

## Case Report

# Struma ovarii simulating ovarian sertoli cell tumor: a case report with literature review

Yan Ning<sup>1,2</sup>, Fanbin Kong<sup>1</sup>, Janiel M Cragun<sup>3,4</sup>, Wenxin Zheng<sup>2,3,4</sup>

<sup>1</sup>Obstetrics & Gynecology Hospital, Fudan University, Shanghai, China; <sup>2</sup>Department of Pathology, University of Arizona College of Medicine, Tucson, AZ, USA; <sup>3</sup>Department of Obstetrics and Gynecology, University of Arizona, Tucson, AZ, USA; <sup>4</sup>Arizona Cancer Center, University of Arizona, Tucson, AZ, USA

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**Abstract:** Struma ovarii, as a monodermal variant of ovarian teratoma, constitutes about less than 3% of ovarian teratomas. It is difficult to be macroscopically recognized. Multiple appearances under microscope serve as another reason to mislead the accurate pathologic evaluation. Here, we report an unusual case of struma ovarii occurred in a 77 years old woman, which is currently known as the oldest age for this disease. The frozen section morphologically showed sex cord like elements and was suspicious for a sex-cord stromal tumor, probably a Sertoli cell tumor. Final pathological diagnosis was confirmed as struma ovarii based on the typical morphologic thyroid follicles and immunohistochemical staining results.

**Keywords:** Struma ovarii, sertoli cell tumor, ovary

## Introduction

Struma ovarii is the most common type of ovarian monodermal germ cell teratoma, accounting for nearly 3% of all ovarian teratoma [1]. Struma ovarii is defined by that the tumor is composed either entirely or predominantly (over 50%) of thyroid tissue [2, 3]. Struma ovarii is benign in general, although a few malignancy arising in the tumor has been reported [2]. It is well known that accurate diagnosis of struma ovarii is difficult pre-operatively due to its non-specific clinical presentation and rare incidence, particularly in elderly women. In addition, rare microscopic features such as paucity of typical thyroid follicles and presence of sex cord like elements can be problematic at the time of intra-operative consultation. We here report an unusual case of a 77-year-old woman with struma ovarii but morphologically showing sex cord like elements at the time of frozen section diagnosis.

## Case presentation

### Clinical information

A 77-year-old women with a history of gravida 4, para 4 was admitted to the University of Arizona

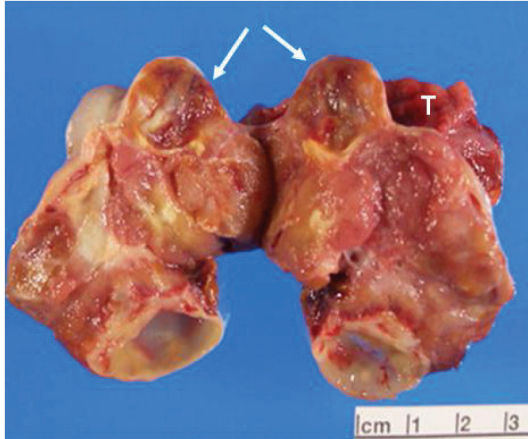
Medical Network. She initially complained of urinary incontinence and un-resolving hematuria and was referred to an urologist. CT scan revealed intracystic bladder masses and an incidental finding of a right adnexal mass. Specifically, the CT scan showed, in the right adnexa, an 8 x 5 x 5cm solid, soft tissue attenuation mass with some associated calcifications as well a 2.6 cm cystic component, and moderate pelvic ascites was noted. Serum level of CA125 was elevated at 521Units/ml, and CA19-9 was normal.

Her family history was negative for any type of cancer. Her medical history had included breast cancer post radiation and chemotherapy for 12 years and significant for a 30 pack year history of smoking, having stopped smoking 27 years prior to presentation.

