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Original Article

Diagnosis and treatment of 11 cases of struma ovarii: a clinical analysis with literature review

Shizhang Yang, Jinjin Yu

Department of Obstetrics and Gynecology, Affiliated Hospital of Jiangnan University, Wuxi 214000, Jiangsu, P. R. China

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Abstract: Objective: To investigate patient demographics, presenting signs and symptoms, laboratory and radiological investigations, surgical methods, histopathology, and follow-up results of 11 patients diagnosed with Struma Ovarii (SO). Methods: The general clinical data, auxiliary examination results, surgical and histopathological findings of 11 patients (aged from 25 to 66 years, mean 45.9 years) with SO admitted to the Department of Gynaecology of the Affiliated Hospital of Jiangnan University from January 1, 2009 to January 31, 2024 were retrospectively analyzed and compared with previous studies in the literature. Results: Most patients are asymptomatic with struma ovarii and it can usually only be detected by physical examination. Common clinical presentations include a pelvic mass, abdominal distension, dyspnoea, or peritoneal dropsy. Cancer antigen 125 levels may be elevated, but the difference in serum tumour markers between benign and malignant patients was not statistically significant. Ultrasonographic findings are not specific for Struma Ovarii. Establishing the diagnosis of SO remains a challenge as ultrasonographic features are non-specific. Ultrasonography suggests the presence of heterogeneous echoes and septations in these patients with ovarian foramen cysts. Computerized tomography (CT) and especially Magnetic resonance imaging (MRI) are advantageous in characterizing adnexal cysts that are sonographically indeterminate. As to the treatment part, surgery is the mainstay of treatment method for ovarian tumours. Adjuvant therapy includes extracorporeal radiotherapy, chemotherapy, and thyroid suppression. Pathological specimen findings reveal that the gross pathology usually presents as multilocular cysts, whether benign or malignant. Macroscopically, it presents as a unilateral, solid mass with a gelatinous, red-brown to green cut surface. It may also show goiter-like multinodular or cystic change. Conclusion: SO is an uncommon type of ovarian teratoma, and preoperative diagnosis is often difficult because it does not have typical clinical features and is poorly recognized. Fortunately, serial measurement of serum thyroglobulin is a sensitive and economical follow-up tool, making SO better managed after surgery.

Keywords: Struma ovarii, treatment, management, clinical analysis, literature review

Introduction

Struma Ovarii (SO) is a teratoma that exclusively or predominantly contains more than 50% thyroid tissue. It is a highly specialized monodermal teratoma, accounting for less than 5% of mature teratomas [1]. Due to the absence of typical clinical signs and symptoms, SO is often misdiagnosed preoperatively, with most cases confirmed through postoperative pathology [2]. The potential for malignancy, including papillary and follicular carcinomas, underscores the importance of understanding this rare condition. This study aims to investigate the clinical symptoms, laboratory results, radiological investigations, surgical methods and histopathology of SO to improve diagnostic and therapeutic approaches.

Subjects and methods

Subjects

Clinical data from 11 patients (aged 25-66 years, mean age 45.9 years) diagnosed with SO at the Department of Gynecology, Affiliated Hospital of Jiangnan University, from January 1, 2009, to January 31, 2024, were retrospectively analyzed. This study was approved by the Ethics Committee of the Affiliated Hospital of Jiangnan University. Written informed consent was obtained from all participants. All proce-

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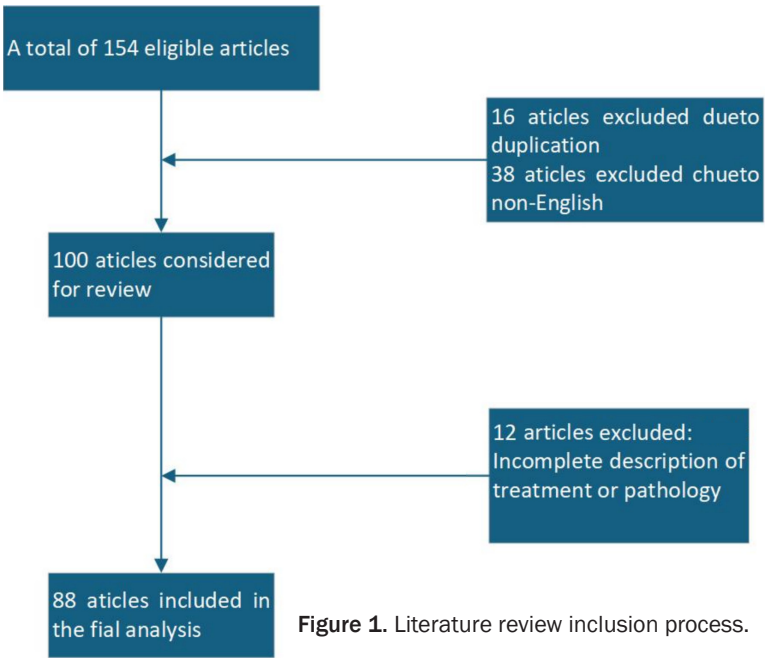

