CASE REPORT

An 81-year-old, Thai woman presented with a large pelvic mass and an intermittent dull pain in her pelvis for one month. Her past medical history included well-controlled hypertension and dyslipidemia. She had no family history of ovarian and endocrine tumors. The pelvic examination and the computed tomography (CT) scan showed a non-calcified solid- cystic mass, 10.4x11.5 x6.7 centimeters, arising possibly from the right ovary (Fig 1). A small well-defined thin wall cyst of

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left ovary, 2.7x1.8 centimeters, was also noted. There was no ascitic fluid, organomegaly and intra-abdominal lymphadenopathy. The tumor markers including cancer antigen (CA) 125 and CA 19-9 were unremarkable (CA125= 38.38 U/mL, CA19-9=27.75 U/mL). Her gynecologic operation was postponed for 3 months because of cerebral infarction. She had a right carotid bulb with severe luminal stenosis and calcified plaque which extended to the right internal carotid artery. She underwent right carotid endarterectomy which was uneventful. Her abdominal pain was not worse and the follow-up of ultrasonography showed the same findings as Fig 2.

Finally, the patient underwent a total abdominal hysterectomy (TAH) with bilateral salpingo-oophorectomy (BSO), omentectomy and ascitic fluid for cytology. There was 1,600 mL of straw colored ascitic fluid. Her right ovary had become a solid-cystic mass. There was a ruptured site on its external surface. Her uterus and left ovary were unremarkable. The tumor was totally removed. The pathologic report revealed poorly differentiated thyroid carcinoma arising in struma ovarii. The ascitic fluid for cytology showed some atypical cells.

Gross pathology

The size of right ovarian mass was 10x8.5x7 centimeters. Its external surface was smooth and glistening with focal nodular area (Fig 3A). Cut surfaces showed non-homogeneous solid-cystic lesion. The solid component was brown-tan, and gelatinous appearance with multiple foci of hemorrhage and necrosis and it occupied approximately 70% of the total mass (Fig 3B, 3C). The inner cystic surface was smooth and glistening without papillary growth. Few small foci of solid gray-white nodules (varing from 1 to 2.5 centimeters) were identified (Fig 3D).

Histopathology

The tumor was composed of mature thyroid tissue which was varying in size of thyroid follicles and containing colloid material. Thyroglobulin and TTF-1 immunohistochemistry were identified in the epithelial cell. In areas corresponding to solid gray-white nodule, the section demonstrated a well-defined solid nest of tumor cells surrounded by thin fibrovascular septa (insular histologic pattern) (Fig 4A). Tumor cells were uniform and contained round vesicular nuclei with indistinct nucleoli, mitotic figure presented approximately

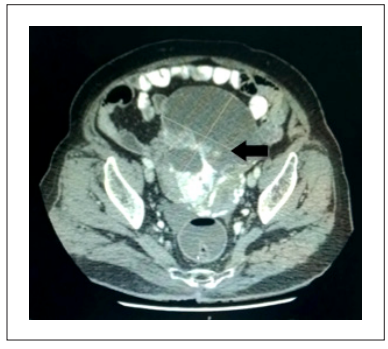

Fig 1. CT imaging showed a non-calcified solid-cystic mass in pelvic cavity (arrow).

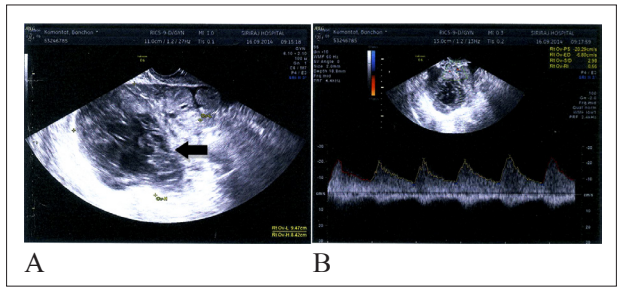

Fig 2. A: Ultrasonography revealed the same size of solid cystic mass (arrow).
B: Doppler ultrasonography showed a low vascular flow (RI=0.66).

