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Urothelial (Transitional Cell) Carcinoma Arising in Mature Cystic Teratoma – A Case Report –

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Mature cystic teratoma (MCT) is one of the most common benign ovarian tumors, but 1-2% of MCTs are transformed to a malignant neoplasm. Urothelial carcinoma (UC) or transitional cell carcinoma is the most common cancer in the urinary tract. However, UC is a very rare component of transformed malignancy of MCT. Here we report a case of UC arising in an MCT in a 52-year-old woman. Grossly, the ovary was partly cystic and partly solid. Microscopically, the cyst revealed the classic features of MCT and the solid area was papillary UC. By immunohistochemistry using cytokeratins and thrombomodulin, the UC showed a similar expression to that of UC arising in the urinary tract, rather than resembling a primary transitional cell carcinoma of the ovary. When UC is found in a component of MCT, the origin of the carcinoma should be evaluated and urinary tract examinations are required to rule out metastasis.

Key Words : Ovarian neoplasms; Teratoma; Carcinoma, transitional cell

Mature cystic teratoma (MCT) is a neoplasm of germ cell origin, and it is one of the most common ovarian tumors in reproductive-age women.[1] All ovarian MCTs are benign, but malignant transformation occurs in 1-2% of MCTs and the most common form of malignancy is squamous cell carcinoma.[1,2] Urothelial carcinoma (UC) or transitional cell carcinoma is the most common malignant neoplasm of the urinary tract including the renal pelvis, ureter or urinary bladder, but UC is extremely rare in MCT with malignant transformation.[3] We now report a case of UC arising in an MCT of the right ovary in a 52-year-old woman.

CASE REPORT

A 52-year-old, premenopausal woman visited Chungbuk National University Hospital with a history of an abdominal mass for 2 months. Computed tomography demonstrated a large unilocular cystic mass with a solid area in the right ovary (Fig. 1A). Other pelvic organs including uterus, large intestine, kidneys, ureters, and urinary bladder were normal. She underwent right salpingo-oophorectomy under the clinical impression of cystic teratoma. Grossly, the resected ovary was 22 × 19 × 5 cm in size and the outer surface was smooth. On the cut surface, the cyst was filled with yellowish creamy fluid and hairs, which are the classic features of mature cystic teratoma. A solid polypoid area was found on the inner surface of the cyst and measured 6 × 6 × 5 cm in size (Fig. 1B). Microscopically, the cut surface of the solid area revealed papillary fronds (Fig. 2A). Each papilla was composed of a central fibrovascular core and covering urothelial cells with eight to twelve cell layers and moderate nuclear atypia, which was consistent with the low grade papillary UC (Fig. 2B). There was no evidence of invasion into the ovarian stroma. By immunohistochemistry, using a formalin-fixed and paraffin-embedded tissue block, the UC cells were positive for cytokeratin (CK)7 (1 : 100, OV-TL 12/30, Neomarkers, Fremont, CA, USA), CK20 (1 : 50, KS20.8, Novocastra, Newcastle, UK), and thrombomodulin (1 : 100, 15C8, Novocastra) (Fig. 2C), and negatve for Wilms tumor protein 1 (1 : 40, WT49, Novocastra), carcinoembryonic antigen (1 : 100, 12-140-10, Novocastra), estrogen receptor (1 : 100, 6F11, DiNonA, Seoul, Korea), and progesterone receptor (1 : 100, 16, Novocastra). The cystic area was composed of squamous epithelia, sebaceous glands, cartilage and