Figure 1. Literature review inclusion process.

dures followed institutional guidelines and regulations. Inclusion criteria: Patients diagnosed with SO during hospitalization, without elevated tumor markers or abnormal thyroid function test results. Exclusion criteria: Patients with non-ovarian tumors or diagnosed ovarian malignancies. Diagnostic Criteria: All forms of struma ovarii are typically found incidentally in imaging studies but may present with symptoms of pelvic mass and lower abdominal pain. Thyroid carcinoma originating in struma ovarii comprises a small minority of all cases of struma ovarii. Importantly, diagnosis is confirmed by pathology. Struma ovarii is defined as an ovarian teratoma comprising at least 50% thyroid stroma [3].

Methods

The study cases were divided into benign and malignant groups and compared for their clinical characteristics, diagnostic methods, treatment approaches, and outcomes between benign and malignant groups. After that, the results were compared with previous literature. Firstly, we collected the 11 cases clinical data like age, presenting symptoms, gestation, menopause, tumor markers, thyroid function, surgical intervention, pathology, metastasis, chemotherapy or radiotherapy after surgery and recurrence. Afterwards, we compared the clinical characteristics of the benign group (n = 9, 81.8%) and malignant group (n = 2, 18.2%). The second step was to collect the literature clinical features of SO patients and analyze the influence factors of death. Thirdly, the overall survival in the literature and our study were analyzed together.

Literature review was conducted using PubMed, ClinicalTrials.gov and Embase databases (1987-2024) with search terms including “malignant struma ovarii”, “struma ovarii” and “therapy”. A total of 88 articles were included, involving 71 (74.0%) benign and 25 (26.0%) malignant cases (**Figure 1**).

Observation indicators: Clinical symptoms, tumor markers, thyroid function tests, surgical methods, pathological results, distant metastasis, postoperative adjuvant therapy, disease recurrence and overall survival.

Data analysis

These data were assessed with SPSS 27.0. Categorical variables were compared using the Man-Whitney U test or Chi-square test and continuous variables were analyzed using the t-test. Survival rates were calculated using Cox regression models. A two-sided p value < 0.05 was considered statistically significant.

Results

Our study

General characteristics of the 11 cases: In this study, all patients with Struma Ovarii (SO) were multiparous, with their ages ranging from 25 to 66 years, and the average age was 45.9 years. The tumor diameter varied from a maximum of 15 cm to a minimum of 3 cm. One patient exhibited symptoms of hyperthyroidism, and the serum thyroglobulin levels of the remaining patients were serially measured. The proportion of malignant tumors was 18.2% (2/11), while that of benign tumors was 81.8% (9/11).

Before surgery, all patients presented with pelvic masses and unconfirmed ovarian cysts as

shown in the imaging examination. One patient was admitted to the respiratory department due to dyspnea caused by ascites and was subsequently referred to the gynecology department for the investigation of Meig's Syndrome or ovarian cancer. In another special case, an ovarian cyst was detected during a caesarean section. Eventually, all patients were diagnosed with SO based on the histopathological examination of the resected specimens. Details are presented in **Table 1**.

Pathologic features of struma ovarii: The histopathologic criteria for thyroid carcinoma originating in struma ovarii mirror those of primary thyroid carcinoma. In terms of gross features, on the cut surface of the SO tissue, the struma component appears beefy red-brown, resembling normal thyroid tissue, and the cystic components are similar to follicular nodular disease of the native thyroid gland. The tumors are predominantly solid but may contain multiloculated or uniloculated cystic components. If a cystic component is present, mucinous/colloid type material can be found within it. Malignant foci tend to recapitulate the findings of carcinoma in the native thyroid gland.

Regarding microscopic features, SO is composed of thyroid follicles of varying sizes that are lined by low cuboidal to columnar cells with pale eosinophilic cytoplasm (**Figure 2**). In foci of malignancy, in terms of microscopic features, the neoplastic epithelial cells exhibit an increased nuclear-to-cytoplasmic ratio with nuclear crowding; the nuclei are round to oval, with powdery to optically clear chromatin and irregular nuclear membranes, which result in nuclear grooves and pseudoinclusions (**Figure 3**). In our study, intraoperative frozen sections were performed in all cases (11/11, 100%) to confirm the diagnosis of SO. One case (1/11, 9.0%) was diagnosed as ovarian cancer, and another case involved a mixed borderline tumor of the ovarian mass.

