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High malignant female adnexal tumor of probable wolffian origin (FATWO): A case report

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Female adnexal tumors of probable Wolffian origin (FATWO) are rare. Although the histological features of the benign tumors are recognized, features of malignancy are not well defined in published work because these tumors are particularly rare. In this study, we report a 52-year-old woman with a High malignant FATWO. The frozen biopsy of the fragile uterine mass, located at the left broad ligament, revealed a malignant FATWO with high mitotic figure (up to 36/10 HPF). The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and paraaortic and pelvic lymph node dissection. Pathologic findings were consistent with malignant FATWO infiltrating to the unilateral salpinx without lymph node metastasis. The patient received three cycles of adjuvant treatment with paclitaxel and carboplatin. There was no clinical evidence of recurrence during the 12 months of follow-up; the patient is currently still being followed-up.

Key Words: Malignant, Female adnexal tumor, Wolffian origin

Female adnexal tumors of probable wolffian origin (FATWO) were first described in 1973 by Kariminejad and Scully.[1] The tumors were microscopically characterized by epithelial cells growing in diffuse, sieve-like, tubular patterns. These tumors were typically located at the broad ligament where wolffian remnants are abundant, and have a different appearance to tumors of Mullerian origin.

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In general, FATWOs are rare diseases and most of FATWO are benign morphological features and biological behavior. Malignant FATWOs are extremely rare neoplasms.[2] There are few cases reported in the English medical literature. This is the first case reported in Korea and a malignant tumor described thus far, with distinctive morphological features being the large size of the tumor, larger than 12 cm, apparent hypercellularity, the highest mitotic activity (up to 36 /10 HPF) with demonstrable tumor implants and metastases.

We report a fortuitously discovered case of a tumor

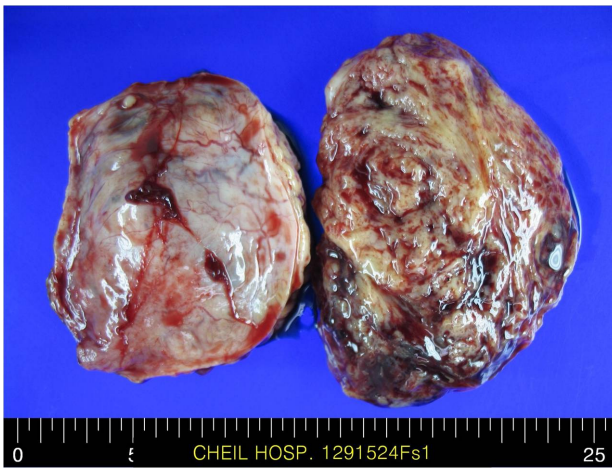

Fig. 1. Gross finding. A well demarcated mass, 12 cm in diameter, showing soft, solid yellow-tan mass with focal hemorrhage.

of the broad ligament having all the pathologic and clinical characteristics of a malignant FATWO displaying the highest mitotic activity.

Case Report

A 52-year-old woman, gravida 4 para 3, was referred to Cheil women's Health Care Center on May 2008 to evaluate a pelvic mass with elevated CA125 (87.8 U/mL). A pelvic examination and an ultrasound showed an 11×9×8 cm semi-solid mass containing a cystic portion at the left uterine wall, with the mass separated from the uterus. An abdomen-pelvic CT

