

Follicular variant of thyroid papillary carcinoma arising from ovarian mature cystic teratoma: a case report

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Summary

Malignant transformation of mature cystic teratoma of the ovary occurs very rarely. As reported in previously published literature, the incidence of malignant transformation is less than 2%. Among them, squamous cell carcinoma is the most common neoplasm; however, a follicular variant of thyroid papillary carcinoma arising from mature cystic teratoma is extremely rare. Here, I have reported a case of a follicular variant of thyroid papillary carcinoma arising from a mature ovarian cystic teratoma. A 65-year-old woman presented to our hospital for an incidentally detected ovarian mass. The patient underwent laparoscopic salpingo-oophorectomy for a suspicion of benign ovarian mass. Postoperative pathologic examination revealed a follicular variant of papillary carcinoma arising in the thyroid tissue of a mature ovarian cystic teratoma. Therefore, this case highlights that there is a possibility of an unusual but malignant transformation in ovarian teratoma.

Key words: Mature cystic teratoma; Papillary thyroid carcinoma; Ovarian neoplasm.

Introduction

Mature cystic teratoma (MCT) is the most common germ cell tumor of the ovary, which comprises 10%-20% of all ovarian tumors [1]. Most MCTs are benign tumors and occur at reproductive age. However, malignant transformation of MCT can develop very rarely and is reported in only 1%-2% of cases [2, 3]. It occurs mainly in postmenopausal women, with an average age of 45-60 years [4]. Symptoms of malignant transformation of MCT are not typical and difficult to diagnose before surgery. Malignant transformation can occur in various histologic types. Of these, 80% and 7% become malignant changes with squamous cell carcinoma and adenocarcinoma, respectively [5, 6]. Although several studies of malignant transformation in MCT have been published, a follicular variant of thyroid papillary carcinoma (FVTPC) arising from ovarian MCT is extremely rare, with only few cases reported. Here, we have described a case of FVTPC arising in ovarian MCT, which was small before surgery and showed no significant examination findings.

Case Report

A 65-year-old, gravida 6, and para 5 woman was referred to our gynecologic oncology department from a local clinic with incidentally detected adnexal mass by pelvic computed tomography (CT). She had a cervical polypectomy history 3 years ago, but no specific medical history. The patient's body mass index was 28.3 kg/m². Pelvic examination revealed no specific symptoms, and transvaginal ultrasonography showed a solid and cystic lesion measuring 2.4 × 3.0 cm. Serum CA-125 was 12.1 U/mL, and ROMA test was 9.73%. Both tests were within normal range. The serum thyroid-stimulating hormone and free T4 levels were within

normal limits, but the serum total T3 level was slightly increased to 3.44 nmol/L (normal range: 1.2-2.8 nmol/L). The CT scan image, which was read back at our hospital, indicated that a 2.5-cm benign tumor was observed in the right adnexa (Figure 1). The test result suggested benign tumor, but the patient had severe anxiety; therefore, laparoscopic salpingo-oophorectomy was performed. During the operation, no specific findings such as nodular lesion or ascites were seen in the pelvic and intra-abdominal cavity. Moreover, a right ovarian tumor measuring 3 cm was revealed. Frozen biopsy was not performed due to strong suggestion of benign nature. The ovarian surface was smooth, and no evidence of malignancy was observed. Macroscopically, the tumor was 4.0 × 2.3 cm in size, and brown nodules were observed inside the tumor (Figure 2). Microscopic examination revealed mature cystic teratoma with atypical thyroid tissues. The nodular areas of the tumors measured 1.2 × 0.9 cm and 0.6 × 0.5 cm, and the tumor cells were arranged as microfollicles with central colloid. The tumor cell nucleus was large and showed a ground-glass appearance (Figure 3A). There was no extra-ovarian extension of tumor cells. In addition, lymphovascular space and perineural invasions were not observed. Immunohistochemistry demonstrated focal membrane staining with HBME-1 (Figure 3B) and strong positivity for TTF1 seen in tumor cells (Figure 3C). Morphology and immunohistochemistry results were consistent with FVTPC. The patient was discharged without any complication 2 days after surgery. Based on the biopsy results, Positron Emission Tomography-Computed Tomography (PET-CT) was performed. No specific findings were observed in PET-CT other than the old inflammatory nodule in the left lung (Figure 4). The patient is undergoing regular follow up without any specific symptoms for 3 months.