Treatment outcomes in struma ovarii: The majority of patients (10/11, 90.9%) presented with a pelvic mass. Some patients complained of abdominal distension (7/11, 63.6%) and abdominal pain (3/11, 27.3%). One case (1/11, 9.1%) exhibited hyperthyroidism, and five cases (5/11, 45.5%) had ascites. None of the patients manifested menstrual changes (0/11, 0%). Fortunately, ovarian benign tumors were the most prevalent histopathological diagnosis among the patients (9/11, 81.8%). However, one case of ovarian epithelial cancer (1/11, 9.1%) and one borderline tumor (1/11, 9.1%) were identified. Five patients (5/11, 45.5%) presented with ascites. Among these ascites cases, two patients (2/5, 40.0%) had light-yellow ascites, and one patient (1/11, 20.0%) had a large volume of peritoneal fluid (7,000 ml). All patients underwent surgery. One case (1/11, 9%) was treated with the TAH + USO + O surgical approach, and four cases (4/11, 36.4%) received the USO + COHE surgical method. In the remaining patients (6/11, 54.5%), two cases underwent the TAH + USO, OCB and TAH + USO + RLD + O surgical procedures, respectively. After surgery, two cases (2/11, 18.2%) were pathologically confirmed as malignant and received chemotherapy (**Table 1**). Up to now, during the follow-up period, no recurrence has been observed in all cases.

We further analyzed the clinical characteristics differentiating malignant from benign tumors. The results indicated a statistically significant difference in age (years) and chemotherapy between the two groups ($P < 0.05$) (**Table 2**). It was demonstrated that the malignancy rate increased with advancing age.

The literature results

From 1987 to 2024, a total of 88 eligible articles were retrieved, covering 96 patients (**Figure 1**). The ages of the patients ranged from 18 to 80 years, with an average age of 48.3 years (**Table 3**). The follow-up period spanned from 36 to 96 months, with an average of 60.07 months. Among the patients, 78 (81.3%) were still alive, while 18 (18.7%) were deceased. The main corresponding literature sources were shown in **Table 4**.

To review the influencing factors of death in the context of SO (presumably some specific condition, though not fully clear from the text) based on the literature, the results show that tumor metastasis, response to chemotherapy, and the malignant nature of the disease are the main factors. There were statistically significant differences in terms of the response to chemotherapy and the malignant status among the influencing factors of death ($P < 0.05$) (**Table 5**).

Table 1. Characteristics of cases with struma ovarii

Age	Presenting symptom	Gestation	Menopause	Seroglycoid	Thyroid function	Surgical intervention	Pathology	Metastasis	Additional treatment	Recurrence	
1	46	Flatulence, Left adnexal mass	G1P1	no	Normal	not done	USO + COHE	struma ovarii	no	no	no
2	47	Flatulence, Pelvic Mass, ascites	G5P1	no	AFP9.02 ng/ml, CA125 68 u/ml	normal	USO + COHE	struma ovarii	no	no	no
3	66	Flatulence, Abdominal pain, Pelvic Mass, ascites	G4P2	yes	CA125 77 u/ml	normal	TAH + USO + O	struma ovarii borderline tumor	no	chemotherapy	no
4	43	Right adnexal mass, ascites	G1P1	no	CA125 75 u/ml	not done	USO + COHE	struma ovarii	no	no	no
5	41	Pelvic Mass	G1P1	no	Normal	not done	USO + COHE	struma ovarii	no	no	no
6	53	Flatulence, Pelvic Mass, ascites	G5P1	yes	CA125 80 u/ml	not done	TAH + USO	Struma ovarii	no	no	no
7	27	Pelvic Mass	G1P1	no	Normal	normal	OCB	Struma ovarii	no	no	no
8	20	Pelvic Mass	G0P0	no	Normal	not done	OCB	Struma ovarii	no	no	no
9	54	Flatulence, Pelvic Mass	G1P1	yes	Normal	normal	TAH + USO	struma ovarii	no	no	no
10	64	Flatulence, Abdominal pain, Pelvic Mass, ascites	G3P2	yes	CA199 28.92 u/ml	not done	TAH+USO + RLD + O	struma ovarii canceration cystic teratoma,	no	chemotherapy	no
11	44	Flatulence, Abdominal pain, Pelvic Mass, ascites, dyspnoea	G4P1	no	CA125 425.6 u/ml	Thyrine13.4 ug/ml, thyroglobulin antibody86.22 ug/ml, thyrotropin 8.5 u/ml	TAH + USO + RLD + O	struma ovarii	no	no	no

TAH, total abdominal hysterectomy; USO, unilateral/right/left salpingo-oophorectomy; O, omentectomy; RLD, retroperitoneal lymph node dissection; COHE, contralateral ovary histopathological examination; OCB, ovarian cystis abscission.