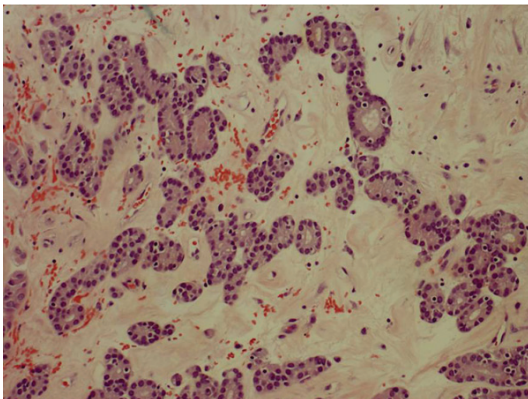
In physical examination, she had non-enlarged freely mobile uterus and palpable mass in lower right side of abdomen. No lymphadenopathy was detected in auxiliary, supraclavicular or inguinal regions.

Transurethral biopsy of the bladder mass revealed a high-grade urothelial carcinoma. Therefore, getting along with high-grade urothe-

## Struma ovarii simulating ovarian sertoli cell tumor

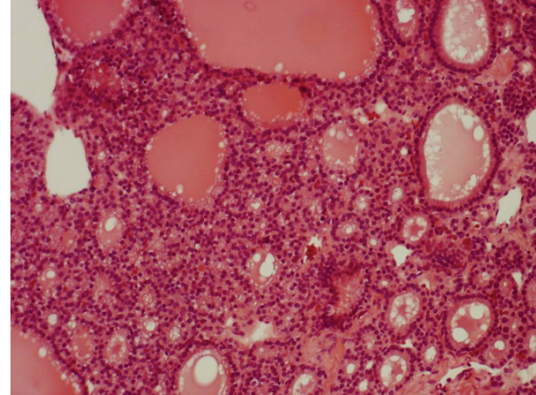


**Figure 1.** Gross finding of the struma ovarii. The tumor is mainly solid showing several nodules that were tan-brown and small areas as dark red (arrows) on cross section. One cyst containing clear straw-colored fluid is shown in the lower part of the figure. The fallopian tube (T) is unremarkable.



**Figure 2.** Microscopic findings of struma ovarii mimicking sex cord like element. Some area of the tumor shows a clear tubular growth pattern, which is lined by single layer of cuboidal cells without significant nuclear atypia 100x.

lial carcinoma, the patient underwent total hysterectomy, bilateral salpingo-oophorectomy, cystectomy, pelvic and periaortic node dissection, omentectomy and peritoneal biopsies. Intra-operatively, there was about 800 ml amber-colored fluid, which was sent for cytological examination. The uterus and left ovary were normal in size. There was an 8 cm in greatest dimension mass on her right ovary that was resected and sent for the frozen section evaluation. The frozen section diagnosis was suspicious for a sex-cord stromal tumor, probably a Sertoli cell tumor.



**Figure 3.** Classic microscopic presentation of struma ovarii. Colloid-containing follicles with varying sizes are seen 100x.

