

Case Report

# The Smallest Reported Malignant Struma Ovarii: A Case Report

Nobuko Yasutake<sup>a</sup> Hirotsugu Noguchi<sup>b</sup> Yuta Ibayashi<sup>c</sup>  
Hiroaki Nakamura<sup>d</sup> Kazuki Tateishi<sup>d</sup> Kotaro Yuki<sup>a</sup> Ryuji Shiina<sup>a</sup>  
Shohei Shimajiri<sup>b</sup> Takuji Fujita<sup>a</sup>

<sup>a</sup>Department of Gynecology and Obstetrics, Tagawa Municipal Hospital, Fukuoka, Japan;

<sup>b</sup>Department of Pathology, University of Occupational and Environmental Health,

Kitakyushu, Japan; <sup>c</sup>Department of Internal Medicine, Kyushu University Beppu Hospital,

Oita, Japan; <sup>d</sup>Department of Clinical Laboratory, Tagawa Municipal Hospital,

Fukuoka, Japan

## Keywords

Struma ovarii · Malignant papillary thyroid carcinoma · *BRAF*

## Abstract

**Introduction:** Malignant struma ovarii is a rare neoplasm. It is usually asymptomatic and not commonly diagnosed preoperatively. In addition, there is currently no established diagnostic and therapeutic approach for malignant struma ovarii. **Case Report:** A 66-year-old asymptomatic female was referred to our hospital. Computed tomography showed the presence of a well-defined mass with enhancement in the internal and peripheral areas. The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, and partial omentectomy. Histopathology revealed the presence of a papillary thyroid carcinoma arising from a 2.5-cm-diameter struma ovarii (malignant struma ovarii). According to the criteria of the International Federation of Gynecology and Obstetrics, the patient had stage IA disease. Subsequently, she underwent a thyroid scan with normal findings. At the 3-month follow-up, the patient was alive, in good clinical condition, and disease free. **Conclusion:** In this report, we present the smallest malignant struma ovarii reported so far in the literature. Because of the

rarity of these tumors and the lack of firm prognostic factors, the treatment decision should be customized for each patient according to the pathological and clinical parameters.

© 2018 The Author(s)  
Published by S. Karger AG, Basel

## Introduction

Struma ovarii is a rare ovarian neoplasm categorized as a monodermal teratoma and is composed, either exclusively or predominantly, of thyroid tissue [1]. These lesions represent 0.5–1% of all ovarian tumors and 2–5% of ovarian teratomas [2]. Most cases of typical struma ovarii are benign [1]. Malignant transformation of struma ovarii is mainly reported in the fifth and sixth decades of a patient's life as a unilateral adnexal mass, often located on the left side [3, 4]. The size of the tumors ranges from 3 to 20 cm [4–6], and it is most frequently associated with follicular variants of papillary thyroid carcinoma (54%) and papillary thyroid carcinoma (21%) [4]. In addition, up to 92% of patients are euthyroid [3]. Hyperthyroidism is found in the remaining patients (approximately 8%); however, even in these patients, signs or symptoms of thyrotoxicosis may be absent [3].

Currently, there is no established diagnostic and therapeutic approach for malignant struma ovarii. In this report, we present a case of a small malignant struma ovarii along with a review of the literature including clinicopathological features, diagnosis, and management.

## Case Presentation

An asymptomatic 66-year-old female (gravida 0) presented with an incidental finding of a 2.7-cm-diameter ovarian tumor during an obstetric examination 3 years prior to admission. The patient was referred to the hospital for further evaluation. Although she had intellectual disability, she was in good physical health. Of note, she had been postmenopausal for 16 years. Her past medical history included left partial mastectomy and radiation for stage I breast cancer (invasive ductal carcinoma) 2 years prior to admission. Examination using transvaginal ultrasound showed the presence of a small solid and cystic mass with a diameter of 3.5 cm in the right ovary. Contrast-enhanced computed tomography revealed a well-defined mass with slight enhancement in the internal and peripheral areas of the right adnexa. There was no lymphadenopathy or peritoneal dissemination. Sedation was deemed challenging for this patient; thus, magnetic resonance imaging was not performed. The serum levels of CA125, CEA, CA19-9, and SCC were within the normal range. However, the presence of malignancy could not be ruled out.

The patient underwent laparotomy with total hysterectomy, bilateral salpingo-oophorectomy, and partial omentectomy. Intraoperatively, the right ovary was converted into a 2.5-cm multiloculated mass with a solid component (Fig. 1a), which was not adherent to other organs. The presence of 7 mL of clear yellowish ascitic fluid was observed. Findings in the uterus and left adnexa were unremarkable. There were no enlarged lymph nodes, metastasis, or disseminated lesions in the intraperitoneal organs.