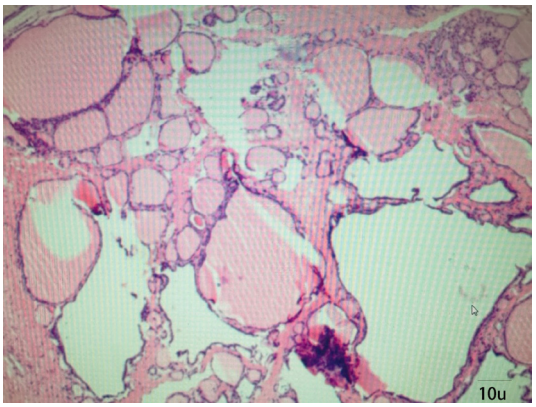

Figure 2. 100X Struma ovarii: ovarian teratoma made up of benign thyroid tissue (Hematoxylin and eosin stain, HE).

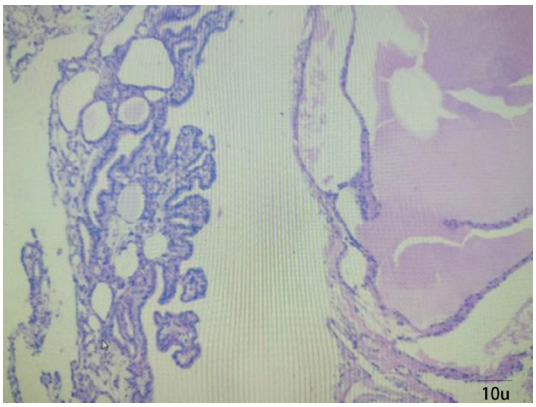

Figure 3. 100X Ovarian mucinous borderline cystadenoma mixed benign thyroid tissue (Hematoxylin and eosin stain, HE).

The differences in study and literature results

The main clinical characteristics of 11 cases were selected and compared with those of 96 patients described in the literature. The results showed that the clinical characteristics and treatment outcomes of the 11 patients were similar to the treatment outcomes reported in the literature, and there was no statistically significant difference (P > 0.05), **Table 6**.

Subsequently, we combined the data of the study group with the data from the literature and carried out a survival analysis. Univariate and multivariate analyses were performed using Cox regression models for overall survival. Tumor metastasis (hazard ratio [HR] = 1.43, 95% confidence interval [CI]: 1.22-1.26, P = 0.043), chemotherapy (HR = 2.49, 95% CI: 1.12-3.88, P = 0.000), and malignancy (HR = 1.40, 95% CI: 1.08-2.93, P = 0.045) were identified as independent risk factors (**Table 7**).

Discussion and literature review about OS

MatSure cystic teratomas constitute approximately 20% of all ovarian tumors. Struma Ovarii (SO), a monodermal variant of ovarian teratoma, comprises more than 50% thyroid tissue [1]. SO accounts for around 2.7% of ovarian teratomas and was initially described by Von Kalden in 1895. It occurs most prevalently in regions where goiter is endemic, with the peak incidence in the fifth decade of life [4]. SO can be categorized as either benign or malignant. Malignant tumors are infrequent, accounting for 5-37% of cases; nevertheless, the criteria for their definition have not been uniformly established. The majority of patients exhibit no overt clinical symptoms and are typically detected during a physical examination due to the presence of an ovarian mass. SO has the potential to transform into a malignant tumor [1]; the most common carcinoma originating from struma ovarii is papillary thyroid carcinoma (PTCSO). Less commonly, the malignant component is follicular variant papillary thyroid carcinoma (FVPTCSO) or follicular thyroid carcinoma (FTCSO) [3]. Based on the analysis of our clinical data, postmenopausal women were more susceptible to disease progression (2/11, 18%), whereas in the literature, the malignant rate is 26% (25/96). Moreover, in a recent review of malignant struma ovarii, 178 cases were evaluated. It was demonstrated that malignant SO was papillary thyroid carcinoma in 72.5% of cases. Among the metastases of SO, the histologic subtypes of the papillary thyroid carcinoma component were papillary classic-type thyroid carcinoma in 74 patients (41.6%) and papillary follicular variant thyroid carcinoma in 50 patients (28.1%) [5].