### Pathological finding

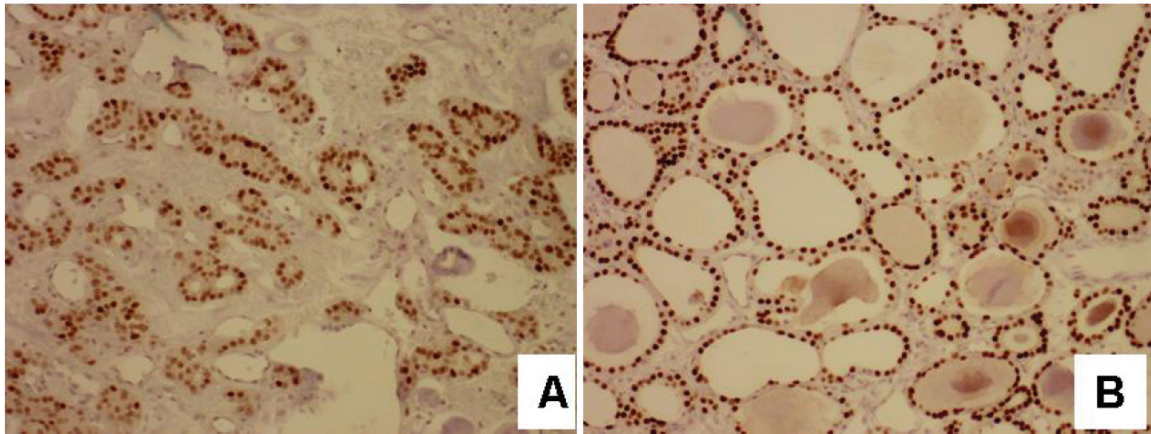
#### Gross features

The right ovarian mass was a solid and cystic tumor measuring 9.0×7.0×5.0cm and had intact and smooth external surface. Cut section (**Figure 1**) showed that the tumor was predominantly (about 75%) solid with several nodules, which appeared majority as tan-brown and small areas as dark red (arrows) in color. The nodules were partially separated by gray whitish fibrous tissue. There were a few cystic spaces filling with yellow-brown or straw-colored fluid. Focal area of calcification was present. Right fallopian tube (T) appeared no abnormality. Left ovary was normal in size and cut section showed a few small cystic structures. Left fallopian tube and uterus were unremarkable.

#### Microscopic and immunohistochemical features

Microscopically, approximately 30% of the tumor including frozen sections showed unusual histological appearance. These included numerous hollow tubules (**Figure 2**) and some semi-solid pseudotubular structures (picture not shown). These tubule-like structures were lined by single layer of cuboidal cells. Some of them contained moderate amount of pale eosinophilic serous like fluid, while others showed empty spaces in the lumen. No significant nuclear atypia was seen.

On the other hand, more classic thyroid follicular structures came out in the remaining sections. These included thyroid follicles of various



**Figure 4.** Immunohistochemical staining of TTF-1 in struma ovarii. TTF-1 is strongly positive in both the Sertoli-like areas (A) and the classic thyroid follicles (B) 100×.

sizes ranging from less than 1 mm to a few mm. Microfollicular pattern was dominant. Majority follicles contained eosinophilic reddish colloid secretions (**Figure 3**). Occasional hollow tubule-like structures were present in those thyroid follicle predominant areas. Cytologically, the tumor cells had uniform oval nuclei without significant nuclear atypia. Nucleoli were sometimes prominent and mitotic figures were not easily identified. In addition, sporadic lymphocytes and fibrous stroma, some of them with dystrophic calcifications were present. One of the small cystic structures from left ovary was filled with keratin debris and sebaceous material without cellular components.

#### Immunophenotype of the tumor mass

Immunohistochemistry was performed and demonstrated diffuse strongly positive for thyroglobulin and TTF-1 (**Figure 4**), negative for inhibin, calretinin, CD99 and others. The immunostaining results are listed in **Table 1**.

#### Final diagnosis

Final pathological diagnosis was made based on the above morphologic and immunohistochemical staining results. The right ovary was a struma ovarii and the left ovary contained an incidental microscopical dermoid cyst. The uterus, fallopian tube, pelvic and periaortic lymph nodes and omentum were histologically unremarkable. Cytological evaluation for peritoneal fluid revealed reactive mesothelial cells without malignant cells.

#### Discussion

Mature cystic teratomas account for approximately 20% of all ovarian tumors. Of these, approximately 15% contain normal thyroid tissue. Struma ovarii, as a monodermal variant of ovarian teratoma, was first described by Boettlin in 1889 and Gottschalk in 1899 [4]. It constitutes about less than 3% of ovarian teratomas. Although thyroid tissue can be identified histologically in up to 20% of cases of mature cystic teratoma, it is difficult to be macroscopically recognized [2]. Multiple appearances under microscope serve as another reason to mislead the accurate pathologic evaluation. The age distribution of patients with struma ovarii ranges from 6 to 74 years with average age of 40s and the peak age at 50s. It is rare in elderly women or in prepubertal girls [2, 5]. There were only a few cases of struma ovarii reported in age 70s [4, 6, 7]. Here, we describe a case of struma ovarii occurred in a 77 years old woman, which is currently known as the oldest age for this disease.

