Primary transitional cell carcinoma of the fallopian tube: 
A case report

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I. Introduction

Primary carcinoma of the fallopian tube is one of the rarest gynecologic malignancies, accounting for 0.18 to 1.6 percent of all malignant neoplasms of the female genital tract.13 The histopathologic features of fallopian tube carcinoma are similar to epithelial ovarian cancer.13 The vast majority are papillary adenocarcinoma but other histologic types including clear cell carcinoma, mixed(glassy cell) carcinoma, and endometrioid carcinoma have been reported.34 Reports of primary transitional cell carcinoma of the fallopian tube are extremely rare50 and clinicopathologic features have not yet been well characterized.7 We report a case of a primary malignant neoplasm of the right fallopian tube with histological features of transitional cell carcinoma with a review of literatures.

II. Case Report

A 58-year-old widow, gravida 2, para 2, 3 years post-spontaneous menopause, was referred
to Asan Medical Center Gynecologic Oncology Clinic for irregular vaginal bleeding and abnormal endometrial biopsy result described as "adenosquamous cell carcinoma, invasive, non-keratinizing small cell type." Soon after menopause, she had experienced intermittent vaginal spotting twice or three times a year. On physical examination, the uterus was of normal size, and no palpable abnormal pelvic mass was detected. The cervix was small and clean. Papanicolaou smear was normal. Investigations, including sigmoidoscopy, cystoscopy, intravenous pyelogram, chest x-ray film and routine laboratory tests revealed normal findings. The CT scan of pelvis showed enlarged right adnexa and normal sized uterus with central lucency which might represent mild endometrial hyperplasia or endometrial secretion. Under the impression of endocervical squamous cell carcinoma of stage Ib, laparotomy was performed, and a $2 \times 3 \times 4$cm sized firm right tubal mass with adhesions to the retroperitoneum and the right ovary was encountered. No ascites was found in the peritoneal cavity and the washing cytology showed negative for malignant cell. The left adnexa, the uterus and the cervix were grossly normal. A frozen section of the tubal mass revealed a poorly differentiated carcinoma and that of paraaortic lymph node was negative for tumor. The tumor infiltrated into the muscularis, but there was no evidence of the serosal involvement. A radical hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic lymph node dissection and an appendectomy were performed and thorough exploration of pelvic and abdominal cavity could not detect any suspicious nodule of metastasis. On pathologic findings, the right fallopian tube was dilated in the ampullary portion by a tan soft papillary tumor encroaching upon the lumen. A transition from malignant to benign tubal epithelium was noted in several foci(Fig. 1). The tumor showed a papillary architecture with papillae covered by multilayers of atypical plump cells exhibiting numerous mitotic figures and scanty fibrovascular cores(Fig. 2). The interce-

Fig. 1. Transitional cell carcinoma of fallopian tube. Intraluminal papillary tumor shows transition to flattened benign epithelium. (H&E, original magnification ×10)

Fig. 2. Transitional cell carcinoma of fallopian tube. The papillae are covered by multilayers of atypical plump cells. (H&E, original magnification ×400)
llular bridge or keratinization was not observed. The base of the tumor showed irregular nest of invasion (Fig. 3). Ultrastructural examination of the tissue retrieved from the paraffin embedded blocks showed polygonal tumor cells with oval or occasionally indented nuclei, abundant cytoplasm containing well developed organelles including mitochondria, free ribosomes, rough endoplasmic reticulum, many lysosomes and interdigitating cell membranes. A few cells contained thick bundles of tonofilaments within the cytoplasm (Fig. 4). The 28 pelvic lymph nodes and the paraaortic lymph nodes revealed no metastasis. The ovaries, the left fallopian tube, the uterine corpus and the cervix were free of tumor. After review of previous endometrial biopsy slides, a diagnosis of a primary, poorly differentiated, papillary squamous cell carcinoma (so-called transitional cell carcinoma variant) of the fallopian tube with extension to endometrium (stage IIa) was rendered. The postoperative course was uneventful except for the delayed restoration of the bladder function till 26th postoperative day and the persistent serous drain from the Hemo-vac over 100cc till 46th postoperative day. On 52nd postoperative day, the patient was discharged without specific problem to be followed up by the oncology service of our Gynecologic Clinic. No additional treatment was recommended, and the patient was well until 68 months later without any evidence of recurrence.