Metastatic SO is a rare condition with a non-negligible recurrence rate [5]. The median time to recurrence is 76.6 months (ranging from 4 to 264 months), and the median overall survival time is 64.5 months (ranging from 0 to 492 months) [6]. Fortunately, among the 11 cases in our study, no recurrence was observed. Metastatic SO is present in 5%-23% of cases, with the most common sites of metastasis being the peritoneum, mesentery, and omentum [5]. The multivariate analysis model for overall survival (OS) incorporated capsular involvement and

Table 2. Man-Whitney U test or Chi-square test and t-test analyses the differences in clinical characteristics

	Benign (n = 9)	Malignant (n = 2)	t/χ^2	*P*
Age (years)	41.7 ± 11.29	65 ± 1.41	-2.797	0.021*
Gestation				
Yes	8 (88.9)	2 (100)	0.00	1.0
No	1 (11.1)	0 (0)		
Flatulence				
Yes	5 (55.6)	2 (100)	0.136	0.712
No	4 (45.4)	0 (0)		
Abdominal pain				
Yes	1 (11.1)	2 (100)	2.807	0.094
No	8 (88.9)	0 (0)		
Ascites				
Yes	4 (45.4)	2 (100)	0.413	0.521
No	5 (55.6)	0 (0)		
Dyspnoeav				
Yes	1 (11.1)	0 (0)	0.00	1.0
No	8 (88.9)	2 (100)		
Seroglycoid unnormal				
Yes	1 (11.1)	0 (0)	0.00	1.0
No	8 (88.9)	2 (100)		
Comprehensive staging surgery				
Yes	3 (33.3)	2 (100)	0.861	0.354
No	6 (66.7)	0		
Chemotherapy				
Yes	0 (0)	2 (100)	5.305	0.021*
No	9 (100)	0 (0)		

*P < 0.05.

Table 3. Summary of the literature clinical features of SO patients

Subject	Number of patients	Mean ± SD
Age (year)	96	48.3 ± 14.58
Age (live)	78	41.7 ± 13.05
Age (death)	18	59.8 ± 17.98
Tumor size (diameter/cm)	60	8.65 ± 5.38
Follow-up time (month)	50	60.07 ± 71.3

age; however, the results indicated that there was no statistically significant independent prognostic factor for predicting OS [5]. In contrast, our research findings suggest that: univariate analysis revealed that age, tumor metastasis, chemotherapy response, and malignancy are risk factors for OS, and multivariate analysis identified tumor metastasis, chemotherapy response, and malignancy as independent risk factors for OS.

In previous studies, ovarian cancer has been found to afflict women aged 65 years or older more frequently than younger women [2]. In this study, the average age of incidence was 45.90 ± 13.8 years, while in the literature, it was 48.3 ± 14.58 years. The temporal trend also indicates an augmentation in the age-specific incidence rates of ovarian teratomas. Fortunately, the prognosis of most SO cases is favorable [6]. Ovarian teratoma predominantly occurs in perimenopausal women, which might be associated with the promotion of protein synthesis by estrogen [7]. SO is largely asymptomatic, and patients usually seek medical attention due to a pelvic mass, approximately one-third of which are accompanied by ascites [8]. Some patients present with concomitant pleural effusion (pseudo-Meig's syndrome) and elevated serum CA125 levels [9]. In our study, patients mainly manifested with pelvic masses (10/11, 90.9%), abdominal disten-

