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Original Article

Ultrasound imaging and clinical pathologic analysis of ovarian strumal carcinoid

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Abstract: This study describes the ultrasound appearances and pathologic characteristics of ovarian strumal carcinoid. Twenty-one patients with ovarian strumal carcinoid, underwent ultrasound and histopathologic examinations and their demographic and clinical characteristics were recorded. A pelvic mass typical of other ovarian tumors was seen on ultrasound, but microscopy revealed proliferating follicular thyroid and carcinoid cells. Via immunohistochemical analysis, carcinoid components stained positively for synuclein, chromogranin A, and thyroid transcription factor-1. In summary, ovarian strumal carcinoid is a rare intermediate germ cell tumor with highly specific clinicopathologic characteristics. Its diagnosis is determined by histopathologic features and immunohistochemical phenotype.

Keywords: Ovarian strumal carcinoid, immunohistochemistry, prognosis

Introduction

Ovarian strumal carcinoid is an extremely rare ovarian tumor consisting of thyroid and carcinoid tissue, but its malignancy is intermediate or benign. The World Health Organization (WHO) classifies strumal carcinoid of the ovary (struma ovarii and carcinoid) among germ cell neoplasms, 9091/1 [1]. Fewer than 200 cases have been reported, and most were stage 1 [2, 3].

Ovarian goiter and carcinoid cannot be diagnosed preoperatively [4]. The present study is a retrospective review of the clinical and pathologic data of 21 patients with treated ovarian strumal carcinoid. Diagnoses and treatments were conducted at the Affiliated Hospital of Qingdao University and the Chinese People's Liberation Army General Hospital, China. Herein we describe patients' demographic and clinical characteristics, imaging and histopathologic findings, and outcomes.

Materials and methods

The Ethics Committee of Affiliated Hospital of Qingdao University approved this retrospective study. All the participants or family members gave informed consent.

Patients

Twenty-one patients received a diagnosis of ovarian strumal carcinoid and were treated between January 2000 and December 2015. Their mean age was 43 years (range 30--75 years); 14 were peri- or post-menopausal.

Methods

Clinical data, laboratory test results, and treatment strategies were recorded, including the results of follow-up visits. The results of hematoxylin-eosin and immunohistochemical staining were also reviewed.

Results

Clinical manifestation

All patients were characterized by degree of disease, duration of abdominal distension, abdominal pain, and constipation. Some patients were found with an abdominal mass upon medical examination. All patients were unilateral onset,

Table 1. Clinical features of 21 patients with strumal carcinoid

		Patients, *n*
Age, y	<50	7
	≥50	14
Constipation	Yes	6
	No	15
Ascites	Yes	3
	No	18
Location	Left	11
	Right	9
CA125/CA199	Elevated	6
	Normal	15
Echography diagnosis	Benign	6
	Malignant	15
Tumor size, cm	<5	3
	≥5	18
Histopathology	Insular carcinoid	9
	Trabecular carcinoid	7
	Discrete	5
Surgery	Extensive hysterectomy, bilateral adnexectomy	11
	Unilateral adnexectomy	8
	Hysterectomy, unilateral adnexectomy	2

and the rates of left and right sides were similar (**Table 1**).

Preoperative serum CA125 and CA199 concentrations were elevated in 6 patients, all of whom had ascites. Postoperatively, serum CA125 and CA199 concentrations returned to normal. None of the patients underwent thyroid function assessment before surgery, but postoperatively serum triiodothyronine, thyroxine, and free thyroxine concentrations were normal. Fifteen patients received provisional diagnoses of malignant ovarian cancer before surgery.

On ultrasound imaging, all the patients were found to have unilateral lesions of diameter 3-15 cm, with a smooth surface and clear boundary. Each lesion was a solid cystic mass. The cystic portions were full of dense point echo. The solid portions were hyperechoic masses, detected at low speed and with resistance flow signals at Doppler examination. They were difficult to distinguish from teratoma, mucinous cystadenoma, or ovarian cancer (**Figure 1**). On contrast-enhanced CT pelvic cavity images of circular lower density, the masses of 9 patients were similar in calcification, fat, soft tissue, and liquid density, with borders (**Figure 2**).