Fig. 3. Transitional cell carcinoma of fallopian tube. The base of tumor shows nests of invasion. (H&E, original magnification ×100)

Fig. 4. Transitional cell carcinoma of fallopian tube. Ultrastructural examination showing a few scattered numerous, thick bundles of tonofilaments within the cytoplasm.
III. Discussion

The incidence of the primary fallopian tubal cancer varies from 0.18 to 1.6 percent in the age group of 18 to 80 years.\(^1\) The greatest incidence occurs in the fifth to sixth decades of life. The age-specific incidence of fallopian tube neoplasms increases in a manner similar to that of ovarian and endometrial tumors, suggesting possible common etiologic factors. A shared association with nulliparity supports this suggestion.\(^6\) The signs and symptoms of carcinoma of the fallopian tube are usually inconsistent and non-specific. As our case, postmenopausal or less frequently intermenstrual bleeding is the most common presenting symptom and the most common physical sign is a pelvic mass in most studies.\(^9\) Correct preoperative diagnosis of the fallopian tubal cancer is very uncommon because of a lack of typical clinical findings, and was made in only two of the 71 patients in the study by Eddy et al.,\(^12\) one of 26 cases reported by Kinzel,\(^13\) and 3 of 30 patients presented by Semrad et al.\(^14\) Abnormal Papanicolaou cytology suggestive of adenocarcinoma was noted in 11 percent of cases in Yoonessi’s study.\(^15\) Abnormal cytology and negative endometrial curettage have led to diagnosis of fallopian tube malignancy in isolated cases.\(^16\) Hirai et al.\(^10\) demonstrated diagnostic endometrial aspiration cytology in 6 of 10 patients. Hysterosalpingography, sonography, hysteroscopy and laparoscopy have been supported as part of the preoperative work-up in case of suspected tubal cancer.\(^20\) In our case, because the patient had normal Papanicolaou smear and positive endometrial biopsy of adenosquamous cell type, the primary tubal cancer could not be suspected preoperatively.

The histopathologic features of fallopian tube carcinoma are similar to epithelial ovarian cancer.\(^2\) The vast majority are papillary adenocarcinoma but other histological types including clear cell carcinoma, mixed (glassy cell) carcinoma, and endometrioid carcinoma have been reported.\(^3\) Reports of primary transitional cell carcinoma of the fallopian tube were extremely rare,\(^6\) but recently Uehira et al.\(^7\) reported that the transitional cell–predominant tubal cancer showed the similar clinical features with regard to patient age, clinical stage, cytology of ascites, and peritoneal washings at initial operation compared to the others, and it showed some characteristic pathologic features, i.e. more frequent solid gross appearance, solid histologic pattern, tumor necrosis, spindle-shaped tumor cells, and sulfomucin-predominant acid mucin secretion. Diagnostic criteria to differentiate fallopian tube malignancy from ovarian and other primary malignancy were established by Hu et al.\(^22\) and modified by Sedlis\(^23\) and these are now generally accepted as principal diagnostic criteria: 1) the tumor arises from the endosalpinx, 2) the histological pattern reproduces the epithelium of tubal mucosa, 3) transition from benign to malignant epithelium is found, and 4) the ovaries and endometrium are either normal or have tumor smaller than that in tube. Our case fulfilled all these four criteria as shown on the descriptions and the figures about pathology. In 10 to 26 percent of cases, tumor may be present in both tubes at presentation.\(^24\) This is considered as a manifestation of multifocal disease rather than metastasis, because in most cases tumors are symmetrical and there is no tumor in the intervening endometrium and no peritoneal spread.\(^20\) The pattern of spread of fallopian tube carcinoma have long been considered similar to those of ovarian epithelial cancer, with the intraperitoneal route being the most frequently encountered. Direct invasion and transmural spread involves the serosa of the ovaries, uterus, and intestines.\(^23\) Recent studies have highlighted the potential for lymphatic, vascular, and transcoelomic spread.\(^25\) Limited understanding of this rare disease has led to disagreement between authors regarding classification and staging. Numerous staging classification have been used, and staging procedures have varied between studies sharing the
same classification. Recently, an official FIGO fallopian tube staging\textsuperscript{27} has been published, largely based on ovarian cancer staging, but incorporating components of Schiller and Silverberg’s classification and the prognostic features of peritoneal washings, tumor nodule size, and node metastasis. This positive step will now enable reliable comparison between future studies.