Table 4. The main corresponding literature sources

Authors	Literature title and the journal.
Dardik RB, et al.	Malignant struma ovarii: two case reports and a review of the literature. Gynecol Oncol 1999; 73: 447-451.
Ostoglou-Athanassiou I, et al.	Malignant struma ovarii: report of a case and review of the literature. Horm Res 2002; 58: 34-38.
Makani S, et al.	Struma Ovarii with a focus of papillary thyroid cancer: a case report and review of the literature. Gynecol Oncol 2004; 94: 835-839.
Roth LM, et al.	Highly differentiated follicular carcinoma arising from struma ovarii: a report of 3 cases, a review of the literature, and a reassessment of so-called peritoneal strumosis. Int J Gynecol Pathol 2008; 27: 213-222.
Goffredo P, et al.	Malignant struma ovarii: a population-level analysis of a large series of 68 patients. Thyroid 2015; 25: 211-215.
Wei S, et al.	Pathology of struma ovarii: a report of 96 cases. Endocr Pathol 2015; 26: 342-348.
Marti JL, et al.	Optimal surgical management of well-differentiated thyroid cancer arising in struma ovarii: a series of 4 patients and a review of 53 reported cases. Thyroid 2012; 22: 400-406.
Ma D, et al.	Struma ovarii with malignant transformation and germline KIT mutation: a case report with review of the literature. Int J Gynecol Pathol 2016; 35: 442-447.
Siegel MR, et al.	Struma ovarii with atypical features and synchronous primary thyroid cancer: a case report and review of the literature. Arch Gynecol Obstet 2019; 300: 1693-1707.
Addley S, et al.	Malignant struma ovarii: surgical, histopathological and survival outcomes for thyroid-type carcinoma of struma ovarii with recommendations for standardising multi-modal management. A retrospective case series sharing the experience of a single institution over 10 years. Arch Gynecol Obstet 2021; 303: 863-870.
Cui Y, et al.	The Clinical and Pathological Characteristics of Malignant Struma Ovarii: An Analysis of 144 Published Patients. Front Oncol 2021; 11: 645156.
Leuştean L, et al.	Management of malignant struma ovarii: is aggressive therapy justified? Case report and literature review. Thyroid Res 2022; 15: 14.
Taelman V, et al.	Metastatic malignant struma ovarii: a case report and review of the literature on the management of malignant struma ovarii. Acta Clin Belg 2022; 77: 721-725.
Vaidya B, et al.	Concurrent Intrathyroidal Follicular Variant of Papillary Thyroid Carcinoma with Malignant Struma Ovarii Presenting 12 Years After Initial Diagnosis. J Nucl Med Technol 2024; 52: 175-176.
Wu Z, et al.	Follicular Thyroid Carcinoma Arising from the Struma Ovarii Coexisting with Papillary Thyroid Carcinoma, Hashimoto's Thyroiditis and Polycystic Ovarian Syndrome-a Case Report and Literature Review. Int J Womens Health 2024; 16: 1187-1198.
Peştean C, et al.	Diagnostic Value of Nuclear Hybrid Imaging in Malignant Struma Ovarii: A Systematic Review of Case Reports. Diagnostics (Basel) 2024; 14: 2630.

Table 5. Man-Whitney U test or Chi-square test analyses relationship between influencing factors and death

Influencing factors	state	Number of deaths	Total	χ^2	*P*
Tumor Metastasis	Yes	5 (62.5%)	8	1.600	0.206
	No	1 (12.5%)			
Chemotherapy Therapy	Yes	6 (26.1%)	23	4.518	0.034*
	No	3 (13.0%)			
Malignant	Yes	7 (28%)	25	8.341	0.004*
	No	3 (12%)			

*P < 0.05.

Table 6. Man-Whitney U test or Chi-square test and t-test analyses the main character comparing in study and literature

	Study (n = 11)	Literature (n = 96)	t/χ^2	*P*
Age	45.90 ± 13.8	48.3 ± 14.58	-0.520	0.604
Positive clinical signs	11 (100)	90 (94)	0.728	0.393
Tumor size (diameter/cm)	10.45 ± 2.38	8.65 ± 5.38	1.094	0.277
Malignant	2 (18.2)	25 (26)	0.323	0.570
Tumor Metastasis	0 (0)	8 (8.3)	0.991	0.320
Chemotherapy Therapy	2 (18.2)	23 (24)	0.184	0.668

Table 7. COX univariate and multivariate analyses of potential prognostic factors for overall survival in literature and our study cases

	Univariate		Multivariate	
	HR (95% CI)	*p*	HR (95% CI)	*p*
Age (≥ 45.90 vs < 49.5)	1.72 (1.01-4.36)	0.035*	1.88 (0.29-1.91)	0.077
Tumor Metastasis (Yes/No)	1.18 (1.37-2.58)	0.047*	1.43 (1.22-3.26)	0.043*
Chemotherapy therapy (Yes/No)	1.68 (1.98-2.24)	0.039*	2.49 (1.12-3.88)	0.000*
Malignant (Yes/No)	2.34 (1.17-3.67)	0.002*	1.40 (1.08-2.93)	0.045*

*P < 0.05.

sion (7/11, 63.6%), and abdominal pain (3/11, 27.3%), which was higher than previously reported in the literature [1]. The possible reasons for our elevated findings could be a larger sample size and earlier diagnosis.

In this study, all patients (11/11, 100%) achieved an uncomplicated recovery, with the resolution of their symptoms observed postoperatively. Preoperative thyroid function examination was normal in 4 cases (4/11, 36.4%), and all patients had normal thyroid function after the operation. Ascites disappeared within two weeks after surgery, and all tumor markers returned to normal postoperatively. CA125 declined the most rapidly among all tumor markers and reached normal levels within four weeks. All patients were followed up for 12-120 months, and the results indicated that all patients had an uneventful recovery with symptom resolution after the operation. The treatment outcomes were consistent with those of a retrospective case series study [5].

