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Female Adnexal Tumors of Probable Wolffian Origin with a Biphasic Histologic Growth Pattern and Positive for C-kit

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Abstract Female Adnexal Tumor of Probable Wolffian Origin (FATWO) is believed to be derived from the mesonephric (Wolffian) remnants commonly located in the broad ligament. Here we report a case of FATWO with unique histologic growth pattern. The tumor has a solid growth pattern with both epithelioid and spindle cell components. Immunohistochemistry (IHC) showed tumor cells to be diffusely positive for Estrogen receptor (ER) and Progesterone receptor (PR). The epithelioid areas were positive for AE1/3, CK-7 and CAM 5.2. The spindle cell areas were positive for Vimentin and CD10. The tumor cells were negative for Inhibin, CK20, P53, CA125, CD99, Calretenin and CK5/6. Interestingly, the tumor cells are positive for C-kit, which provides additional evidence for possible therapy using tyrosine kinase inhibitors (TKI). However, the frequency of c-kit expression in this tumor and its relevance to therapeutic efficacy using TKI for the recurrent and metastatic tumor are unknown and merit further study.

1. Introduction

Female Adnexal Tumors of Probable Wolffian Origin (FATWO) are rare. They are first reported in 1973 by Kariminejad and Scully [1]. More than 80 cases have been reported so far. They are believed to arise from the remnants of the mesonephric duct. Although mesonephric or Wolffian ducts are crucial in the formation of the vas deferens in the male, in females they degenerate and persist only as occasional inclusions in the lateral walls of the vagina (Gartner's duct), cervix and consistently in the broad ligament [2]. FATWOs are usually found in the same location where mesonephric remnants are commonly found. It has been shown that the tumor shares similar histological and immunohistochemical features with mesonephric remnants [3,4]. These features are distinctive and are not found in other adnexal tumors.

FATWO has generally been observed to behave in a benign fashion. However, among the more than 80 reported cases, the recurrent/metastatic rate is 23%. Therefore, the tumor should be considered to be of low malignant potential. Limited data indicate that recurrent/metastatic tumors do not respond to chemotherapy or radiation [5–7]. However, the immunoactivity of the tumor provides a possibility that the c-kit positive tumors may respond to tyrosine kinase inhibitors (TKI) such as Gleevec (Novartis Pharmaceuticals Corporation, One Health Plaza, East Hanover, NJ) [6].

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2. Case report

2.1. Clinical history

Patient is a 47-year-old woman who had amenorrhea following placement of Mirena Intrauterine device (IUD) in 2009. In 2011, she was diagnosed with complex hyperplasia without atypia. In June of 2012, she started to have irregular vaginal bleeding with intermittent left lower quadrant (LLQ) pain/discomfort. An endometrial biopsy (EMB) was performed and found to be benign. An ablation and IUD removal was performed, and meanwhile, long-term reliable contraception methods were discussed with the patient. The patient agreed to undergo a laparoscopic bilateral tubal ligation in May of 2013. During the procedure, an incidental left paratubal/broad-ligament mass lesion was identified. Multiple fragments of the lesion were removed at that time.

2.2. Gross and histologic findings

Grossly, the tumor was homogenously tan, firm and solid measuring 4.5 × 4 × 2 cm in aggregates with a segment of left fallopian tube (Fig. 1). Microscopically, the tumor displays a biphasic growth pattern in which nests of epithelioid cells grow in spindled cell background (Fig. 2a and b). Nuclei are bland with fine, evenly dispersed chromatin with indistinct nucleoli. The tumor has a low mitotic rate (0–3 mitoses/10 high power fields). Immunohistochemistry (IHC) showed tumor cells to be diffusely positive for ER and PR (Fig. 3). The epithelioid areas were positive for AE1/3, CK-7 and CAM 5.2. The spindle cell areas were positive for Vimentin and CD10 (Fig. 3). The tumor cells were negative for Inhibin, CK20, p53, CA125, CD99, Calretenin and CK5/6. Interestingly, the tumor cells are positive for C-kit with more prominent staining in the epithelioid areas (Fig. 4).