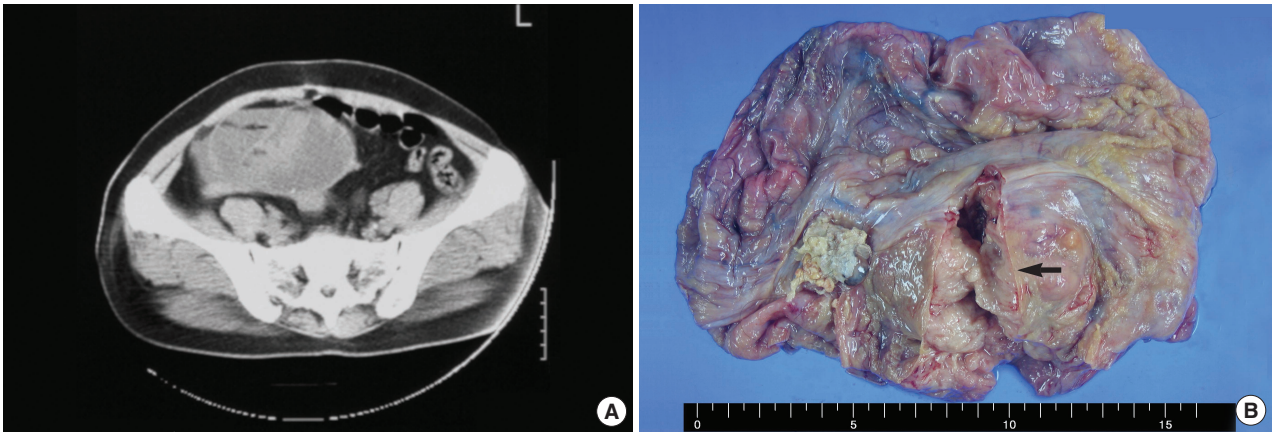

Fig. 1. (A) Pelvic computed tomography demonstrates a cystic mass in the right ovary. (B) Cut section of the cyst reveals a solid polypoid area (arrow) on the inner surface. Yellowish creamy fluid and some hairs are also seen.

adipose tissue. Benign urothelial cells were also found adjacent to the papillary UC (Fig. 2D, E).

After the operation, the patient exhibited no recurrence or metastasis after 15 months of follow-up.

DISCUSSION

UC arising in an MCT is very rare, and only three cases have been reported so far.[4-6] Microscopic findings of UC, however, were described in only one of them.[5] Because of its rarity, we report this case with an emphasis on immunohistochemical findings, and review the literature regarding the pathogenesis of UC arising in an MCT.

The pathogenesis of malignant transformation of MCT is not fully elucidated yet. Lee *et al*.[5] found normal urothelial epithelium adjacent to UC, which was similar to our case, and they suggested that prolonged stimulation of epithelial cells by lipid material induced secondary malignancy. Iwasa *et al*.[7] demonstrated that squamous cell carcinoma in MCT may be derived from metaplastic squamous epithelium rather than teratomatous squamous epithelium using immunohistochemical analysis. Therefore, we believe that prolonged and persistent stimulation of teratomatous or metaplastic urothelial epithelium by some irritating materials within the teratoma may cause UC in MCT.

Generally, malignant transformation of MCT occurs in older patients (range, 47 to 55 years) than patients who have MCT without malignancy (range, 35 to 38 years).[2,6,8] Serum levels of squamous cell carcinoma antigen (17.01 ng/mL vs 1.82 ng/mL) and cancer antigen 125 (33.0 U/mL vs 17.1 U/mL) and preoperative measurement of tumor size (15.2 cm vs 8.8 cm) are also important factors distinguishing between malignancy arising in MCT and pure MCT.[8] However, menopause itself does not seem to be a risk factor for malignancy arising in MCT: Kikkawa *et al*.[8] noted that six of 11 patients were postmenopausal, while Al-Rayyan *et al*.[6] demonstrated that only three out of 11 were postmenopausal.

Due to the rarity of UC arising in MCT, there is no consensus regarding treatment and prognostic factors. Several studies reviewed the prognostic factors of secondary malignancy in MCT.[2,5,9] They concluded that surgical staging is the most important prognostic factor. They recommended conservative surgery and close follow-up for patients with International Federation of Gynecology and Obstetrics (FIGO) stage IA disease. The carcinoma component of our case was confined to the ovary with no involvement of the ovarian surface, which was consistent with FIGO stage IA. Therefore, the best treatment plan after surgery may be close follow-up without adjuvant chemotherapy or radiotherapy, although the UC in our case was different from malignancies in the previously studied cases.

It is important to differentiate UC arising in MCT from primary transitional cell carcinoma of the ovary (TCC-O). TCC-O is a distinct subtype of surface epithelial-stromal tumor which is histologically similar to UC.[10] Some studies tried to compare the expression of several markers between TCC-O and UC of the urinary tract.[11-13] Most UCs of the urinary tract were positive for CK20, uroplakin III and thrombomodulin, and were negative for Wilms tumor protein 1 (WT1). In contrast, TCC-Os frequently expressed WT1, but fewer than 20% of TCC-Os showed immunoreactivity with thrombomodulin and/or uroplakin III, and none of them expressed CK20. Our case was positive for CK20 and thrombomodulin, but negative for WT1,