How do significant amounts of pleural effusion and ascites develop? Currently, the etiology of pleural effusion and ascites is predominantly explained as follows: Firstly, the tumor's action stimulates the peritoneum, inducing interstitial exudation into ascites, which alters the osmotic pressure gradient and diminishes the peritoneal absorptive capacity [10]. Secondly, in certain individuals, there exists sufficient mechanical communication between the pleura and the peritoneum to permit the passive transfer of fluid from the abdomen to the chest. Thirdly, tumor compression of blood vessels or lymphatic vessels leads to impaired reflux. Lastly,

the tumor itself may secrete substances [11]. In this study, 6 cases (54.5%) had ascites and 1 case (9%) had pleural effusion.

There is no unified or standardized diagnostic and therapeutic approach for malignant struma ovarii. Hybrid imaging modalities may hold substantial value in initial diagnosis, and the combination of F-18 FDG PET/CT and I-131 NaI SPECT/CT represents a successful diagnostic strategy [12]. Savelli et al. [13] described the sonographic features of SO in their study. The sonographic characteristics of ovarian tumors are variable and uncommon, rendering sonographic diagnosis highly challenging. SO should be suspected when a pleomorphic solid adnexal mass containing one or more "struma pearls" is detected. Studies have shown that ultrasonography revealing an abundant blood-flow signal in the ovary is not indicative of malignancy in ovarian tumors. Therefore, in cases of polycystic ovaries or cystic ovarian tumors, when ultrasonography demonstrates an abundant, low-resistance blood-flow signal, the possibility of an ovarian tumor should be considered. Although ultrasound is typically the first-line technique for investigating pelvic diseases in women, CT and MRI possess particular advantages in characterizing sonographically indeterminate adnexal masses [14]. The combination of CT and MRI has revealed unilateral fibrous ovarian masses containing punctate calcifications, often associated with multilocular cystic tumors [13]. In our study, all patients underwent ultrasonography, and the results suggested ovarian cysts or the presence of solid heterogeneous echoes, a diaphragm in ovarian cysts, and pelvic effusion in four patients.

Nevertheless, there are no specific tumor markers for SO. In some patients, serum CA125 levels are several times higher than the normal upper limit. In fact, the levels of CA125, CA199, AFP, and CEA may fall within the normal range [11]. Currently, CA125 is widely employed in the diagnosis of ovarian cancer and has emerged as a significant prognostic factor in the treatment outcomes of women with advanced ovarian cancer following chemotherapy [15]. Given that SO is a type of ovarian teratoma, this might account for the elevation of CA125, although the specific mechanisms necessitate further investigation [16].

Thyroglobulin has been detected in both benign and malignant phyllodes tumors. The value of thyroglobulin as a "tumor marker" for malignant recurrence is well-documented. It has been utilized to detect recurrence after cervical thyroid ablation and in patients receiving thyroid-suppressive therapy [1]. In our study, serial serum thyroglobulin levels exceeded the normal range in one patient. The plasma thyroid indices in patients with abnormal thyroid function varied. Thyroxine was elevated to 13.4 μg/ml, thyroglobulin antibodies to 86.22 μg/ml, and thyrotropin to 8.5 μg/ml.

The treatment of SO remains contentious as both benign and malignant tumors are rare and challenging to distinguish [17]. Currently, surgery constitutes the primary treatment modality for SO. Surgical options span from total abdominal hysterectomy plus bilateral salpingo-oophorectomy, salpingo-oophorectomy, to conservative procedures such as unilateral salpingo-oophorectomy for fertility preservation [1]. Adjuvant therapies encompass extracorporeal radiotherapy, chemotherapy, and thyroid suppression [5].

The pleural effusion of the patient dissipated rapidly, and CA125 promptly approached normal levels, signifying a favorable prognosis in our study. However, it has been reported that benign SO may also undergo malignant transformation and metastasize [11]. Consequently, patients should undergo a comprehensive examination of all surrounding organs and be closely monitored over an extended period. For malignant patients, some scholars contend that they can be managed in accordance with the treatment principles of ovarian germ-cell tumors. The prognosis of malignant SO is relatively favorable, and young patients with fertility requirements may initially consider unilateral salpingo-oophorectomy and subsequently undergo radical surgery after childbearing. In this paper, we employed multiple and multivariate Logistic model analyses for overall survival in the literature and our study cases. Tumor metastasis, chemotherapy, and malignancy were identified as independent risk factors (**Table 5**).