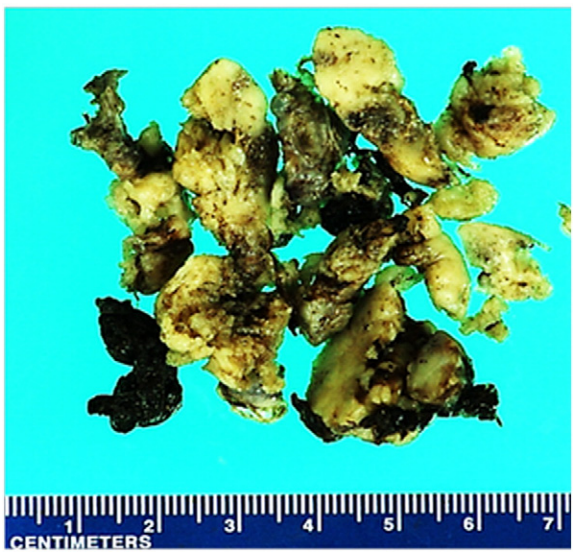

Fig. 1 A case of FATWO observed incidentally at laparoscopy. The tumor is located in the broad ligament and the specimen is submitted in fragments. Grossly, the tumor is white-yellow, solid with focal hemorrhage.

3. Discussion

The majority of patients with FATWO are parous women with a median age of 50 years (range 15-83 years old). The clinical presentations are variable. Most patients have no symptoms and the tumor is found incidentally on imaging studies or laparoscopy. The case we reported here is discovered at laparoscopy for tubal ligation. In subsets of reported cases, the patients present with abdominal pain, and may also have with genitourinary symptoms. However, the source of pain in these cases is unclear.

In majority of the reported cases, the tumor is located in the broad ligament as reported in this case; however, it has been reported that the tumor can also be found in the rete ovarii [8–11], retroperitoneum [12], in a paravaginal location and rarely in the ovary itself [13,14].

Histologically, four different histopathologic patterns are described by Devouassoux-Shisheboran et al [3]: 1) Diffuse – solid nests of spindle cells; 2) Epithelioid – a tubular pattern of packed, winding, branching and anastomosing tubules; 3) Cribriform – a sieve like pattern of epithelioid cells; 4) Multicystic. In our case, the unique biphasic growth pattern in which nests of epithelioid cells grow in spindled cell background has rarely been reported.

The differential diagnosis of FATWO includes ovarian sex cord stromal tumors, such as Sertoli cell tumor, Sertoli-Leydig cell tumor, granulosa cell tumor, well differentiated endometrioid ovarian adenocarcinoma, and endometrioid adenocarcinoma of the fallopian tube. Sertoli-Leydig cell tumors have not been reported in the paratubal site or in the broad ligament. Therefore, our case is unlikely Sertoli-Leydig tumor due to its location and histologic pattern. There have been reported cases of granulosa cell tumor in the broad ligament. Nuclear grooving is an important but non-specific feature of granulosa cell tumors. Nuclear grooving is not a feature of our tumor. In addition, inhibin, which is positive in granulosa cell tumor, is negative in our tumor. Endometrioid adenocarcinoma arising from the fallopian tube and ovary needs to be differentiated from FATWOs arising within the broad ligament and ovary. The bland cytology with a low mitotic activity in our tumor excludes endometrioid adenocarcinoma in which the degree of nuclear atypia and mitotic activity are more impressive.

The immunohistochemistry staining pattern in our tumor also supports the diagnosis of FATWO. Almost all reported FATWOs are strongly positive for Pan-cytokeratin, CAM 5.2 and vimentin. Majority of FATWOs stains diffusely with calretinin, CD10 and CK7. Variable immunoreactions to inhibin, estrogen receptor, progesterone receptor, androgen receptor and EMA have been observed