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Case Report

Recurrent Thyrotoxicosis of Extrathyroidal Origin due to Struma Ovarii: A Case Report and Review

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Abstract

Struma ovarii (SO) is a recognized, albeit infrequent, cause of ectopic thyroid hormone secretion. Due to its rarity, only a few cases had been reported with fairly detailed information on thyroid function test (TFT) results. Furthermore, data are limited in the extent of local spread, surgical approach, and postoperative management. A 41-year-old woman from Libya presented with tremor, nervousness, weight loss, heat intolerance, and palpitation. She had also complained of lower abdominal pain and delayed periods. Two years earlier, she was diagnosed with hyperthyroidism, treated with a 12-month course of antithyroid medications resulting in full resolution of symptoms. Her TFTs revealed elevated serum triiodothyronine, thyroxine (T4), free T4, and low thyroid-stimulating hormone (TSH). Pelvic ultrasonography showed a left ovarian cystic mass and a suspicious of ectopic pregnancy was suggested. Abdominal surgical exploration with left salpingo-oophorectomy was performed. Gross and microscopic examinations confirmed the diagnosis of SO. Four weeks later, TFTs were repeated and revealed a high level of serum TSH, and low total T4 and free T4 levels. L-thyroxine replacement was started. In conclusion, Determination of the cause of thyrotoxicosis is essential for proper management. If clinical data and initial investigations are not consistent with common causes of hyperthyroidism, whole-body radioactive iodine scan should be considered. The definitive treatment for patients with SO is surgical resection via laparoscopic approach.

Keywords: Atypical hyperthyroidism, pelvic mass, struma ovarii

Introduction

Struma ovarii (SO) is a rare type of germ cell derived ovarian neoplasm, mainly a cystic teratoma.[1] It was first described by R Boettlin in 1889 followed by Von Klden in 1895 and Gottschalk in 1899.[2-4] Probably, it is the most common type of monodermal teratoma[2,5-7] and comprises 2.7% of all ovarian dermoid tumors.[8] The pathological examination reveals that the tumor is composed of predominately matures thyroid tissue[4] that comprised over 50% of the total mass tissue[2] or forms a macroscopically recognizable aspect of mature cystic teratoma that is identical to cervical thyroid gland microscopic morphology and biology.[5] In a total of 500 cases reported, hyperthyroidism was found in about 5%–15% of cases.[4,9]

Atypical forms of hyperthyroidism represent a diagnostic and management challenge to the treating physicians and may cause delays in management.[1] We report a rare case of recurrent hyperthyroidism resulting from SO and complicated possibly permanent hypothyroidism. A concise review of the relevant literature is presented.

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Case Report

A 41-year-old married Libyan woman presented in 2011 with tremor, nervousness, weight loss, heat intolerance, and palpitation. Hyperthyroidism was confirmed biochemically, and she received antithyroid drugs for 1 year. Two years later, she had symptoms suggestive of recurrent thyrotoxicosis (namely tremor, nervousness, weight loss, heat intolerance, and the palpitation) together with abdominal pain and delayed period. Thyroid function test (TFT) revealed high serum triiodothyronine (T3) and serum thyroxine (T4) with low serum TSH level (TSH 0.01 μIU/ml [0.5–4.2], serum T3, 147 ng/dL [70–130 ng/dL], T4, 17 μg/dl [normal, 6.5–12 μg/dL], free T4, 2.9 ng/dL [0.7–1.8]). Pelvic US scan showed a left ovarian cystic mass with suspicion of ectopic pregnancy. The

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patient underwent urgent abdominal surgical exploration with left salpingo-oophorectomy. Gross pathology demonstrated a multilocular soft tissue cyst of 8 cm × 6 cm × 3 cm in size with Fallopian tube on the surface of 6 cm in length. Microscopic examination detected features of mature thyroid tissue with colloidal material and no evidence of malignancy. The Fallopian tube showed no pathological changes. Symptoms of hyperthyroidism subsided, and 4 weeks later, high levels of TSH and low levels of total T4 were evident. Replacement therapy with Levothyroxine was initiated.