Histological sections demonstrated a 2.5-cm-diameter struma ovarii characterized (>60%) by the classic features of a well-differentiated papillary thyroid carcinoma (tumor size: 1 cm) (Fig. 1b). The lesion was characterized by the formation of crowded, branching papillae lined by abnormal thyroid follicular cells (Fig. 1c). These cells exhibited enlarged, irregular nuclei with pale (optically clear) chromatin, nuclear grooves, and intranuclear

cytoplasmic invaginations (Fig. 1d). Mitotic figures were <1 per 10 high-power fields. The presence of necrosis and marked cell atypia was not evident. Moreover, there was no histological evidence of other germ cell elements or vascular, lymphatic invasion. The thyroid adenomatous lesion was evident in the right fallopian tube, but the carcinomatous lesion was not observed. The papillary thyroid carcinoma was confined to the right ovary. The left adnexa, omentum, uterus, and ascitic fluid were negative for malignancy. Immunohistochemical staining showed that the tumor was positive for thyroglobulin (Fig. 2a), thyroid transcription factor-1 (Fig. 2b), and *BRAF* V600E (Fig. 2c).

The serum levels of thyroglobulin were >500 ng/mL 3 h after surgical resection of the ovarian mass. Thyroid function tests (thyroid-stimulating hormone: 0.58  $\mu$ IU/mL, free T3: 2.53 pg/mL, free T4: 1.16 ng/mL) and the levels of thyroglobulin and thyroid peroxidase antibodies were within the normal range. Thyroid ultrasonography did not reveal the presence of a nodule. Following the operation, the patient underwent whole-body fluorodeoxyglucose positron emission tomography-computed tomography to investigate the possibility of lymph node or distant metastasis. The results of this analysis did not show the presence of metastasis.

According to the criteria established in 2014 by the International Federation of Gynecology and Obstetrics, the patient was diagnosed with stage IA ovarian carcinoma (pT1aNxM0) also termed malignant struma ovarii. One month after the operation, the levels of thyroglobulin returned to normal. At the 3-month follow-up, there was no evidence of recurrence. We therefore decided to carefully perform thyroglobulin monitoring.

## Discussion

Struma ovarii lesions may be benign or malignant. The distinction between them is challenging because of the rarity of these lesions and the lack of uniform criteria [1]. However, most studies advocate the diagnosis of struma ovarii based on the histopathological criteria of entopic thyroid carcinoma, i.e., “ground glass” overlapping nuclei and nuclear grooves, or mitotic activity and vascular invasion [7]. In the present case, the diagnosis was based on these criteria. In previous reports, the size of malignant struma ovarii tumors ranged from 3 to 20 cm [4–6]. In this case, the size of the tumor was merely 2.5 cm. This is the smallest malignant struma ovarii tumor reported so far in the literature.

Similar to entopic thyroid carcinoma, papillary thyroid carcinoma arising from struma ovarii is associated with a good prognosis. The 5- and 25-year survival rates were shown to be 92 and 79%, respectively [8]. Shaco-Levy et al. [9] reported that histopathological predictors of a poor prognosis are tumor size of  $\geq 10$  cm, >80% of the stromal tissue affected by carcinoma, presence of necrosis,  $\geq 5$  mitoses per 10 high-power fields, and marked cell atypia. DeSimone et al. [4] and Jean et al. [10] recommended the use of thyroidectomy as an adjunct to radioactive iodine ( $I^{131}$ ) therapy in the first-line management following surgery. The absence of a primary lesion in the thyroid is necessary to exclude metastatic thyroid carcinoma to the ovary. This is a reasonable approach considering that  $I^{131}$  therapy is used to reduce the risk of recurrence in cases with entopic thyroid carcinoma. However, there is controversy regarding the therapeutic approach for the management of malignant struma ovarii. Given the favorable prognosis typically associated with this disease, our case had no poor prognostic factors. Therefore, we decided to monitor the levels of thyroglobulin without performing thyroidectomy or introducing adjuvant therapy.

*BRAF* is the strongest activator of the downstream MAPK signaling pathway. The constitutive activation of this pathway leads to tumorigenesis [11]. Multiple molecular abnormalities have been described in thyroid carcinomas arising from ovarian teratomas, including *BRAF* mutations and *RET/PTC* rearrangements, as observed in patients with entopic papillary thyroid carcinoma [1]. Schmidt et al. [12] have reported that *BRAF* V600E mutations were present in 2 of 6 (33%) cases of malignant struma ovarii. Zhang et al. [13] demonstrated a high concordance between immunohistochemistry and molecular methods for detecting *BRAF* V600E mutations in formalin-fixed and paraffin-embedded tissues of entopic papillary thyroid carcinoma. Our case was positive for *BRAF* V600E on immunohistochemistry. In entopic papillary thyroid carcinoma, *BRAF* mutations are associated with poorer clinicopathological outcomes and may independently predict disease recurrence [14]. However, so far, there are no studies demonstrating a correlation between the *BRAF* mutational status and clinical behavior in malignant struma ovarii. Investigation of additional cases is warranted to examine this relationship.

