



A rare case of squamous cell carcinoma *in situ* arising in mature cystic teratoma

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Mature cystic teratoma (MCT) is the most common ovarian tumor. Secondary malignant tumors rarely arise in MCTs, and squamous cell carcinoma (SCC) is the most common form of such tumors. MCT-derived SCC *in situ* (CIS) is mostly found together with invasive SCC; it is seldom detected alone. A 44-year-old woman with breast cancer was found to have a left ovarian cyst (size >8 cm) before treatment. She underwent bilateral salpingo-oophorectomy, and frozen biopsy showed MCT with focal proliferation of squamous epithelium and mild atypism. However, definitive pathologic diagnosis confirmed CIS arising in MCT. In addition, germline BRCA 1/2 test and human papillomavirus test of tumor tissue yielded negative results. This report is the first case of its kind in Korea. Our report can aid in clinical decision making and serve as a basis for follow-up studies on this rare type of CIS arising in MCT.

Keywords: Carcinoma *in situ*; Teratoma, mature; Malignant transformation; Germ cell tumor

Introduction

Mature cystic teratoma (MCT) is the most common germ cell tumor arising in the ovary. It comprises well-differentiated tissues derived from the 3 germ layers and has a potential for malignant transformation [1]. Generally, malignant changes rarely occur in MCTs (incidence, 1–2%). Invasive squamous cell carcinoma (SCC) is one of the most commonly detected malignant tumors in MCTs, followed by adenocarcinoma and carcinoid [2,3]. However, it is very difficult to diagnose malignant alterations in MCTs before surgery, and such cases have poor prognosis [4].

MCT-derived SCC *in situ* (CIS) is generally detected together with invasive SCC, although its incidence alone is observed in very rare cases [5-7]. Here, we report a case of CIS occurring alone in an MCT.

Case report

The patient was a 44-year-old woman with the following characteristics: gravida 4, para 2 (2 spontaneous deliveries), abortus 2, widowed, menarche at age 14 years, and regular menstruation. Her height, weight, and body mass index were 155 cm, 66 kg, and 27.47 kg/m², respectively. Due to

her low socioeconomic status, she did not undergo regular gynecologic examination. She was diagnosed with asthma 10 years previously. However, she had no asthma symptoms at the time of this report. Recently, she was diagnosed with breast cancer (left, intraductal carcinoma, T2N3M0, estrogen receptor [ER] positive/progesterone receptor negative) at the age of 44 years. She had a family history of breast cancer involving her grandmother. She underwent abdominopelvic computed tomography (AP-CT) for breast cancer staging, which revealed a well-defined bilocular mass 8.5 cm in size, composed of fat, fluid, and calcifications in the left adnexa. Left ovarian cyst was diagnosed, suggesting an asymptomatic

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MCT. Gynecologic consultation for the left ovarian cyst was postponed because the ovarian tumor was suspected to be benign. After neoadjuvant chemotherapy, the patient underwent left breast-conserving surgery. Before starting adjuvant radiotherapy and chemotherapy, she visited the gynecologic outpatient clinic and underwent a gynecologic examination and preoperative evaluations, including transvaginal ultrasonography, Papanicolaou (Pap) smear test, tests for human papillomavirus (HPV), risk of ovarian malignancy algorithm (ROMA), SCC-related antigen (SCC Ag), carbohydrate antigen (CA) 19-9, CA 15-3, and germline BRCA mutations, and follow-up AP-CT. The results of Pap smear and HPV testing were negative. Transvaginal ultrasonography showed a solid left ovarian cyst of size >8 cm. The uterus was normal with a

4.8-mm-thick regular endometrium. The right ovary showed no alteration. The CA 19-9 and SCC Ag levels were elevated (1,948 U/mL and 1.8 ng/mL, respectively). Levels of other serum tumor markers, including ROMA and CA 15-3, were normal (8.0 ROMA% and 12.65 U/mL, respectively). AP-CT revealed no interval change in the ovarian cyst compared with the values obtained 6 months previously (Fig. 1A). It showed a well-defined bilocular mass measuring 8.5 cm, composed of fat, fluid, and calcifications in the left adnexa. After a preoperative diagnosis of MCT was made, she underwent laparoscopic surgery. Before surgery, we decided to perform bilateral salpingo-oophorectomy (BSO) because of the patient's ER+ breast cancer, and she was prescribed tamoxifen for >5 years.