Histopathologic features

The lesions comprised varying proportions of carcinoid and thyroid tissue; tumor cells were mainly small gland cells or solid nests. There were varying sizes of follicular thyroid tissue, with a flat follicular lining and cuboid epithelium that contained colloid. The transition was visible between carcinoid cells and thyroid follicular epithelium. Immunohistochemical staining was positive for thyroglobulin and thyroid transcription factor-1 (TTF-1) in the thyroid follicular epithelium, and for TTF-1, synuclein, and chromogranin A (CgA) in the carcinoid component (**Figure 3**, **Table 2**).

Treatment and prognosis

The patients were treated with the following: hysterectomy and bilateral salpingo-oophorectomy, (11 patients); ipsilateral oophorectomy, (4 patients); laparoscopic ipsilateral oophorectomy (4 patients); or uterine and ipsilateral oophorectomy (2 patients). All patients had stage I disease and required no postoperative adjuvant treatment.

Until now, no patient has experienced a recurrence, and no metastases were detected during follow-up. Five patients died of other diseases, and the surviving 16 patients remain under regular follow-up. Follow-ups are conducted annually.

Discussion

Ovarian strumal carcinoid is a rare ovarian teratoma, a monodermal or highly specific germ cell tumor with both thyroid characteristics and carcinoid neuroendocrine features [5]. Strumal carcinoid of the ovary was first described by Scully in 1970 [6] and it has attracted considerable attention due to its unique morphology.

Island carcinoid accounts for ~26-53% of primary ovarian carcinoid tumors and is the most common type; trabecular carcinoid is less prev-

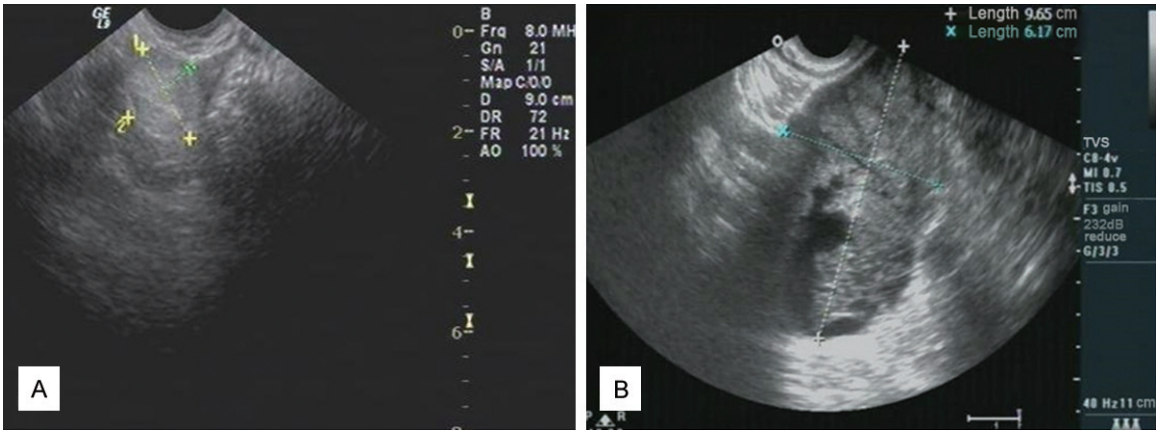

Figure 1. Representative ultrasound appearance of ovarian strumal carcinoid. A. Teratoma-like left ovary. B. Cystic mass in the left adnexa, which does not exclude a malignant tumor of the left ovary.

