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Malignant female adnexal tumor of Wolffian origin (FATWO)

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Summary

Female adnexal tumors of Wolffian origin (FATWOs) are rare tumors arising in the leaves of the broad ligament from the remnants of the mesonephric duct. Most FATWOs behave in a benign fashion, and there are only 11 cases reported in the literature showing malignant FATWOs. In this study, the authors report a 50-year-old woman with a malignant FATWO, positive for calretinin, CD34, CD56, focal positive for CK, and CD117 (c-Kit). The tumor cells were negative for alpha-inhibin, actin, S-100, CK 19, and EMA. The tumor showed a high mitotic count (17/10HPF), necrosis, capsular invasion, high cellularity, and moderate cytologic atypia. Review of literature showed that about 10% of FATWOs pursued an aggressive course and were generally regarded to be at least low malignant potential. Adverse prognosis factors include large side, capsular invasion and rupture, hypercellularity, nuclear pleomorphism, and increased mitotic activity. Because of the few reported cases, there are no clear recommendations regarding initial evaluation, treatment, and follow-up. A larger retrospective study is needed to support to establish diagnostic criteria and the scale of malignant potential.

Key words: Adnexa uteri; Wolffian tumor; Malignant neoplasms.

Introduction

Female adnexal tumors of probable Wolffian origin (FATWOs) are exceptionally rare neoplasms and were first described in 1973 by Kariminejad and Scully[1]. They are thought to originate from the remnants of the Wolffian (mesonephric) remnants [2]. The location of the tumor is usually in the broad ligament, but occasionally can be found in the mesosalpinx, fallopian tube, ovarian hilum, and peritoneum [3, 4]. Most FATWOs behave in a benign fashion, but recurrence or metastasis despite treatment has been reported in a few cases. The evaluation of the distinctive immunohistochemical markers in a patient with a FATWO known to be malignant at initial diagnosis are helpful in differentiating benign from malignant tumors. Owing to the rarity of these tumors, there are no clear recommendations regarding initial evaluation, treatment, follow-up, and adjuvant therapy.

Case Report

A 50-year-old nulliparous woman was referred to this hospital with pelvic pain in December 2017. The pelvic mass was found in her routine pelvic examination. Her past and medical history were unremarkable. She had never used any contraceptives and hormone therapy. She was current smoker with 0.5×10 pack-year. A transvaginal ultrasonography (USG) revealed a 8.8×4.8-cm sized right adnexal mass. The echogenicity of the mass was heterogeneous with irregular contour.

Abdomino-pelvic CT showed a heterogeneous enhancing solid mass in right adnexa 9 cm in diameter (Figure 1).

MRI of the pelvis demonstrated a 4.8×7.8 cm sized, heterogenous SI on T2WI and high SI on T1WI, enhancing mass with diffusion restriction around right adnexa (Figure 2). Its findings indicated that sex-cord stromal tumor such as granulosa cell tumor or subserosal myoma with secondary degeneration that should be ruled out. There was no evidence of significant LN enlargement in MRI images. The serum cancer antigen 125 (CA-125) level was 20.0 U/ml (normal: < 35.0 U/ml). Threre were no abnormalities in other blood chemistry.

In view of the scan findings, a laparotomy was performed; about 7-cm sized tumor was found in right mesosalpinx with ruptured state. The uterus and contralateral ovary were normal and

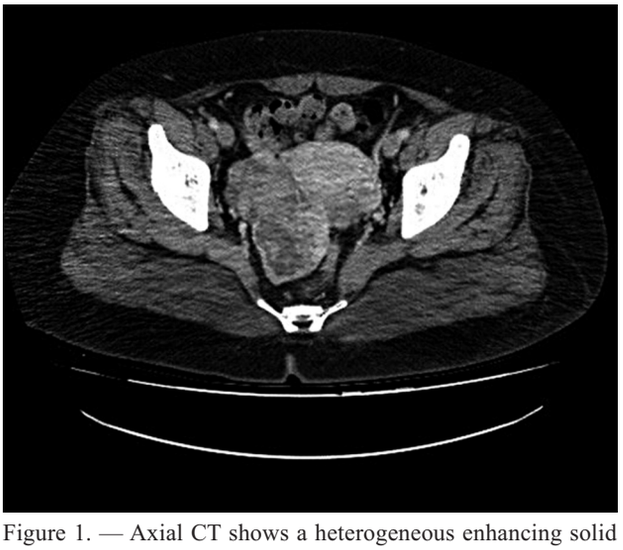

Figure 1. — Axial CT shows a heterogeneous enhancing solid mass in right adnexa (9 cm).