Tumors of struma ovarii are typically unilateral, ranging from 4 to 25 cm with an average of 12 cm in size. Macroscopic appearance typically shows solid and cystic structures with red-brown or tan or yellowish in color in the solid area, while clear to green-brown fluid in cystic spaces. Microscopic examination on lower power shows a diffuse pattern of tumor cells distributed by typically small numbers of the thyroid follicles, usually microfollicle separated by fibrous septae. The microfollicle usually con-



## Struma ovarii simulating ovarian sertoli cell tumor

**Table 1.** Immunophenotype of the tubular and follicular structures of right ovarian tumor

	Tubular Structures	Follicular Structures
Inhibin	negative	negative
Calretinin	negative	negative
CD99	negative	negative
GFAP	negative	negative
CK7	diffusely positive	diffusely positive
TTF-1	diffusely positive	diffusely positive
Thyroglobulin	diffusely positive	diffusely positive

tain eosinophilic colloid. The tumor cells usually have moderate amount of eosinophilic cytoplasm, uniform oval nuclei without pleomorphism, conspicuous nucleoli, and sporadic mitotic figures [2, 8].

When a struma ovarii shows all the above pathologic features, it is hard to miss the diagnosis. However, diagnostic problem is frequently encountered when presence of paucity of the classic histologic features and at the same time showing unusual microscopic findings, particularly in an elderly patient from whom struma ovarii is extremely rare. In our case, the initial pathologic presentation was mainly a solid tumor with several large nodules and microscopically showed many hollow tubules with some pseudotubular appearance and eosinophilic cytoplasm as well as secretions. A wide spectrum of differential diagnosis should be considered in that setting. These included tubule containing sex-cord stromal tumors, epithelial carcinomas with tubular cystic structures such as clear cell carcinoma, tumors with abundant eosinophilic cytoplasm and secretions such as yolk sac tumor, and ovarian metastatic cancers [2, 8]. Among the entities in the differential diagnosis list, Sertoli cell tumor diagnosis at the frozen section time seemed more logic than the others. This impression turned out to be a wrong diagnosis when typical histologic features of thyroid follicles appeared on permanent sections and confirmed by immunostaining.

Morphological variations of struma ovarii leading to the misdiagnosis as a Sertoli cell tumor have been occasionally reported [2, 5, 8, 9]. Based on information from the literature and experience of our own from this case, we think the following points may help us to avoid potential mistakes in future. First, careful gross examination by finding the dark-red thyroid like

tissue, even in a less dominant amount, should raise a concern of struma ovarii. Second, additional sections with various gross appearances at the frozen section time are necessary to consolidate the diagnostic process whenever the diagnosis is uncertain. Third, microscopic clues to the correct diagnosis of struma ovarii also include that unusual histologic patterns are commonly associated with typical thyroid follicles in cystic wall or fibrous septae or associated with components of mature cystic teratoma in focal areas. Finding such areas through examining more sections will certainly aid the diagnosis. In a few problematic cases, a panel of immunohistochemical markers such as inhibin and thyroglobulin or TTF-1, which show opposite results will help to secure the diagnosis [10]. Fourth, age distribution is an important parameter for the diagnosis. However, pathologist should pay more attention to the observed facts to formulate the diagnosis since tumors commonly present in an unexpected way.

Malignant transformation is rare, occurring in 0.3% to 5% of all struma ovarii tumors [1, 11]. The diagnostic criterion of malignant struma ovarii is the same as that in thyroid carcinoma [12, 13]. Although not yet uniformly defined, these criteria include cellular atypia and increased cellular proliferation, nuclear pleomorphism, mitotic activity, and vascular and/or capsular invasion. Recently, Shaco-Levy et al. found that the clinical outcome of struma ovarii could not be predicted based on the microscopic diagnosis of thyroid tissue or on specific histologic features [14]. The most common form of thyroid malignancy in a struma ovarii is papillary followed by follicular thyroid carcinoma. Peritoneal dissemination or recurrence of either papillary or follicular carcinoma from a struma ovarii is rare, too. Distant metastasis is extremely uncommon in malignant struma cases [1, 2]. In our case, there were no patho-

logic findings of above mentioned malignant changes. Therefore, malignancy was ruled out.