Makani et al. [15] reported that disease recurrence was observed after an average of 4 years. Although the present patient did not undergo thyroidectomy or adjuvant therapy, long-term monitoring of the levels of thyroglobulin is necessary.

## Conclusions

Malignant struma ovarii is a rare gynecological tumor most often diagnosed through histological analysis after surgery for suspected ovarian masses. We present the smallest malignant struma ovarii reported so far in the literature. This case also emphasizes the importance of operation for diagnosis. However, currently, there is no established therapeutic approach for the management of malignant struma ovarii. Further study is necessary to establish a uniform therapeutic approach.

## Acknowledgement

The authors thank H. Yanai (Okayama University, Okayama) and Y. Nozaki (Tagawa Municipal Hospital). The authors would like to thank Enago (www.enago.jp) for the English language review.

## Statement of Ethics

The authors have no ethical conflicts to disclose.

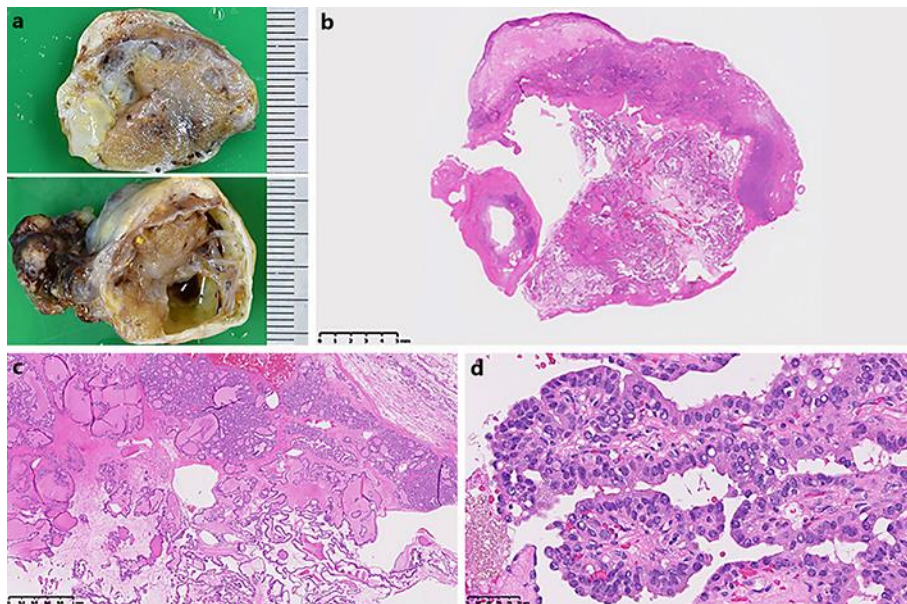
## Disclosure Statement

All authors declare that there is no conflict of interest regarding the publication of this paper.