Intraoperatively, an approximately 9-cm cyst containing fat

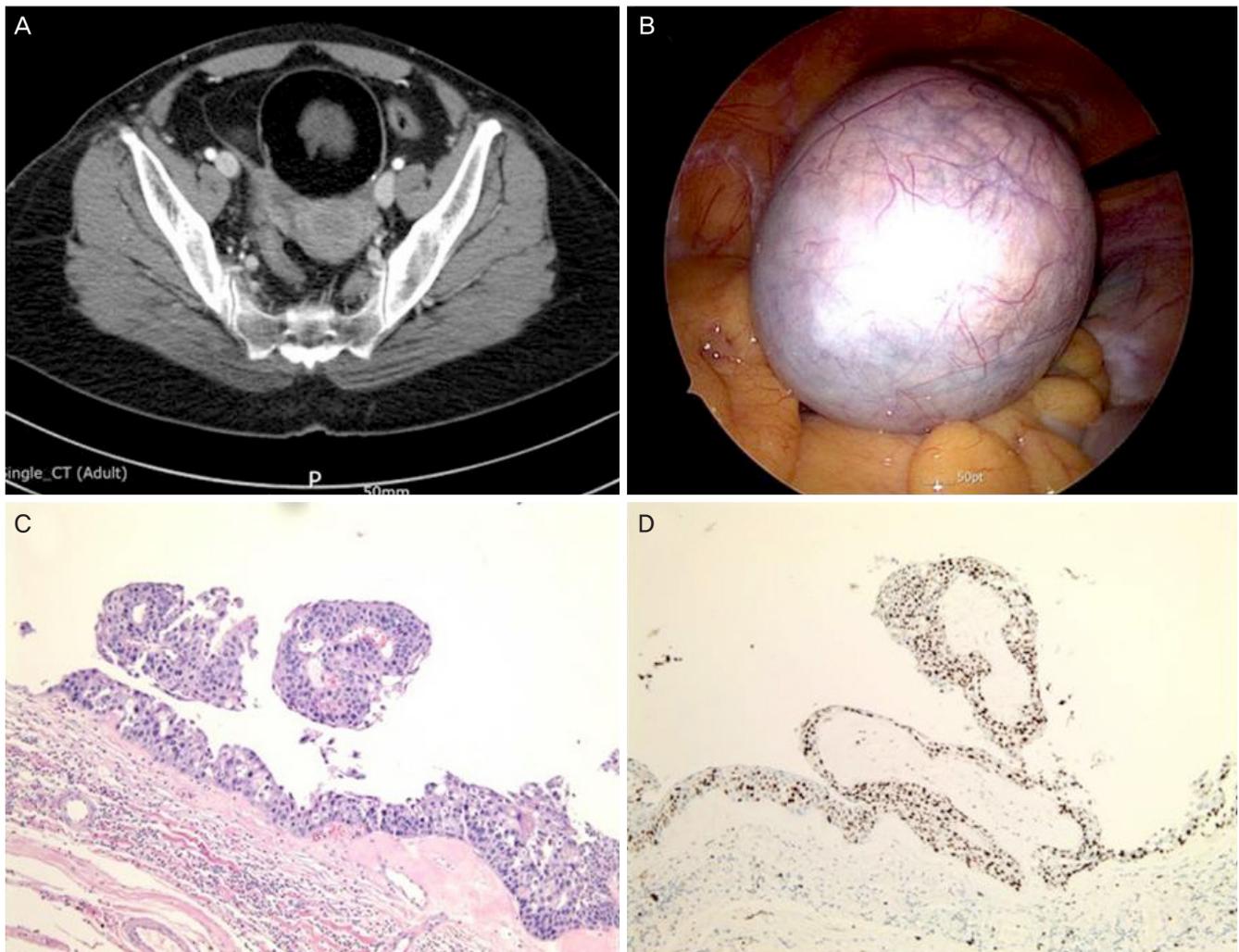


Fig. 1. (A) Abdominopelvic computed tomography scan showing an 8.5-cm well-defined bilocular mass composed of fat, fluid, and calcifications in the left adnexa. (B) Operative findings. (C) Atypical keratinocytes across the complete thickness of the skin. (D) Histopathologic image showing the high rate of proliferation of lesion cells.

and hair was found in the left ovary (Fig. 1B). There was no adhesion. The uterus and contralateral adnexa were grossly normal. No evidence of peritoneal tumor implants was seen. BSO was performed. Intraoperative frozen biopsy showed MCT with focal proliferation of squamous epithelium and mild atypism. No complication occurred in her postoperative course. She was discharged on the 2nd postoperative day. The diagnosis of CIS arising in MCT was confirmed by the histopathologist in permanent biopsy (Fig. 1C and D). HPV test of tumor tissue was conducted using real-time polymerase chain reaction, which showed a negative result. In addition, the germline BRCA 1/2 test was negative.