Discussion and Mini-review

Pathology

SO is an infrequent ovarian teratoma, comprises 0.3%–1% of all ovarian tumors and 2%–5% of all ovarian teratomas.[1-4,10] The majority is benign, about 90%–95%; however, malignant SO was reported in a few cases.[11] The benign lesions are histologically identical to that of normal thyroid tissue. Although no uniform criteria exist for diagnosis of malignant SO, pathologists rely on the presence of histologic features such as cellularity, cellular atypia, and hyperplasia, mitotic activity,[3,8,10] and also vascular or ovarian capsule invasion. The pathological criteria for the diagnosis of thyroid carcinomas are currently used as the standard for malignant SO diagnosis.[9,12] Therefore, histologic criteria are typical for either papillary thyroid cancer (commonest type) or follicular pattern or follicular variant of papillary carcinoma.[9,13] Immunohistochemical staining for thyroglobulin (Tg), T3, and T4 could confirm the diagnosis. Although several authors reported hyperthyroidism caused by SO,[3,4] the mechanisms underlying hyperthyroidism are still generally unknown. Coexisting Graves' disease is rare in the literature.[14,15] Serum thyroid-stimulating immunoglobulins (TSHR-Ab) were expected to stimulate thyroid tissue function in each, the ovary and within the neck. Moreover, cases associated with thyrotoxicosis could be as a result of autoimmune stimulation of the normal thyroid gland. Moreover, malignant SO reported to produce hyperthyroidism,[16] nevertheless, no reports concerning hypothyroidism incidence following SO resection.

SO occurs more frequently in premenopausal females. Its incidence peaks at age of 50 years.[16] The clinical features of SO were obtained mainly from retrospective case reports and small case series.[2,9] The symptoms are a quite nonspecific and mimic other ovarian tumors.[6] Most of patients are asymptomatic, and almost always incidentally discovered during pelvic imaging or unexpectedly after a resection of pelvic mass.[11,14] In one series, 14 patients (41.2%) had no precise symptoms, in whom the ovarian mass was discovered incidentally in ultrasonographic (USG) studies.[2] The patient could present with torsion cyst, lower abdominal pain, and less frequently with ascites;[2,16] ascites reported in about one-third of the cases.[2] It would possibly associate with hydrothorax, the pseudo-Meigs' syndrome. Moreover, patient uncommonly presented with clinical features of hyperthyroidism that occur in 5%–8% of cases,[2,10,16] typically associated with low uptake in RAI scan as shown in Table1 or the hyperthyroidism may be subclinical. In USG, a heterogeneous, predominantly solid mass with multiple cystic lesion may even be obvious. Moreover, a contrast CT scan of the abdomen and pelvis also indicated, to assess the extent of disease and the lymph nodes. It appears as a multicystic ovarian mass with or without some enhancement of the cystic wall.[17] Positron emission tomography might even require in selected cases. Magnetic resonance imaging scan typically appears as a multilocular cystic mass with variable signal intensity on T1- and T2-weighted images. In suspected cases of struma, preoperative whole-body radioactive iodine (RAI) scan requested to assess thyroid RAI 123u within the pelvis. However, there was no or minimal RAI-uptake within thyroid in the neck. Consequently, RAI scans confirmed that SO was bilateral in 5%–10% of patients.[4] The diagnosis necessitates confirmation by the HP finding of the resected ovarian tissues.[17] Serum CA-125 level rise was reported in each benign and malignant lesions[18] also high in other tumor of the intestine, endometrium, breast and lung, and nonmalignant gynecologic diseases. Moreover, high serum Tg level, similarly, secreted by each benign and malignant tumors.[8]

Table 1: Classification of thyrotoxicosis on the basis of radioactive iodine uptake (high versus low)

Thyrotoxicosis with high 24-h RAI uptake	Thyrotoxicosis with low 24-h RAI uptake
Graves' disease	Factitious hyperthyroidism
Multinodular goiter	Subacute thyroiditis
Toxic adenoma	Ectopic secretion of thyroid hormones
	Iodine-induced hyperthyroidism
	Deposits of functioning thyroid cancer metastases

RAI: Radioactive iodine

Management

Initially, treatment with antithyroid drugs for thyrotoxic patients before surgery,[4] also, the iopanoic acid can be used if rapid preoperative preparation is needed.[14] For benign SO, resection of the mass is usually adequate.[2,5-7,13] It allows the histopathological diagnosis and to rule out ovarian malignancy.[2,5-7] Due to its rarity, there is a paucity of evidence in the literature to guide the optimal management for malignant SO. Moreover, there is a controversy regarding whether radical or conservative surgery should be practiced. Consequently, limited evidence exists concerning conservative surgeries (unilateral salpingo-oophorectomy) for patient's desired future fertility, in cases with no capsular or vascular invasion or metastasis, with a strict follow-up.[13] Moreover, in advanced or disseminated malignant SO, patients who are not looking for future fertility, necessitates an approach to ovarian malignancy surgical staging. Radical surgery, namely a total abdominal hysterectomy with bilateral salpingo-oophorectomy, with intraoperative diagnosis by frozen section sampling, staging (e.g., peritoneal washing, omental biopsy, appendectomy, lymph node sampling, and

macroscopic survey of intra-abdominal organs).[13,19] Many authors favored this multimodal approach management, to decrease the recurrence chance and overall survival improvement.[16,17] However, if an intraoperative frozen section indicated no malignancy with staging procedures, thus resulted in conversion to more conservative surgeries.[19] Furthermore, some authors recommended a total abdominal hysterectomy and contralateral salpingo-oophorectomy in a malignant SO patient who operated initially for a fertility sparing approach after complete childbearing or no more potential or desire for fertility.[8,10] Ultimately, a total thyroidectomy recommends poststaging completion, to enhance the effects of RAI-131 ablation therapy and to certain delivery to the malignant cells (as the normal cells of thyroid preferentially uptake also confirm that the struma is definitely ovarian in origin).[13] Conjointly facilitate detection of recurrence or metastases throughout follow-up.[16,17] In addition, as the investigators recommend, exclusion of the primary thyroid cancer is a must.[10,11]