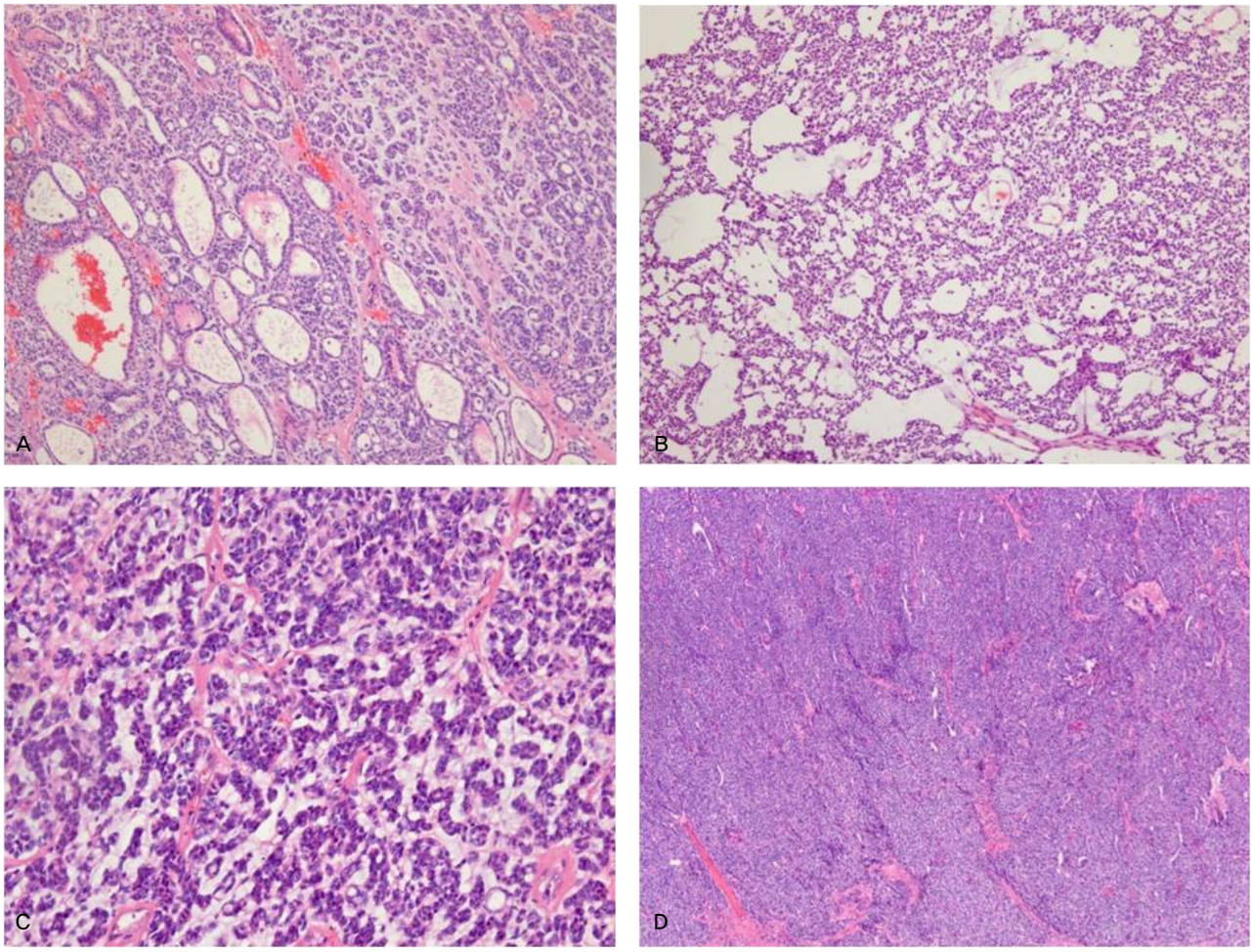

Fig. 2. Microscopic finding. Low-power view showing closely packed variable sized hollow tubules lined by cuboidal epithelial cells (A), sieve-like pattern (B), cord-like arrangement (C), and solid growth (D). Hematoxylin and eosin ×40.

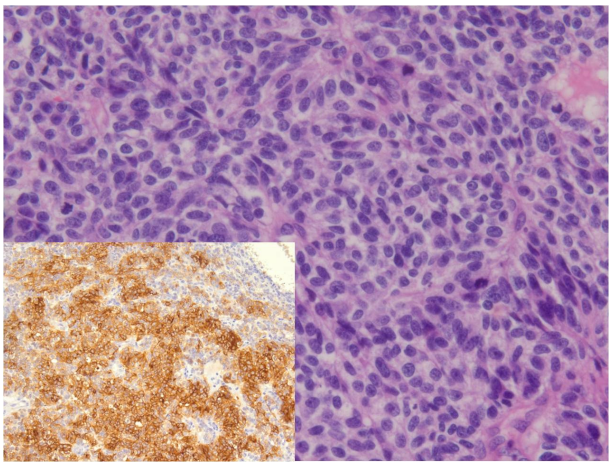

Fig. 3. Immunohistochemical finding. Tumor cells having regular oval nuclei with dispersed chromatin, occasionally conspicuous nucleoli, and frequent mitoses (arrows), and showing positive reaction for CD10 which is supportive finding of probable Wolffian origin tumor.

scan showed a heterogeneously-enhancing pelvic mass in close contact with the upper portion of the uterus; this tumor was thought to be a degenerating exophytic, subserosal uterine myoma. Explo-laparotomy was performed under the clinical impression of uterine myoma with second degeneration. A very large solid and yellow mass measuring 12×9×7.5 cm with suspicious infiltration of the ipsilateral salpinx was located between the right round ligament and ovarian ligament. Microscopic evaluation of a frozen biopsy revealed a FATWO with high mitotic figures (up to 36/10 HPF). A total abdominal hysterectomy and bilateral salpingo-oophorectomy, para-aortic and pelvic lymph node dissection, and omentectomy were performed. The pathologic diagnosis was malignant FATWO with tumor infiltration of the ipsilateral salpinx. There was no evidence of tumor in sections taken from 35 lymph nodes and the omentum. Adjuvant chemotherapy with three cycles of paclitaxel (175 mg/m^2) and carboplatin (AUC 5) was administered. In the 10 months after adjuvant treatment, the patient has shown no evidence of recurrent or metastatic disease. Follow-up is ongoing at Cheil General Hospital and Women's Healthcare Center.