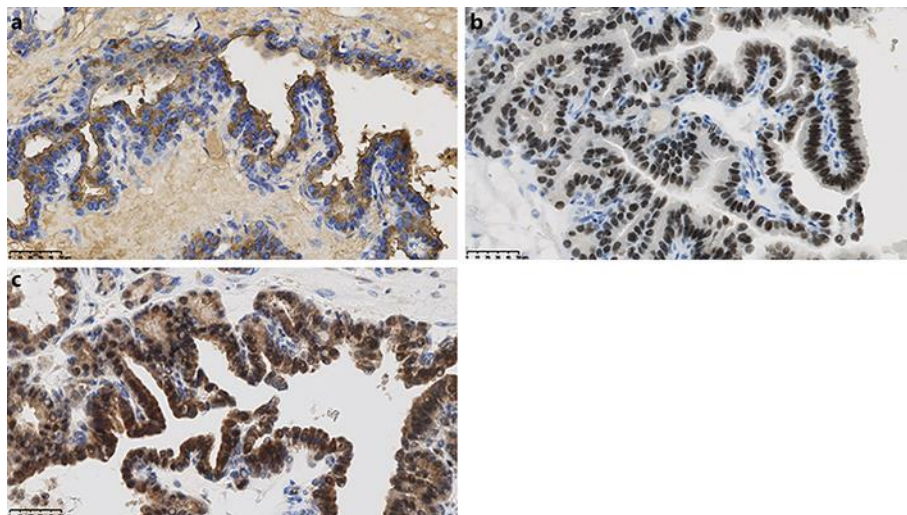
## References

- 1 Prat J, Nogales FF, Cao D, Vang R, Carinelli SG, Zaloudek CJ. Monodermal teratomas and somatic type tumors arising from a dermoid cyst. In: Kurman RJ, Carcangiu ML, Herrington CS, Young RH, editors. WHO Classification of Tumours of Female Reproductive Organs. Lyon: IARC Press; 2014. pp. 63–6.
- 2 Yoo SC, Chang KH, Lyu MO, Chang SJ, Ryu HS, Kim HS. Clinical characteristics of struma ovarii. *J Gynecol Oncol*. 2008 Jun;19(2):135–8.
- 3 Matsuda K, Maehama T, Kanazawa K. Malignant struma ovarii with thyrotoxicosis. *Gynecol Oncol*. 2001 Sep;82(3):575–7.
- 4 DeSimone CP, Lele SM, Modesitt SC. Malignant struma ovarii: a case report and analysis of cases reported in the literature with focus on survival and I131 therapy. *Gynecol Oncol*. 2003 Jun;89(3):543–8.
- 5 Oudoux A, Leblanc E, Beaujot J, Gauthier-Kolesnikov H. Treatment and follow-up of malignant struma ovarii: regarding two cases. *Gynecol Oncol Rep*. 2016 Aug;17:56–9.
- 6 Zhu Y, Wang C, Zhang GN, Shi Y, Xu SQ, Jia SJ, et al. Papillary thyroid cancer located in malignant struma ovarii with omentum metastasis: a case report and review of the literature. *World J Surg Oncol*. 2016 Jan;14(1):17.
- 7 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 Oct;12(4):333–43.
- 8 Barrera JR, Manalo LA, Ang FL. Papillary thyroid-type carcinoma arising from struma ovarii. *BMJ Case Rep*. 2012 Jul 11;2012. pii: bcr0320126145.
- 9 Shaco-Levy R, Bean SM, Bentley RC, Robboy SJ. Natural history of biologically malignant struma ovarii: analysis of 27 cases with extraovarian spread. *Int J Gynecol Pathol*. 2010 May;29(3):212–27.
- 10 Jean S, Tanyi JL, Montone K, McGrath C, Lage-Alvarez MM, Chu CS. Papillary thyroid cancer arising in struma ovarii. *J Obstet Gynaecol*. 2012 Apr;32(3):222–6.
- 11 Davies H, Bignell GR, Cox C, Stephens P, Edkins S, Clegg S, et al. Mutations of the BRAF gene in human cancer. *Nature*. 2002 Jun;417(6892):949–54.
- 12 Schmidt J, Derr V, Heinrich MC, Crum CP, Fletcher JA, Corless CL, et al. BRAF in papillary thyroid carcinoma of ovary (struma ovarii). *Am J Surg Pathol*. 2007 Sep;31(9):1337–43.
- 13 Zhang X, Wang L, Wang J, Zhao H, Wu J, Liu S, et al. Immunohistochemistry is a feasible method to screen BRAF V600E mutation in colorectal and papillary thyroid carcinoma. *Exp Mol Pathol*. 2018 Aug;105(1):153–9.
- 14 Xing M, Westra WH, Tufano RP, Cohen Y, Rosenbaum E, Rhoden KJ, et al. BRAF mutation predicts a poorer clinical prognosis for papillary thyroid cancer. *J Clin Endocrinol Metab*. 2005 Dec;90(12):6373–9.
- 15 Makani S, Kim W, Gaba AR. Struma Ovarii with a focus of papillary thyroid cancer: a case report and review of the literature. *Gynecol Oncol*. 2004 Sep;94(3):835–9.





**Fig. 1.** Macroscopic and microscopic views of the papillary thyroid carcinoma in the struma ovarii. **a** On gross examination, the resected right ovary shows a multilocular cyst with a solid area. Malignant struma ovarii with classic variant papillary thyroid cancer. Areas of normal or adenomatous differentiation (**b**, top) and classic papillary thyroid carcinoma (**b**, bottom). Epithelial cells lining papillary structures (**c**) with nuclear grooves and intranuclear inclusion bodies (**d**) characteristic of the tumor. **b–d** HE. **b** Loupe. **c** ×25. **d** ×400.



**Fig. 2.** Immunohistochemical staining of malignant struma ovarii. Thyroglobulin (**a**), thyroid transcription factor-1 (**b**), and *BRAF* V600E (**c**) -positive staining with ×400 magnification.