Figure 1. – Contrast-enhanced computed tomography scan shows a heterogeneously enhancing solid mass measuring 2.5 cm.

Discussion

Most MCTs are benign tumors that occur at reproductive age. MCTs consist of well-differentiated derivatives of three germ layers known as the ectoderm, mesoderm, and endoderm. It has been reported that approximately 15% of MCTs contain thyroid tissue [7]. Complications of mature cystic teratomas include torsion, malignant transformation, rupture, and infection. Malignant transformation of MCT tended to occur at postmenopausal age, with a median age at diagnosis of 51.6-61.5 years [8-12]. Other malignant transformations include squamous cell carcinoma, adenosquamous cell carcinoma, melanoma, sarcoma, basal cell carcinoma, and undifferentiated carcinoma. However, FVTPC arising in MCT of the ovary is extremely rare. The presence of thyroid tissue in the ovaries was first described by Von Kahlden in 1895 [13]. Papillary thyroid cancer (PTC) arising from ovarian teratomas is a rare occurrence, with an estimate of 0.1%-0.3% [14]. In 2012, a literature re-

view of PTC cases in teratoma was published by Dane *et al.* [15]. There were 15 cases in total, and 3 cases were reported after according to the English literature on PubMed [16-18]. PTC occurring in MCTs, excluding that occurring in the struma ovarii, is very rare. Malignant transformation of the thyroid tissue in MCT can be divided into three types of histopathology [19]. The most common type is PTC (44%), and other histologic types are follicular carcinoma (30%) and FVTPC (26%).

Clinical manifestations of this disease include abdominal pain, vaginal bleeding, abdominal discomfort, and palpable mass. However, there is no specific symptom to be observed in the malignant transformation of MCT. According to the cases of PTC arising in MCT, abdominal pain and bleeding were mostly observed, and only 3 cases were incidentally found as in our case.

Most malignant transformations are usually histologically diagnosed after surgery. The imaging features of