We planned another operation, including hysterectomy, for the following reasons: First, several reports of MCT-derived SCC showed better prognosis in patients treated with hysterectomy, BSO, and lymphadenectomy. Second, our patient had an increased risk for endometrial cancer because of her surgical menopause, tamoxifen use, and obesity. However, hysterectomy was postponed considering her chemotherapy and radiotherapy schedule. The CA 19-9 level decreased to 113.5 U/mL. The levels of other serum tumor markers, including SCC Ag, were normal. The patient is currently undergoing chemotherapy for breast cancer.

Discussion

MCT is a well-differentiated tumor originating in the 3 germ

layers. It accounts for 10–20% of all ovarian tumors and has malignant potential. Secondary malignant alterations very rarely occur in MCTs, with an incidence of 1–2% [1,2]. Among such alterations, invasive SCC is the most common, accounting for almost 75% of malignant tumors in MCTs, followed by adenocarcinoma, carcinoid, carcinosarcoma, and melanoma [2,3,8].

CIS arising in MCT is generally found around the site of invasive SCC. It is very rarely detected alone, with only 6 cases reported since 1972. The clinical features of the 6 reported cases are summarized in Table 1 [2,5-7,9-11]. Similarly, our study presents a case of CIS detected alone in MCT. This is the first reported case of its kind in Korea.

Hackethal et al. [3] reported that 277 patients diagnosed with MCT-derived SCC had an average age of 55 years. In our study, the patient was 44 years old. The most common symptoms of MCT-derived SCC include abdominal pain and a palpable abdominal mass, similar to those of benign MCT. In addition, symptoms may be caused by the tumor pressing against adjacent organs, such as the intestine and bladder. These symptoms are more commonly observed during malignant transformation of MCT because malignant MCTs tend to be larger than benign MCTs [1,3].

CT and magnetic resonance imaging are widely used for the diagnosis of MCT, generally before surgery. The extent of the disease can also be determined with these modalities. However, it is very difficult to differentiate between benign MCT and malignant MCT with imaging modalities [12].

Table 1. Clinical characteristics of patients with squamous cell carcinoma *in situ* arising in a mature cystic teratoma in previous case reports

Author (yr)	Age (yr)	Country	Mean tumor diameter	Symptoms at diagnosis	Treatment	Follow-up
Klionsky et al. (1972) [9]	57	USA	10 cm	Palpable mass ^{a)}	Hysterectomy ^{a)} and LSO	9 years
Peuchmaur and Reynes (1989) [2]	30	France	6 cm	No functional symptom	Right ovarian cystectomy	4 years
Tobon et al. (1991) [10]	62	USA	17 cm	Abdominal pressure, increased abdominal girth, weight gain, pain in the right leg and lower back	Hysterectomy, BSO, and peritoneal washing	1 year
Dadhwal et al. (2002) [7]	58	India	12.5 cm	Palpable mass	Hysterectomy and infracolic omentectomy	Follow-up loss
Gurrera et al. (2008) [11]	48	Italy	14.5 cm	Pelvic swelling	Hysterectomy and BSO	NA
Zakkouri et al. (2011) [6]	62	Morocco	10 cm	Abdomino-pelvic pain	LSO hysterectomy, RSO, and omentectomy	NA

NA, not available; BSO, bilateral salpingo-oophorectomy; RSO, right salpingo-oophorectomy; LSO, left salpingo-oophorectomy.

^{a)}Multiple leiomyomas of the uterus were also present.

When the tumor size is 10 cm or larger, there is a high risk of malignant transformation [4,13].

In a study by Chiang et al. [14], HPV was detected immunohistochemically with a monoclonal antibody for HPV and with *in situ* hybridization of tissues from 4 patients diagnosed with SCC arising in MCT. The results suggested that high-risk HPV might be a cause of the malignant transformation of MCT [14]. In contrast, however, HPV was not identified in the tumor tissue and cervix in this case.

CIS arising in MCT is very rare, and there are no established guidelines for its treatment. Several studies have recommended complete tumor resection in patients with MCT-derived SCC [3,13,15]. Patients treated with hysterectomy, BSO, and lymphadenectomy showed better prognosis [3]. According to a review of the literature on MCT-derived SCC from 1976 to 2005, the rate of complete tumor resection was 100% for CIS arising in MCT and the 5-year survival rate was 100%. Meanwhile, in stage IA, there were no statistically significant differences in survival with respect to cystectomy or oophorectomy and resection of larger areas [5]. Thus, conservative surgery might be a treatment choice for CIS, although additional data are needed to establish the efficacy of this strategy.

In conclusion, this is the first case of CIS arising in MCT reported in Korea. Our report can aid in clinical decision making and serve as a basis for follow-up studies on this rare type of CIS associated with MCT.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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