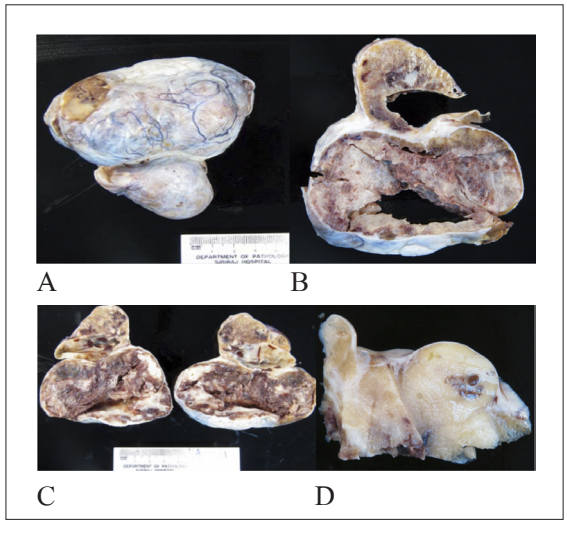

Fig 3. A, B and C, Gross photography of the specimen showing non-homogeneous solid-cystic lesion with brown tan gelatinous appearance, hemorrhage and necrosis. D, A focus of solid gray with nodule.

8/10 HPF (Fig 4B), and obvious vascular invasion and necrosis was present (Fig 4C, 4D). Immunohistochemistry demonstrated that these tumor cells were diffusely strongly reactive with TTF-1, Thyroglobulin and CK7, but they did not mark with CK20, CDX-2, Calcitonin, Synaptophysin, Chromogranin A, Galectin3, CK19, or HBME1. Based on these findings together with Turin proposal this tumor was fulfilling the criteria diagnostic of poorly differentiated thyroid carcinoma arising in struma ovaii.

The consulting Head-Neck surgeon and radiotherapist agreed to treat this patient as a thyroid carcinoma rather than ovarian cancer. Her thyroid function test was normal. Imaging scan revealed no residual tumor. Therefore, we decided to treat her with thyroxine therapy. Currently she has been free of disease for 5 months from the diagnosis.

DISCUSSION

Thyroid carcinoma arising in struma ovarii is a rare disease. The age of presentation is usually from the 5th to 6th decade of life[3]. The symptoms and signs include a pelvic mass (45%), abdominal pain (40%), ascites (17%) in which the fluid rarely contained tumor cells, menstrual irregularities (9%), hyperthyroidism (5-8%) and deep vein thrombosis (4%). CA125 may be elevated as found in germ cell tumors. The diagnosis is usually made post-operatively. There are no imaging specific characteristics for this tumor[4]. Ultrasonography usually shows a heterogeneous solid-cystic mass. The Doppler imaging reveals abundant low resistance blood flow within the highly vascular central portion of the tumor. CT imaging depicts a multiloculated cystic mass with different densities among the locules and solid portion. Calcification may be found. Magnetic resonance imaging finds multiloculated cystic mass with variable signal intensity (stained glass appearance) and solid component.

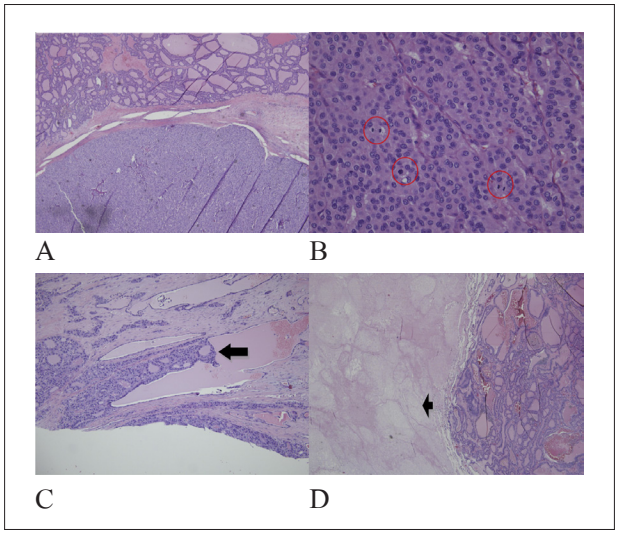

Fig 4. A, Histologic section showed both classic struma ovarii and a well-defined solid nest of tumor cells surrounded by thin fibrovascular septa (insular histologic pattern). B, Insular histologic growth pattern with frequent mitotic figure (circle). C, Obvious vascular invasion (arrow). D, Tumor necrosis (arrow head).

Primary thyroid carcinoma with ovarian metastasis can be differentiated by clinical examination and thyroid ultrasonography. In the case of bilateral ovarian masses without teratomatous features, these favor ovarian metastasis. The other differential diagnosis of malignancy arising in struma ovarii includes strumal carcinoid, Brenner tumor, granulosa cell tumor and papillary serous cystadenoma or cystadenocarcinoma[5]. The immunohistochemistry, such as thyroglobulin TTF-1 inhibin WT1 and CA 125, will aid to differentiate these tumors.