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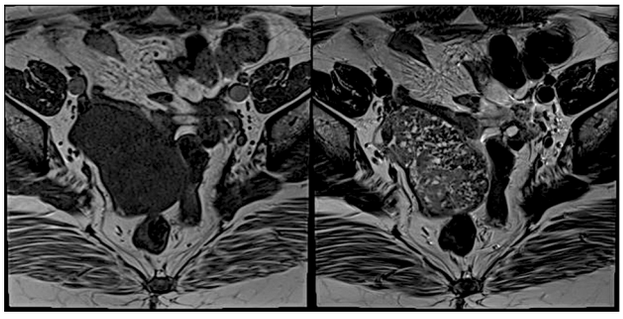

Figure 2. — MRI demonstrates a 4.8×7.8 cm sized enhancing mass with diffusion restriction around right adnexa (heterogenous SI on T2WI and high SI on T1WI).

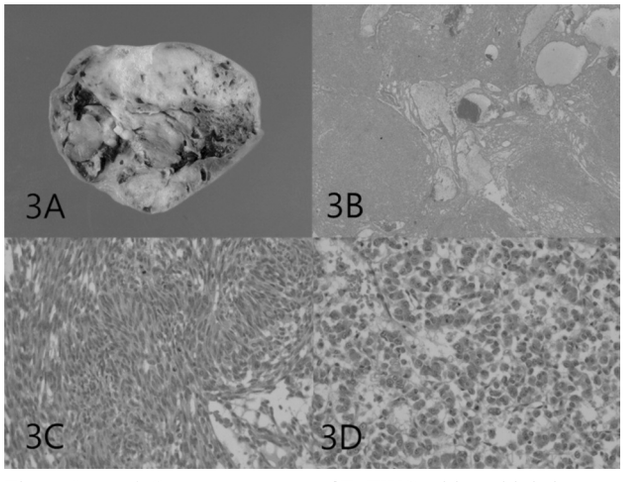

Figure 3. — A) Gross appearance of FATWO with multiple hemorrhage with small cystic change. B) Uniform solid area with variable sized cystic lesion (Hematoxylin & Eosin; ×50). C) Spindle cells with increased mitosis (Hematoxylin & Eosin; ×200). D) Epithelioid cells with moderate cytologic atypia (Hematoxylin & Eosin; ×200).

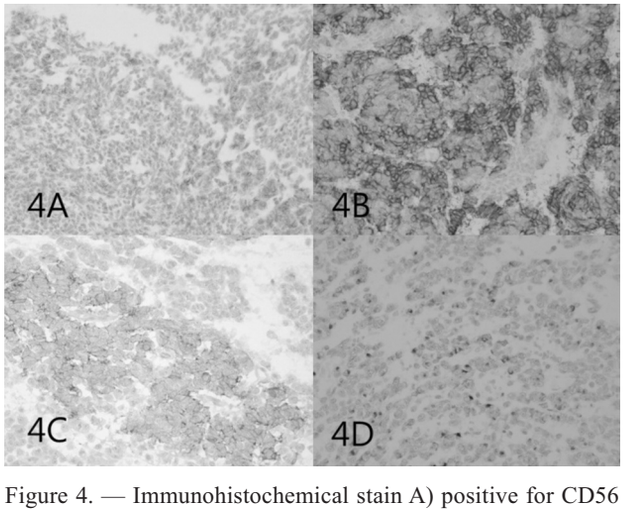

Figure 4. — Immunohistochemical stain A) positive for CD56 (×200). B) Positive for CD34(×200). C) Focal positive for CD117 (c-kit, about 5%, ×200). D) Pan-cytokeratin (CK, ×200). Of note the cytoplasmic dot-like pattern of CK staining.

there was no other visible macroscopic tumor or lymphadenopathy. Intraoperative frozen section histology of tumor indicated possible mesenchymal tumor.