The cell origin of teratomas has been a matter of interest for a long time. It is believed that ovarian mature cystic teratoma arises from a single germ cell after the first meiotic division [15]. This theory has been widely accepted mainly because of the following facts. The main location of the teratomas occurs predominantly along the line of migration of the primordial germ cells from the yolk sac to the primitive gonad. These tumors occur most commonly in reproductive aged women, when germ cell activity is at peak. People believe that struma ovarii derives from germ cells. However, it is completely unknown how this teratoma comprises only thyroid tissue without other germ layer derived components. In the present case, the uniqueness of the struma ovarii occurred in a 77 year old patient and microscopically a dermoid cyst found in the contralateral ovary. The best interpretations of such finding probably remain incidental. Hopefully, molecular studies with a large number of such cases may shed insights of its histogenesis.

In summary, although struma ovarii may exhibit a wide spectrum of histologic changes, which likely mislead pathologic diagnosis, understand those unusual pathologic presentations, careful examinations of the specimen with possible additional sections will certainly improve the accuracy of diagnosis. Immunohistochemical staining for thyroglobulin and/or TTF-1 is useful to aid the diagnosis when a morphologic appearance is ambiguous.

**Address correspondence to:** Dr. Yan Ning, Obstetrics & Gynecology Hospital, Fudan University, No. 419 Fang Xie Road, Shanghai, 200011, China. Tel: +8602133189900; E-mail: nyiping@yahoo.com.cn

## References

- [1] Garcia A, Castellvi J, Lopez M, Gil A, de la Torre J, Ramon y Cajal S. Malignant struma ovarii mimic clear cell carcinoma. *Arch Gynecol Obstet* 2005; 271: 251-255.
- [2] Roth LM, Talerma A. The enigma of struma ovarii. *Pathology* 2007; 39: 139-146.
- [3] Selvaggi SM. Tumors of the ovary, maldeveloped gonads, fallopian tube, and broad ligament. *Arch Pathol Lab Med* 2000; 124: 477.
- [4] Yoo SC, Chang KH, Lyu MO, Chang SJ, Ryu HS, Kim HS. Clinical characteristics of struma ovarii. *J Gynecol Oncol* 2008; 19: 135-138.
- [5] Roth LM, Talerma A. Recent advances in the pathology and classification of ovarian germ cell tumors. *Int J Gynecol Pathol* 2006; 25: 305-320.
- [6] Loizzi V, Cappuccini F, Berman ML. An unusual presentation of struma ovarii mimicking a malignant process. *Obstet Gynecol* 2002; 100: 1111-1112.
- [7] Mui MP, Tam KF, Tam FK, Ngan HY. Coexistence of struma ovarii with marked ascites and elevated CA-125 levels: case report and literature review. *Arch Gynecol Obstet* 2009; 279: 753-757.
- [8] Szyfelbein WM, Young RH, Scully RE. Struma ovarii simulating ovarian tumors of other types. A report of 30 cases. *Am J Surg Pathol* 1995; 19: 21-29.
- [9] Oliva E, Alvarez T, Young RH. Sertoli cell tumors of the ovary: a clinicopathologic and immunohistochemical study of 54 cases. *Am J Surg Pathol* 2005; 29: 143-156.
- [10] McCluggage WG, Young RH. Immunohistochemistry as a diagnostic aid in the evaluation of ovarian tumors. *Semin Diagn Pathol* 2005; 22: 3-32.
- [11] Gould SF, Lopez RL, Speers WC. Malignant struma ovarii. A case report and literature review. *J Reprod Med* 1983; 28: 415-419.
- [12] Boutross-Tadross O, Saleh R, Asa SL. Follicular variant papillary thyroid carcinoma arising in struma ovarii. *Endocr Pathol* 2007; 18: 182-186.
- [13] Devaney K, Snyder R, Norris HJ, Tavassoli FA. Proliferative and histologically malignant struma ovarii: a clinicopathologic study of 54 cases. *Int J Gynecol Pathol* 1993; 12: 333-343.
- [14] Shaco-Levy R, Peng RY, Snyder MJ, Osmond GW, Veras E, Bean SM, Bentley RC, Robboy SJ. Malignant struma ovarii: a blinded study of 86 cases assessing which histologic features correlate with aggressive clinical behavior. *Arch Pathol Lab Med* 2012; 136: 172-178.
- [15] Linder D, McCaw BK, Hecht F. Parthenogenic origin of benign ovarian teratomas. *N Engl J Med* 1975; 292: 63-66.