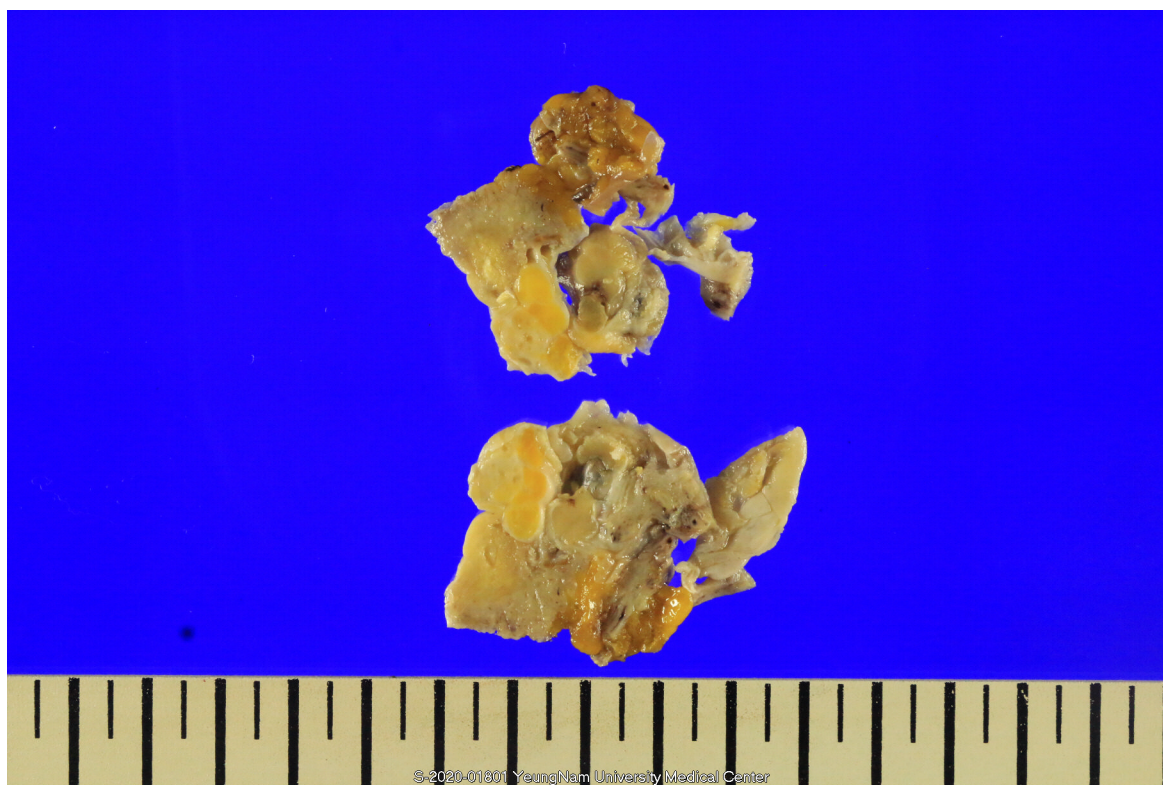


Figure 2. – The postoperative gross appearance of the right ovarian tumor. The tumor has brown nodules inside measuring 4 cm in diameter.

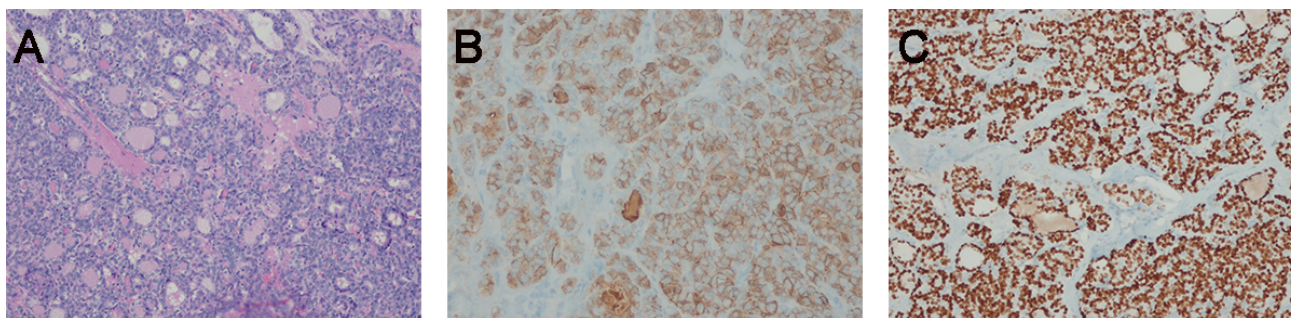


Figure 3. – (A) The size of the tumor nucleus is large and shows a ground-glass appearance (H&E, $\times 100$). (B) Tumor cells show focal positive for HBME-1 staining. (C) Strong positivity for TTF1 seen in tumor cells.