Niloff et al.\textsuperscript{30} pioneered research into tumor markers in fallopian tube carcinoma, describing elevated CA-125 levels in four patients associated with recurring disease, and Lootsma-Miklosava et al.\textsuperscript{30} were first to monitor changes in CA-125 level with treatment and recurrence. Immunohistochemical techniques were employed by Neu-nteufel and Breiteneccker\textsuperscript{30} to assess sections of formalin-fixed tissue from normal tubes, tubo-ovarian abscesses and tubal carcinomas for presence of the tumor markers CA-125, CA19-9, and CEA, and failed to illustrate the specificity of these proteins as tumor markers. Uehira et al.\textsuperscript{7} showed no difference in immunohistochemical findings for cytokeratines, vimentin, EMA, Leu-MI, CEA, and CA-125 between transitional cell-predominant tubal cancer and the others.

The rarity of primary fallopian tube carcinoma has prevented prospective controlled trials of treatment regimens. Management has generally been individualized based on fashions in epithelial ovarian carcinoma treatment.\textsuperscript{31} Surgery remains the principal treatment for primary fallopian tube carcinoma. Following the ovarian epithelial cancer model, initial surgery has included hysterectomy, bilateral salpingo-oophorectomy and omentectomy.\textsuperscript{20} Peters et al.\textsuperscript{320} demonstrated residual disease of greater than 2cm to be a statistically significant poor prognostic factor. Gurney et al.\textsuperscript{31} and Baraket et al.\textsuperscript{320} reported the comparative survivals whether a visible residual tumor was present or not, stressing the importance of debulking surgery. Cytological washings, and biopsy of any suspicious sites including peritoneal surfaces and the diaphragm, are mandatory for staging.\textsuperscript{29} Pelvic lymphadenectomy and paraaortic node sampling are also considered mandatory by many authors even in early stage disease,\textsuperscript{32} although others recommended biopsy of only suspicious nodes.\textsuperscript{22} In our case, we performed radical hysterectomy due to preoperative suspicion of endocervical lesion. Radiotherapy was the traditional adjuvant therapy for disseminated or recurrent primary fallopian tube carcinoma. Results from the Mayo Clinic suggest adjuvant radiotherapy is effective if performed using a whole abdominal external beam or intraperitoneal colloids.\textsuperscript{34} However, results from radiotherapy have generally been disappointing.\textsuperscript{35,36} The most promising development in the treatment of fallopian tube carcinoma is the introduction of cisplatin-containing chemotherapy regimens following their acceptance for ovarian cancer in the 1970s. The almost 4-fold increase in survival with advanced disease compared with studies over the preceding decade was attributed to platinum-based therapy.\textsuperscript{33} McMurray et al.\textsuperscript{11} recommended combination chemotherapy for all patients presenting with stages II, III, or IV and also high-risk stage I with tumor invading beyond the mucosa. Second-look laparotomy may contribute to successful salvage therapy in patients with microscopic disease,\textsuperscript{24,25} although limited effectiveness of current second-line therapy in patients found to have residual disease is argued by critics of the procedure as limiting its value.\textsuperscript{12}

The advantages of extensive staging and debulking surgery, and platinum-based combination chemotherapy, are likely to have vastly improved the prognosis for all disease stages.\textsuperscript{27} The recent report by Muntz et al.\textsuperscript{30} presented overall 5-year survival rates of 100 percent for stage I, 65 percent for stage II, 40 percent for stage III, and 25 percent for stage IV from 35 patients treated from 1960 to 1988. Uehira et al.\textsuperscript{7} demonstrated that transitional cell-predominant tubal cancers tended to relapse later (mean, 31.2 months after diagnosis) than the others (mean, 14.4 months after diagnosis), resulting in a significant difference in the 2-year disease free su-
rvival rate, and suggesting a more favorable re-
sponse of the transitional cell-predominant tubal
cancers to the chemotherapy, but significant di-
fference in overall survival was not clear. In our
case, because we were assured of no residual
disease on surgical and pathologic findings, no
adjuvant treatment was performed and the patient
had a favorable prognosis without any evidence of
recurrence until 68 months after the primary
surgery.

IV. Conclusion

A primary transitional cell carcinoma is extre-
mely rare histologic subtype of the fallopian tubal
cancer, and has never been reported in Korea.
We experienced a case of primary papillary squa-
rnous cell carcinoma (so-called transitional cell
carcinoma variant) of the fallopian tube in 58-
year-old widow with complaint of irregular va-
ginal bleeding, and present it as the first case in
Korea with a review of literatures.

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