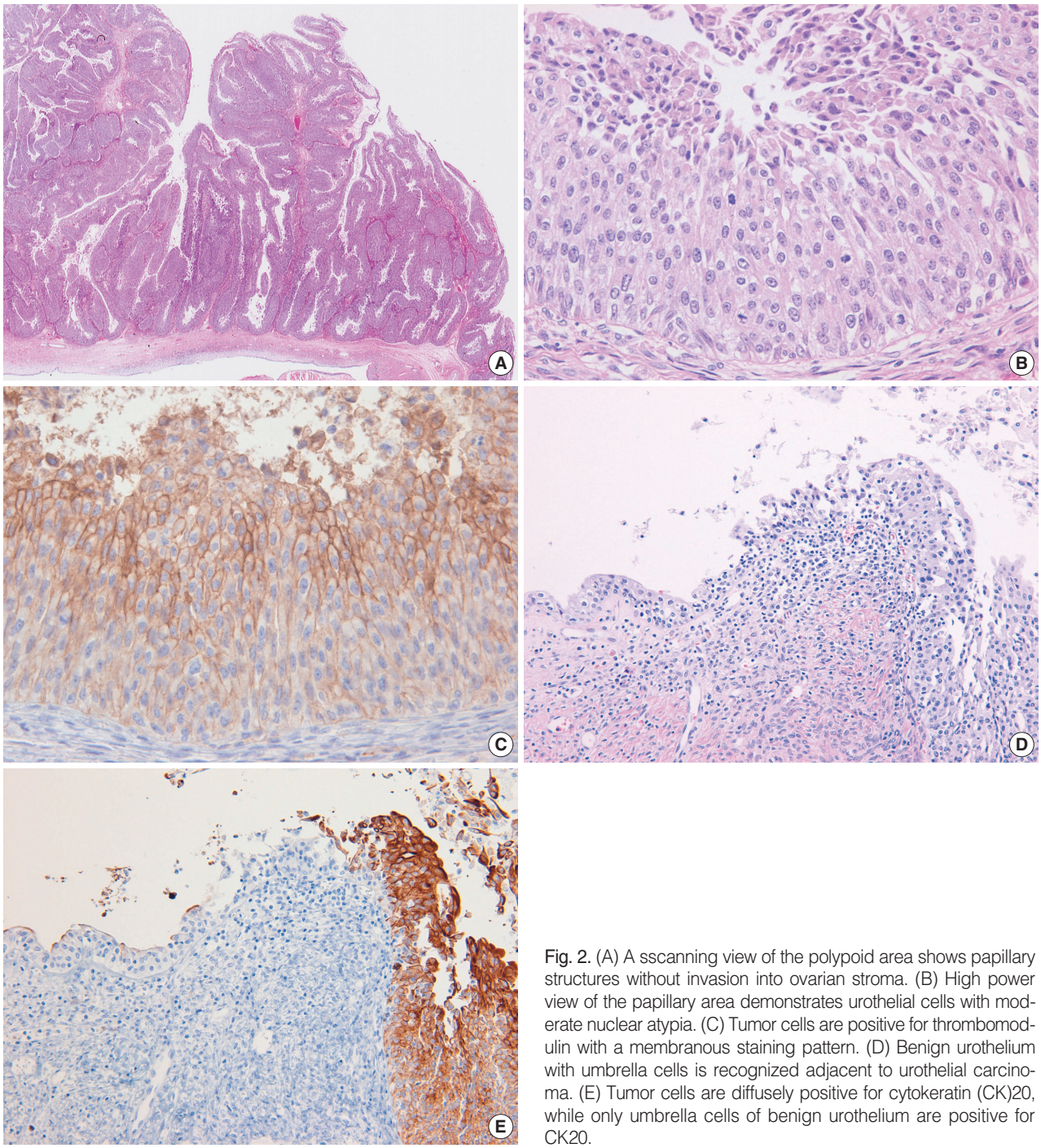

Fig. 2. (A) A sscanning view of the polypoid area shows papillary structures without invasion into ovarian stroma. (B) High power view of the papillary area demonstrates urothelial cells with moderate nuclear atypia. (C) Tumor cells are positive for thrombomodulin with a membranous staining pattern. (D) Benign urothelium with umbrella cells is recognized adjacent to urothelial carcinoma. (E) Tumor cells are diffusely positive for cytokeratin (CK)20, while only umbrella cells of benign urothelium are positive for CK20.

which showed identical expression to those of UCs of the urinary tract. These findings supported the notion that the UC arose in the urothelium within the MCT. However, we should rule out the possibility of metastatic UC from the urinary tract. It is very difficult to distinguish UC arising in MCT, such as our case, from metastatic UC judged by pathologic features. Because there was no evidence of malignancy in the urinary tract, the possibility of metastatic UC was excluded.

In conclusion, UC is a very rare form of secondary neoplasm arising in MCT. When UC is found in MCT, it is important to evaluate the origin of the carcinoma cells, whether the tumor is combined MCT and TCC-O or UC arising in MCT. To avoid an erroneous diagnosis, urinary tract examinations are required, and the possibility of metastatic UC should be excluded.

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