MCT with malignant transformation have been difficult to diagnose. This is because the imaging features of malignant transformation are not prominent. According to Park *et al.*, approximately 82% of malignant transformation of MCTs showed soft tissue, and 89% of tumors with soft tissue showed obtuse angle between the soft tissue and inner wall cyst [20]. In addition, the maximum diameter of the tumor exceeded 9.9 cm in 82% of patients aged 45 years or older [20]. Furthermore, there is no sensitive tumor marker to diagnose for malignant transformation of MCT. However, there have been reports that SCC antigen may help diagnose squamous cell carcinoma arising in MCT. SCC antigen is a useful tumor marker for diagnosing and monitoring cervical squamous cell carcinoma. Tseng *et al.* reported

that 67% (16/24) of patients with squamous cell carcinoma arising in MCTs exceeded the SCC antigen level of 2 ng/mL [9]. It is helpful to follow up the thyroglobulin level to diagnose metastasis or recurrence of PTC arising in MCT [21]. Because thyroglobulin is produced in the thyroid tissue, it can be traced to predict metastasis or recurrence when the serum level changes. However, if thyroidectomy is not performed, it may be ambiguous to diagnose the recurrence or metastasis. Therefore, in patients undergoing thyroidectomy, it seems desirable to follow the thyroglobulin level as well as the anti-thyroglobulin antibody [17].

There is no gold standard for treatment because the malignant transformation of MCT is very rare. However, in the case of postmenopausal women, hysterectomy with both



Figure 4. – No specific findings are observed in PET-CT images other than the old inflammatory nodule of the left lung.

salpingo-oophorectomies is most desirable. Furthermore, if fertility sparing is required, follow-up observation after unilateral salpingo-oophorectomy appears to be desirable without capsular metastasis [17].

The long-term prognosis of papillary thyroid carcinoma arising from mature cystic teratoma is unclear, with a limited number of reports on follow-up time (6-33 months) [18]. However, for stage 1 squamous cell carcinoma arising in MCT, the 5-year survival rate was reported to be 93% (n = 52), indicating that the early detection of MT before the occurrence of invasion or metastasis is essential for treating malignant transformation of MCT [10].

In summary, this article reviewed a rare case of FVTPC in a 65-year-old woman. Malignant transformation in MCT is a rare, especially FVTPC in MCT, which is extremely rare. Preoperative diagnosis is difficult, and no gold standard has been established for treatment. It should be recognized that malignant transformation can occur in MCT. If MCT is diagnosed and shows aggressive features, malignant transformation should be included in the differential diagnosis.

Ethics approval and consent to participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and

the protocol was approved by the Ethics Committee of Yeung-Nam University Hospital (approval number: 2020-11-012)

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Conflicts of Interest

The authors declare to have no conflict of interest.