A study by DeSimone *et al*., what is more, supports the conservative surgery consideration for malignant SO patients who had a desire for fertility.[16] This is in agreement with Ayhan *et al*., who suggested that fertility-conserving approach for patients with benign SO, and radical operation for patients with malignant SO and not desire future fertility.[3,19] Due to the lack of the experience concerning adjuvant RAI131 ablation therapy in malignant SO, it remains controversial. Therefore, the results addicted to the individual case and treating team.[16,20] Although some authors recommended the employment of adjuvant RI therapy to lower the recurrence rate.[16] Along with Levothyroxine suppression therapy, each in its initial presentation of malignant SO or any subsequent recurrence with favorable outcomes and efficacy.[13] Effective laparoscopic surgery recently delineated,[20,19] and therefore the resection of large ovarian cysts via laparoscopy is currently technically possible and established an approach.[15,21,22] Consequently, a clear trend of increasing publicity of the laparoscopic approach.[19] It is evident that with the laparoscopic procedure, patients, none suffer any intraoperative complications, and nor needed conversion to laparotomy. Moreover, less hospital admission duration and low morbidity, fewer investigations postoperative unless symptomatic patients, no recurrence noted as compared to laparotomy throughout follow-up. Furthermore, postoperative complications (including infection, wound inflammation, and subsequent incisional hernia) might discover in patients who underwent laparotomy surgery.[19] Identical to a result of a review done by Medeiros *et al*. that studied the disadvantages and advantage of laparoscopy and laparotomy for benign ovarian tumors.[23] There is disquiet that the resection of a probably malignant ovarian mass through laparoscopy might decrease the staging accuracy and increase the port site metastasis prospect and spill in the abdominal cavity. Nevertheless, Ezon *et al*.[15] concluded that using laparoscopy was not associated with port site metastasis and spillage content of the tumor during surgery did not negatively effect on disease-free or overall patient survival. Postoperative TFT was to ascertain the thyroid function status as previous reports suggested that hypothyroidism requiring replacement therapy may occur after SO resection. However, some workers reserve TFT monitoring for symptomatic patients only.[19]

Postoperative follow-up

Usual surgical follow-up is enough for patients with a benign SO. However, patients with malignant disease, postoperative adjuvant RAI-131 ablation therapy in its initial presentation, and any recurrence emphasized with excellent effect.[2,17] Moreover, follow-up by the serum Tg level, consecutively after surgery and ablation, which is the preferred tumor marker,[13] (especially following fertility-sparing unilateral salpingo-oophorectomy). Providing that, the progressive serum Tg level elevation, usually followed by whole body RAI scan to detect the presence of recurrence or metastases.[10] Recombinant human TSH is used to enhance RAI-131 uptake for treatment and scan.

Prognosis

The majority of the SO are benign, whereas malignant change appears to occur in about a third of cases.[12] Even more, SO is of low metastatic capabilities and low malignancy,[3,7,16,19] metastasis occurring in approximately 5% of malignant cases.[11,12] The spread may occur in the peritoneum, liver,[11,24] mesentery, and omentum, and hematogenous spread may involve the contralateral ovary, bone, brain, mediastinum, or lung.[24]

The prognosis is excellent.[25] Even in malignant cases, postoperative RI-131 ablation therapy has proven curative. Furthermore, recurrences detected by RI-123 scan and repeat RAI ablation therapy[2] will result in extended disease-free survival. Moreover, the recurrence of the malignant SO in patients who underwent surgical resection without subsequent RAI therapy is as high as 50%.[16]

Conclusions

SO cases are difficult to diagnose by clinical features or imaging studies only. However, the final diagnosis was confirmed by histopathological findings. Surgical resection remains the definitive management for benign SO. However, surgery with adjuvant RI therapy achieves success in treating metastatic and recurrent disease. In addition, laparoscopic surgery has been suggested as an option, most of the patients recovered without complications.

Authors' contribution

The authors are responsible for the conduct of the study, data collection, and analysis. They drafted and revised the manuscript and approved its final version.

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Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

The patient provided verbal consent for her case to be published. No formal IRB approval for single "anonymous" case reports are required in our institutions.

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