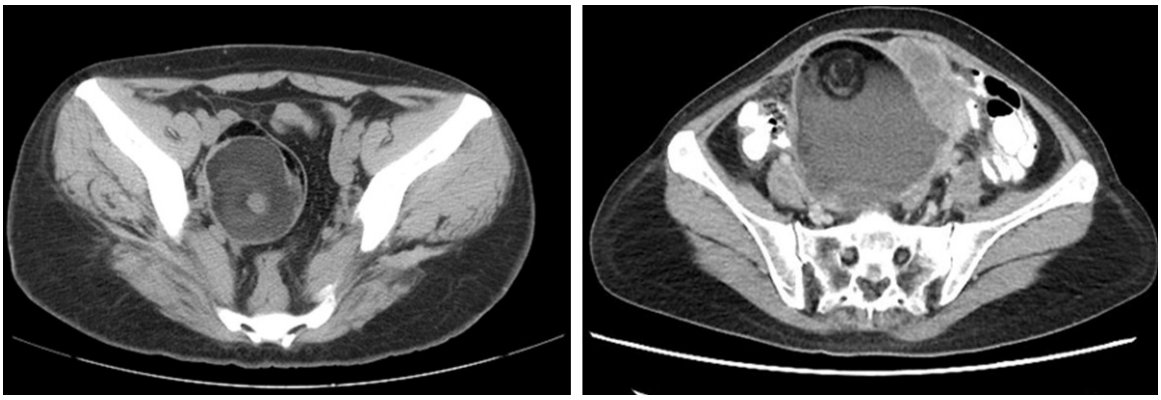

Figure 2. Enhanced CT performance: cystic or solid density, fat, obvious heterogeneity reinforcement.

alent (~23-29%). Island carcinoid is mainly composed of small gland cells and solid nests. The solid nests may be round or oval, and small glandular cells are located around the nests. In trabecular carcinoid, cells are arranged in strips, wavy bands, or parallel trabeculae and the tumor is surrounded by a fibrous matrix. Thyroid carcinoid refers to an ovarian carcinoid-related island or trabecular carcinoid, carcinoid and goiter components can be mixed or dispersed [1]. Thyroid carcinoid is found in ~26-44% of patients with ovarian carcinoid tumor.

Investigation and diagnosis of ovarian carcinoid tumors is normally prompted by the detection of an occult pelvic mass, but large tumors can cause lower abdominal pain and intractable constipation. Kawano and colleagues [7] reported that there was an association between constipation and peptide YY secretion by tumor cells. The mean age of diagnosis is reportedly 42.9 years [8]; most women treated for ovarian strumal carcinoid are peri- or post-menopausal. Some patients reportedly develop carcinoid syndrome [9], but none of the patients in our cohort complained of symptoms consistent with this diagnosis.

The elevation of serum carcinoembryonic antigen, CA125, and CA199 concentrations in ovarian strumal carcinoid [10] can be explained by the tumor's epithelial component, and in some patients there may be pleural effusion and ascites [2]. Thyroglobulin can be used as a serum biomarker of ovarian strumal carcinoid, although the extent of the change in serum concentration would not be expected to affect thyroid function.

Ovarian strumal carcinoid can be classified into 3 types based on the tumor's growth pattern and location [11]: tumor wall nodule simple