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References

- [1] Lai P., Hsieh S., Chien J.C., Fang C., Chan W.P., Yu C.: "Malignant transformation of an ovarian mature cystic teratoma: computed tomography findings". *Arch. Gynecol. Obstet.*, 2005, 271, 355-357.
- [2] Yamaguchi K., Mandai M., Fukuhara K., Higuchi T., Hamanishi J., Takakura K., et al.: "Malignant transformation of mature cystic teratoma of the ovary including three cases occurring during follow-up period". *Oncol. Rep.*, 2008, 19, 705-711.
- [3] Al-Rayyan E.S., Duqoum W.J., Sawalha M.S., Nascimento M.C., Pather S., Dalrymple C.J., et al.: "Secondary malignancies in ovarian dermoid cyst". *Saudi Med. J.*, 2009, 30, 524-528.
- [4] Tangjitgamol S., Manusirivithaya S., Sheanakul C., Leelahakorn S., Thawaramara T., Jesadapatarakul S.: "Squamous cell carcinoma arising from dermoid cyst: case reports and review of literature". *Int. J. Gynecol. Cancer*, 2003, 13, 558-563.
- [5] Kelley R.R., Scully R.E.: "Cancer developing in dermoid cysts of the ovary - a report of 8 cases, including a carcinoid and a leiomyosarcoma". *Cancer*, 1961, 14, 989-1000.
- [6] Climie A.R.W., Heath L.P.: "Malignant degeneration of benign cystic teratomas of the ovary. Review of the literature and report of a chondrosarcoma and carcinoid tumor". *Cancer*, 1968, 22, 824-832.
- [7] Peterson W.F.: "Malignant degradation of benign cystic teratomas of the ovary-a collective review of the literature". *Obstet. Gynecol. Surv.*, 1957, 12, 793-830.
- [8] Kikkawa F., Nawa A., Tamakoshi K., Ishikawa H., Kuzuya K., Suganuma N., et al.: "Diagnosis of squamous cell carcinoma arising from mature cystic teratoma of the ovary". *Cancer*, 1998, 82, 2249-2255.
- [9] Tseng C., Chou H., Huang K., Chang T., Liang C., Lai C., et al.: "Squamous cell carcinoma arising in mature cystic teratoma of the ovary". *Gynecol. Oncol.*, 1996, 63, 364-370.
- [10] Chiang A.J., Chen M.Y., Weng C.S., Lin H., Lu C.H., Wang P.H., et al.: "Malignant transformation of ovarian mature cystic teratoma into squamous cell carcinoma: A Taiwanese gynecologic oncology group (TGOG) study". *J. Gynecol. Oncol.*, 2017, 28, e69.
- [11] Dos Santos L., Mok E., Iasonos A., Park K., Soslow R.A., Aghajanian C., et al.: "Squamous cell carcinoma arising in mature cystic teratoma of the ovary: a case series and review of the literature". *Gynecol. Oncol.*, 2007, 105, 321-324.
- [12] Kashimura M., Shinohara M., Hirakawa T., Kamura T., Matsukuma K.: "Clinicopathologic study of squamous cell carcinoma of the ovary". *Gynecol. Oncol.*, 1989, 34, 75-79.
- [13] Von Kahliden C.: "Ueber eine Eigenthumliche Form des Ovarialcarcinoms". *Zentralbl allg Path.*, 1895, 7, 257.
- [14] Rim S.M., Kim S.M., Choi H.S.: "Malignant transformation of ovarian mature cystic teratoma". *Int. J. Gynecol. Cancer*, 2006, 16, 140-144.
- [15] Dane C., Ekmez M., Karaca A., Ak A., Dane B.: "Follicular variant of papillary thyroid carcinoma arising from a dermoid cyst: a rare malignancy in young women and review of the literature". *Taiwan. J. Obstet. Gynecol.*, 2012, 51, 421-425.

- [16] Hong K., Han A.K.W., Kim M., Yun B.S., Jun H.S., Seong S.J., *et al.*: "Successful in vitro fertilization pregnancy and delivery after a fertility-sparing laparoscopic operation in a patient with a papillary thyroid carcinoma arising from a mature cystic teratoma". *Clin. Exp. Reprod. Med.*, 2019, 46, 140-145.
- [17] Cokmez H., Gulbahar A., Yigit S., Aydin C.: "Oncocytic and tall columnar type papillary thyroid carcinoma arising on a mature cystic teratoma: a case report and literature review". *J. Pak. Med. Assoc.*, 2019, 69, 116-119.
- [18] Iwahashi N., Deguchi Y., Horiuchi Y., Noguchi T., Yahata T., Ota N., *et al.*: "Live birth following laparoscopic fertility-sparing surgery for papillary thyroid carcinoma arising from mature ovarian cystic teratoma: a case report". *Mol. Clin. Oncol.*, 2018, 9, 613-616.
- [19] Kurman R., Telinde R.: "Blaustein's pathology of the female genital tract". 5th ed. New York: Springer Verlag, 2002.
- [20] Park S.B., Kim J.K., Kim K.R., Cho K.S.: "Preoperative diagnosis of mature cystic teratoma with malignant transformation: analysis of imaging findings and clinical and laboratory data". *Arch. Gynecol. Obstet.*, 2007, 275, 25-31.
- [21] DeSimone C.P., Lele S.M., Modesitt S.C.: "Malignant struma ovarii: a case report and analysis of cases reported in the literature with focus on survival and I131 therapy". *Gynecol. Oncol.*, 2003, 89, 543-548.

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