Devaney et al,[6] proposed that the pathologic diagnosis of thyroid carcinoma arising in struma ovarii should adhere to the same criteria used for primary thyroid cancer. These include papillary carcinoma, follicular carcinoma, poorly differentiated carcinoma and undifferentiated (anaplastic) carcinoma. Papillary carcinoma is the most common form (44%), followed by follicular carcinoma (30%) and follicular variant of papillary carcinoma (26%). Recently, Roth et al,[7] described an extraovarian dissemination of thyroid elements and histological resemblance to non-neoplastic thyroid tissue as highly differentiated follicular carcinoma of ovarian origin (HDFCO). It has a very good prognosis.

Treatment and management of thyroid carcinoma arising in struma ovarii

The paucity of published data makes it difficult to find the best treatment modality for

these tumors. For women who wish to preserve fertility, conservative surgery (unilateral oophorectomy) should be considered if there is a unilateral tumor without evidence of capsular invasion or gross metastasis. In the case presenting with gross metastasis, capsular invasion or an intraoperative frozen section confirming thyroid carcinoma arising in struma ovarii should have complete surgical staging for ovarian cancer[2].

DeSimone et al,[8] studied the postoperative management for patients with malignant struma ovarii. In his review of 24 cases, there were 8 recurrences and all occurred in the patients without postoperative treatment. Hence, they suggested that treatment with thyroidectomy and Iodine 131 (I^{131}) should be considered as the first line of management.

Yassa et al,[9] classified the patients according to the risk stratification. In low risk patients with thyroid carcinoma of less than 2 centimeters in size, no worrisome histologic features and pelvic imaging studies showed no evidence of extraovarian disease should receive thyroxine therapy to suppress thyroid stimulating hormone secretion and periodic total body scintiscanning with I^{131} and serum thyroglobulin. Patients with serum thyroglobulin over 10 ng/mL are more likely to have recurrence, based on primary thyroid carcinoma[10]. I^{131} diagnostic whole body scanning is recommended. Conversely, patients with more than 2 centimeters in size of thyroid carcinoma, aggressive histologic characters or extraovarian disease should be considered as high risk group. Near-total thyroidectomy with radioactive iodine therapy is recommended.

Makani et al,[2] reported an average of 4 years for detection of recurrence. They recommended at least 10 years for follow-up. I^{131} radioablation, external beam radiotherapy, chemotherapy and thyroid suppression therapy have been used for treatment of recurrent or metastatic disease[2,5].

In our case, the diagnosis of poorly differentiated thyroid carcinoma was based on the Turin proposal for the use of uniform diagnostic criteria[11]. These include (1) presence of a solid/trabecular/insular pattern of growth, (2) absence of the conventional nuclear features of papillary carcinoma and (3) presence of at least one of the following features: convoluted nuclei, mitotic activity $\geq$ 3/10 high power fields (HPF) and tumor necrosis. In primary thyroid carcinoma, the behavior of poorly differentiated carcinoma lies between well differentiated and undifferentiated carcinoma. Table 1 showed the clinical course of 7 patients with poorly differentiated thyroid carcinoma arising in struma ovarii. Because of the small number of patients and variety of surgeries and post-operative treatments, there is currently no agreement for treatment of these patients. Robboy et al,[12] found that there was no correlation between histologic morphology and clinical features. Even when clinically malignant, the patient is often associated with long survival as evidenced by 89% 10-year and 84% 25-year survival. Since our patient had a recent stroke, we decided to

TABLE 1. Cases of poorly differentiated thyroid carcinoma arising in struma ovarii.

Reference	Age, yrs	stage	Treatment of extraovarian disease	Follow-up
Werth[13], 1928	36	III	Radiation	AW 6 months
Gonzalez-Angulo[14], 1963	60	I	None	NA
Zakhem[15], 1990	52	IA	NA	NED 1.7 yrs
Zakhem[15], 1990	30	IA	NA	NED 2.7 yrs
Roth[16], 2008	70	II	Chemo, RAI	DOD 3 yrs
Garg[17], 2009	40	IA	None	NED 1.1 yrs
Garg[17], 2009	47	IA	None	NED 5 yrs

AW, alive and well; DOD, dead of disease; NA, not available; NED, no evidence of disease; RAI, radioactive iodine therapy following thyroidectomy

postpone the operation for 3 months and undergo the shortest time for surgery to remove the tumor (TAH, BSO, omentectomy and ascitic fluid for cytology). In the multidisciplinary meeting, it was decided that because there was no residual tumor postoperatively, her associated disease was quite severe and she is 81 years old, the patient should be followed up with thyroxine therapy.

In conclusion, based on case series and case report, treatment modalities of thyroid carcinoma arising in struma ovarii depend on the stage of disease and the risk stratification. Limitation for the recommendation of treatment was founddue to the rarity of the disease. A prospective trial is not likely feasible.

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