Pathologic findings

On gross examination, the tumor was well encapsulated, and the surface of the 12×9×7.5 cm solid mass was yellow-tan, smooth and glistening with focal hemorrhage (Fig. 1). Microscopically, the tumor is characterized by epithelial cells growing in various architectural patterns including tubules, cords, serve-like arrangement and solid growth. There was an eosinophilic secretion within the lumens of the cysts and tubules (Fig. 2). There was no cytoplasmic mucin product. Reticulum staining highlightened the tubular pattern. The tumor cells were cellular and slightly atypical having relatively uniform round to oval hyperchromatic nuclei and frequent mitotic activities up to 36 per 10 HPF at active areas. There was focal hemorrhage, but no necrosis. Immunohistochemical stains were positive for pan-cytokeratin, CD10 (Fig. 3), inhibin-alpha, estrogen receptor, C-kit, but negative for cytokeratin7 and cytokeratin20. Immunostaining for Ki-67 showed increased proliferation index (10~40%). The tumor invaded to salpingeal serosal wall.

Discussion

Features that appear typical of FATWO cases that have been observed to date include (a) the location that they are found, which is typically same as that of mesonephric remnants (b) their morphological dissimilarity to other ovarian tumors of either epithelial-stromal or sex cord-stromal types (c) some ultrastructural and immunohistochemical homology with the mesonephric duct (immunohistochemical evidence in support of a wolffian origin).[3]

In benign FATWO, the most common treatment procedure is total abdominal hysterectomy with bilateral salpingo-oophorectomy. It is unclear at this point if adjuvant chemotherapy or radiation therapy provides benefits. A patient's physical characteristics and per-

sonal preference, such as her age and desire for fertility, should certainly be considered when formulating a treatment plan.

Although most FATWO behave in a benign fashion, there have been reports of malignant tumors. It is difficult to characterize malignant tumors due to the extremely low number of reported cases. However, FATWO with high mitotic activity, cellular atypia, and necrosis generally behave in an aggressive manner.[4] Furthermore, certain characteristics of malignant FATWO including hypercellularity, cellular pleomorphism, and an increased number of mitotic figures are associated with an increased risk of tumor recurrence. Our case had the highest level of mitotic figures reported to date.

It is important to examine frozen tumor sections to determine if the tumor is benign or malignant in nature, as this will determine the surgical approach that can affect the possibility of recurrence, and can also result in a drastically different prognosis. Any irregular mass discovered in a wolffian remnant location that has a different appearance to a myoma should be examined further by microscopic analysis of frozen sections. In addition to the number of mitotic figures, characteristics such as a large tumor size, increased cellularity, capsular invasion, and rupture of the capsule may predict an adverse course.[5]

Typically, a patient with the malignant FATWO experiences multiple recurrences and does not respond to conventional treatment. Steed et al. suggested Gleevac therapy as a targeted molecular therapy in a recurrent malignant FATWO with a c-kit-positive.[3] Harada et al. also reported a FATWO that responded well to response to Gleevac treatment.[4] However, in contrast to our case, the tumor in Harada et al.'s patient had a low mitotic figure. FATWO may be hormone-dependent tumors, and suggested that hormonal therapy be used in tumors with aggressive histological characteristics such as the presence of necrosis or a high mitotic index, or upon conventional treatment failure.[6]

In our case, the tumor was a large, malignant tumor with an unusually high number of mitotic figures that invaded the ipsilateral serosa of fallopian tube. Because of the highest mitotic figure and the tubal invasion, the patient underwent the surgical staging and three cycles of adjuvant chemotherapy.

Although the biological behavior of benign FATWO is, in general, benign, malignant FATWO's behavior is unpredictable. This report serves to remind us of the existence of female adnexal tumors of probable Wolffian origin and, in particular, their malignant potential.

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= 국문초록 =

양성에 비해 악성 중신관 기원 추정의 여성 부속기 종양 (FATWO)은 매우 드문 질환이다. 따라서 양성과 달리 악성 FATWO의 치료와 예후에 관한 임상적 결과물들의 거의 없는 상태이다. 매우 드문 질환의 진단, 치료 및 예후들을 정립하기 위해 증례보고는 매우 중요하다. 이에 저자들은 높은 유사분열을 갖는 악성 중신관 기원 추정의 여성 부속기 종양 환자의 증례를 보고하는 바이다. CT scan상 이차적 퇴행성 자궁 근종 추정 진단을 받은 52세의 여환이 본원에 방문하여 시험적 개복술을 받았다. 수술 시 시행한 동결절편 조직 검사에서 고 유사분열의 중신관 기원 추정의 여성 부속기 종양으로 판명되어, 전자궁 적출술, 양측 부속기 절제술, 대망 절제술 그리고 골반 및 대동맥 임파절 곽청술을 시행하였다. 수술 후 조직 검사상 높은 유사분열 (up to 36/10 HPF)을 갖는 FATWO로 확진 되어, paclitaxel과 carboplatin을 이용한 보조적 항암 치료를 3회 시행하였다. 이후 12개월의 추적 경과상 재발 소견은 보이지 않았다.

중심단어: 악성, 중신관 기원 추정의 여성 부속기 종양 (FATPWO)