It should be emphasized that all malignant SO cases should undergo postoperative I^{131} whole-body scanning to evaluate the presence of residual disease in the abdominal cavity, and serum thyroglobulin levels should also be monitored [6]. Residual disease and malignant recurrence respond remarkably well to I^{131} radioablation [17]. For residual malignant dis-

ease, adjuvant therapy, including total thyroidectomy followed by I^{131} radioablation, should be implemented, after which thyroid hormone supplementation is essential [1-17].

Serum thyroglobulin is a protein that serves as a substrate for thyroid hormone synthesis. It should be undetectable after total thyroidectomy and I^{131} ablation [2]. It is recommended that when elevated serum thyroglobulin levels are detected during at least a 10-year follow-up in these cases, both methods (I^{131} whole-body scanning and serum thyroglobulin level check) are advised to detect residual disease, confirm recurrence, or identify the presence of metastases [6-18].

Recent studies have proposed that the pathophysiological mechanism underlying a functional SO may involve either an autonomous hormone-secreting tumor or the stimulation of ovarian thyroid tissue by antibodies directed against thyrotropin receptors [19]. Malignant papillary thyroid tumors might share a similar oncogenic mechanism with papillary thyroid carcinoma [20]. Multiple reports have indicated that mutations in the tumor-suppressor gene BRAF occur frequently in malignant phyllodes tumors with papillary carcinoma but are absent in benign tumors. Additionally, mutations in the tumor-driver gene RAS have also been observed in malignant phyllodes tumors with a follicular variant of capillary carcinoma [21]. In our study, intraoperative frozen sections were carried out in all cases (11/11, 100%) to confirm the diagnosis of SO (**Figure 2**). One case [1/11, 9.0%] was diagnosed as ovarian cancer, and another case was a mixed borderline tumor of the ovarian mass (**Figure 3**). Contralateral ovarian biopsies in all cases revealed normal ovarian tissue. The diagnosis of malignant SO should adhere to histopathologic criteria analogous to those for primary thyroid disease. A teratoma must contain more than 50% thyroid tissue to be categorized as a phyllodes tumor SO.

Subsequently, we further examined the clinical features differentiating malignant from benign cases. The results demonstrated that the incidence rate of malignant SO rises with age (**Table 2**). However, significant discrepancies were noted in adjuvant therapy and the malignant ratio between the literature cohorts and our study (**Figure 3**). We hypothesize that this is due to the fact that most SO cases have been reported anecdotally, and there have been no large-scale studies on benign cases. Concurrently, the two malignant cases in our study were both in patients over 60 years old. This may imply a close association between the incidence, prognosis, and the patient's age as well as distal metastasis.

Later in the article, we contrasted our results with those of previous literature. The average age at diagnosis was 48.3 years (**Tables 3**, **4**), and the patients' ages spanned from 18 to 80 years. A statistically significant correlation was identified between influencing factors and mortality. Nevertheless, substantial differences in adjuvant therapy and the malignant ratio persisted between the literature groups and our study. Furthermore, the Logistic model analyses of overall survival in the literature and our study cases indicated that tumor metastasis, chemotherapy, and malignancy were independent risk factors, which concurred with the literature [6].

Strengths and Limitations: This study harbors several potential limitations. The number of clinical cases is restricted, and there is a pronounced imbalance in the numbers of benign and malignant cases. Consequently, the analysis results may be skewed. In subsequent investigations, we will augment the sample size, mitigate bias, and derive more comprehensive conclusions.

The strengths of this study encompass a meticulous analysis of 11 cases and a comparison of the disparities in clinical features between benign and malignant cases. Moreover, we compared and dissected our research findings with those in the literature, augmenting the scientific validity and reliability of our research inferences.

In summary, SO represents a rare subtype of ovarian teratoma. Preoperative diagnosis is frequently arduous as it lacks characteristic clinical manifestations and is not widely recognized. CA125 can serve as a tumor marker, although the specific mechanisms warrant further exploration. For patients with polycystic or solid ovarian tumors, preoperative attention should be paid to thyroid abnormalities, and thyroid function should be routinely examined. Serial measurement of serum thyroglobulin constitutes a sensitive and cost-effective follow-up tool. It is recommended to monitor these cases for a minimum of 10 years.

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Disclosure of conflict of interest

None.

Address correspondence to: Shizhang Yang and Jinjin Yu, Department of Obstetrics and Gynecology, Affiliated Hospital of Jiangnan University, Wuxi 214000, Jiangsu, P. R. China. E-mail: yangsz1986@126.com (SZY); yujjwx@126.com (JJY)

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