A total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO) and omentectomy were performed, with removal of the mass present in the right tube.

Grossly, the ruptured tumor located in right mesosalpinx measuring 8.5×5.5×4.5 cm. The mass was grey-tan colored, soft, solid, and encapsulated. Cut surface revealed focal hemorrhage and small cystic change (Figure 3A). Microscopically, the tumor was solid area with macro- and microcystic change. Solid area composed of spindle and epithelioid cells with moderate cytologic atypia. It revealed short fascicle, tubular, cord-like, and sieve-like pattern. Lining of cyst were cuboidal or hobnail cells similar to that of solid area. Myxoid change was also identified. Tumor showed capsular invasion, but lymphovascular invasion was not identified. Mitotic count was high (up to 17/10 HPF) and necrosis were also identified (Figures 3B-D).

Immunohistochemical stains were positive for calretinin, CD34, CD56, focal positive for CD117 (c-Kit), and cytokeratin (CK). The tumor cells were negative for alpha-inhibin, actin, S-100, CK-19, EMA (Figures 4A-D).

In consideration of the anatomical location, histologic features and results of immunohistochemical staining, the tumor was diagnosed as FATWO with malignant potential. The patient's postoperative period was uneventful. She is under the close follow-up without any chemotherapy or radiation.

Discussion

FATWO are rare neoplasms arising in the broad ligament from the remnants of mesonephric/Wolffian ducts. The median age was 50 years, ranging from 18 to 83 years. Most cases are discovered incidentally during pelvic examination or at laparotomy. Although most cases in the literature are benign, there are 11 reported cases of malignant tumors [5, 6].

A diagnosis of malignant FATWO is vexing particularly because of the rarity of this tumor, small cases in the literature are available. Large tumor size, capsular invasion with rupture, increased mitotic activity, hypercellularity, and nuclear atypia indicates aggressive clinical course [3, 7, 8].

The reported immunohistochemical study of primarily benign FATWOs describe positivity for vimentin (100%), pancytokeratin (AE 1/3, CK1) (100%), anti-cytokeratin 5.2 (100%), calretinin (91%), cytokeratin 7 (88%), inhibin (68%), and epithelial membrane antigen (12%), among others [9, 10].

There is no reliable immunohistochemical stain suggesting malignant potential. On review of literature, one report suggested that CD56 positivity may indicate malignancy [11]. Present case also expressed CD56 positivity; it could be a helpful diagnostic marker to diagnosis malignant FATWOs.

The two patients with malignant FATWOs positive for c-kit were reported by Steed *et al.* and Syriac *et al.* [6, 12]. One of them was a recurred case considered as malignant FATWO. Authors suggested that a molecular targeted ther-

apy, such as tyrosin kinase inhibitor, could be considered in case of no response for chemotherapy and radiation therapy in metastatic or recurrent FATWO [12]. The present case was focal positive for c-kit, about 5%. There is still controversy the usefulness of c-kit immunohistochemical stain to differentiate between benign and malignant lesions. However it also may be helpful diagnostic biomarker to determine malignancy and could be one of the treatment choice as targeted therapy.

Because of the rarity of these tumors, there are no clear recommendations regarding initial evaluation, treatment, follow-up or adjuvant therapy. Various treatments have been described, of which the majority involve debulking surgery, including total abdominal hysterectomy and bilateral salpingo-oophorectomy. However, chemotherapy and radiation therapy have not proven to be effective in recurrent FATWOs.

In conclusion, FATWOs are rare and generally benign tumors and some of them follow a malignant course with recurrences. Therefore, long-term follow-up is required for patients with FATWOs, especially those with malignant disease.

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