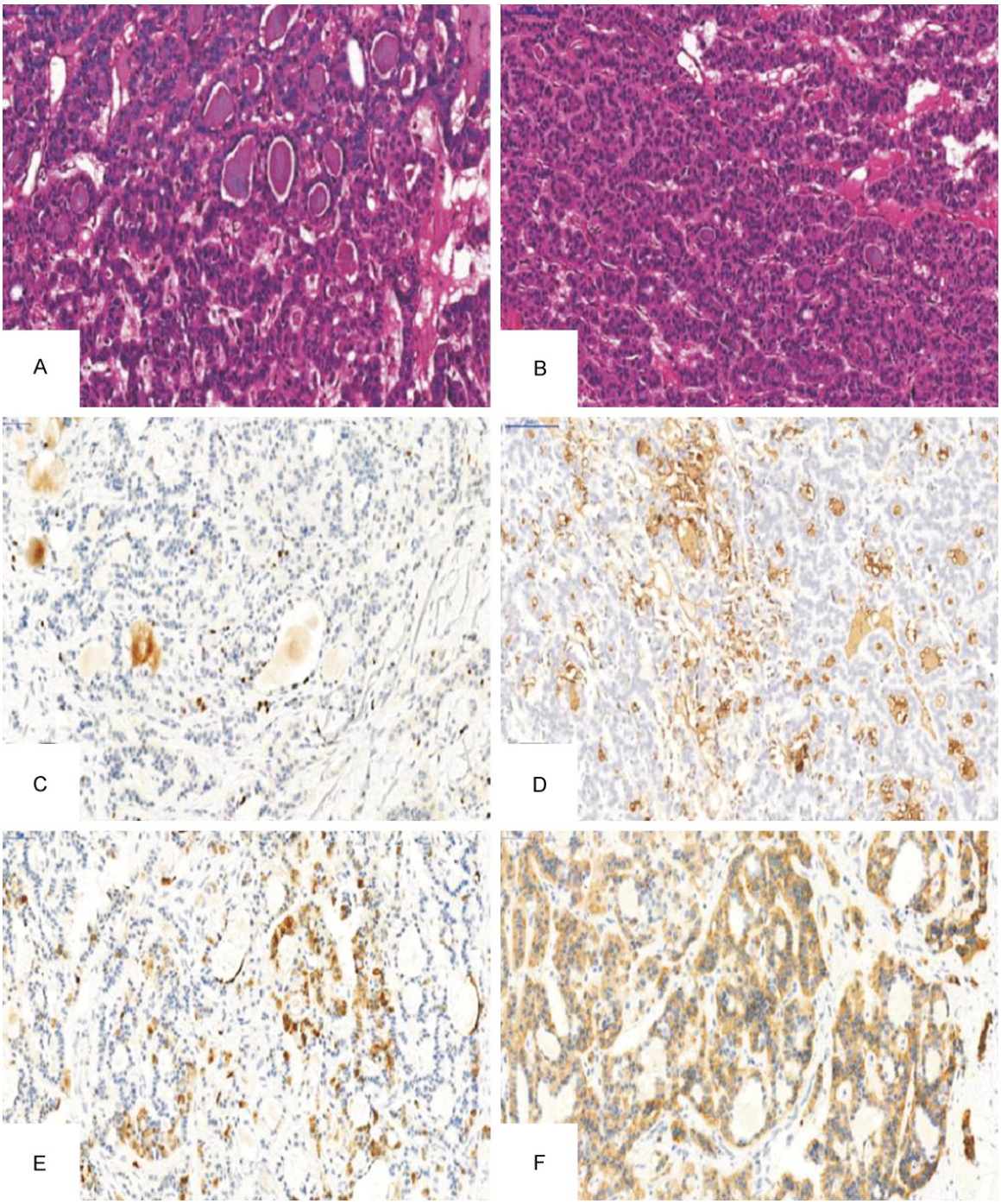

Figure 3. Histopathologic findings of ovarian strumal carcinoid: (A, B) Mixed carcinoid and goiter tissue with cells arranged in strips and trabeculae; (C) Expression of thyroid transcription factor-1 in carcinoid tissue; (D) Tumor tissue did not stain for thyroglobulin, but thyroid follicular tissue stained positively; (E) Carcinoid tissue expressed cytokeratin 19 and (F) stained strongly for synuclein. Magnification: (A, C-F) ×400; (B) ×200.

type; and mixed type. In our cohort, 9, 12, and zero patients, respectively, had the tumor wall nodule, simple, and mixed types. The tumor wall nodule type (diameter 1-8 cm), is located at the dermoid cyst wall and protrudes into the cavity. The tumor tissue has a diffuse distribution, with thickening of the cystic wall.

The tumor of the simple type of ovarian strumal carcinoid is homogeneous with a gray or pale

Table 2. Immunohistochemical results for strumal carcinoid, *n*

		Positive	
Antibody		Weak/dispersed	Strong/diffuse
Thyroid globin	21		
CD56	5	9	7
Thyroid transcription factor-1	21		
Synaptophysin	1	10	10
Chromogranin A	2	9	10
Neuron-specific enolase	8	7	6
Ki-67	2-5%		

yellow carcinoid area with bleeding and necrotic lesions, and the thyroid follicular cavity is filled with a glue-like substance.

In the mixed type of ovarian strumal carcinoid, the carcinoid and teratoma components are mixed, the tumor tissue consists of carcinoid, thyroid follicular, or other ingredients, and the carcinoid is generally beam-like and island-like. The single island-like carcinoid is rare [12]. In the present study, immunohistochemistry showed that: specimens from all 21 patients were positive for synuclein and partially positive for CgA.

Most cases of ovarian strumal carcinoid are detected but not diagnosed by ultrasound examination, as it lacks sufficient specificity [13-15]. Regarding cystic dense point echo, Savelli [16]. Hink the room with follicular colloid containing different concentrations of thyroglobulin and thyroid hormone and so on, this is the same as CT performance high-density capsule principle is, the other solid part in rich blood flow signal, it has to do with the mass in nodular goiter and thyroid rich blood supply. The ultrasound examination, of 15 of our patients revealed a unilateral echo-mixed mass in the adnexa that was initially thought to be a malignant tumor. In six patients, there were signs of teratoma.

Ovarian strumal carcinoid is difficult to diagnose before surgery, as it is rare and has no pathognomonic clinical manifestations or imaging findings. It is most often diagnosed on postoperative pathologic examination. The majority of cases are diagnosed as carcinoid mixed with thyroid tissue. Carcinoid cells are argyrophilic, while thyroid tissue expresses thyroglobulin or TTF-1 [17].

Ovarian strumal carcinoid can be differentiated by elimination of features that typify other suspected neoplasms. Malignant goiter, has clear follicular or papillary structures and a lack of trabecular and island carcinoid structures. In ovarian goiter, only thyroid tissue is visible on pathologic examination and there is no carcinoid component. Teratoma with thyroid medullary carcinoma, contains amyloid, and stains positively with Congo red and is positive for cancer or testis antigens. Finally, metastatic carcinoid, is histologically similar to primary ovarian carcinoid, with the primary tumor outside the ovaries and ovarian involvement unrelated to a teratoma component, and carcinoid syndrome may persist after oophorectomy.

Ovarian strumal carcinoid grows slowly and has low malignant potential [18]. Over 90% of tumors are confined to the ovaries (stage I) and advanced cases (stage II or III) are rarely seen [19]. The treatment strategy is generally bilateral oophorectomy and hysterectomy for uncomplicated disease, with unilateral oophorectomy in patients who wish to preserve fertility. All patients must be closely monitored postoperatively. In our cohort of 21 patients, 14 were peri- or post-menopausal, and all underwent bilateral oophorectomy and hysterectomy, or uterine and ipsilateral oophorectomy.

If the thyroid follicular component is a papillary or follicular cancer, additional chemotherapy or radiation therapy is necessary after surgery. Whether chemotherapy or radiation therapy is needed for non-stage I tumors is not known. Some investigators have suggested chemotherapy in cases of advanced primary ovarian carcinoid [20] to address concurrent metastasis or carcinoid syndrome. Resection of metastases in combination with chemotherapy has also been described.

The 10-year survival rate of stage I thyroid carcinoid is reportedly 100%, but the 5-year survival rate of stage III and IV patients is only 33%, with a median survival of 1.2 years [21]. Robboy and Scully [22] followed 46 patients with ovarian strumal carcinoid of a cohort of 50 for 6 months to 20 years, and reported the fol-

lowing outcomes: 40 patients were still alive without recurrence; 23 survived >5 years; 15 survived >10 years; 6 died (cause of death was unrelated to the tumor in 5 patients); and one patient relapsed. The autopsy of the patient who died showed extensive peritoneal and liver metastases of a poorly differentiated adenocarcinoma with carcinoid components.

In conclusion, ovarian strumal carcinoid is a rare germ cell tumor with unique clinical and pathologic features and associated thyroid tissue components. It has a good prognosis, but its diagnosis depends on its histopathologic features and immunohistochemical phenotype.

Disclosure of conflict of interest

None.

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