Gynecologic Oncology Reports 33 (2020) 100612

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Case report

Female adnexal tumor of probable Wolffian Origin – A report of two cases at one institution

Megan E. Bunnell[a], Bridget M. Donovan[a], Paige H. Parrack[b], Michael G. Muto[c], Neil S. Horowitz[c], Shuk On Annie Leung[c,*]

[a] Department of Obstetrics, Gynecology and Reproductive Biology, Brigham and Women's Hospital, Harvard Medical School, Boston MA 02115, United States
[b] Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston MA 02115, United States
[c] Division of Gynecologic Oncology, Department of Obstetrics, Gynecology and Reproductive Biology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA; Dana-Farber Cancer Institute, Boston MA 02115, United States

ARTICLE INFO

Keywords:
FATWO
Adnexal mass
Wolffian duct
Benign

1. Introduction

Female Adnexal Tumor of Probable Wolffian Origin (FATWO) is a rare gynecologic neoplasm of low malignant potential. There are under 100 cases of FATWOs described in the literature (Shalaby and Shenoy, 2020). These tumors are thought to be derived from mesonephric (Wolffian) duct remnants. Patients with FATWO are most often described as presenting with vague abdominal symptoms or remain asymptomatic with these tumors discovered incidentally during imaging or abdominal surgery performed for other indications (Shalaby and Shenoy, 2020; Liu et al., 2018). The mean age of diagnosis is reported to be 50 years, with a range of 15 to 83 reported in the literature (Shalaby and Shenoy, 2020). The most common location of a FATWO is in the broad ligament, but they can be identified in any of the female reproductive organs that house remnants of the Wolffian duct system including the broad ligament, mesosalpinx, fallopian tubes, ovaries or peritoneum (Cossu et al., 2017). There are, at present, no tumor markers associated with FATWO, and CA-125 levels are most often normal in published cases (Shalaby and Shenoy, 2020). In general, FATWOs require no additional management beyond initial surgical intervention.

Herein we describe two separate cases of FATWO, in a pre-menopausal and a post-menopausal woman, that were diagnosed on final pathology at the Brigham and Women's Hospital in Boston, MA.

2. Case Presentation

2.1. Case A

A 43-year-old pre-menopausal G4P3 woman with no past medical history presented to the emergency department with acute right lower quadrant abdominal pain without vaginal discharge, bleeding or other systemic symptoms. Human chorionic gonadotropin (hCG) was negative. During her workup she had an abdominal computed tomography (CT) which noted a 7x4x4cm "soft tissue and fluid containing structure with a contained 2.5 cm rim calcified component, most likely representing the right ovary with a contained dermoid cyst" (Supplementary figure 1). A follow up pelvic ultrasound noted similar findings with flow to both ovaries. Her pain was controlled with Toradol and she was referred for outpatient management of this lesion. Repeat pelvic ultrasound noted a "6.5x3.0x4.5 cm lobulated solid mass, partially calcified (2.8 cm) and partially solid with color flow located in posterior cul-de-sac. Mass adjacent to but seemingly separate from right ovary. Could be *para*-ovarian vs. bowel etiology" (Fig. 1). Of note, this patient had pelvic ultrasounds dating back to pregnancy 9 years prior identifying a 4.0x2.0x2.0 cm "heterogenous solid-appearing right adnexal mass with areas of increased echogenicity, felt to possibly represent a broad ligament fibroid."

Given the ultrasound findings, patient was counseled to undergo surgical management with a gynecologic oncologist. Her CA 125 was

* Corresponding author at: Brigham and Women's Hospital, Division of Gynecologic Oncology, 75 Francis Street, ASB1, 3rd Floor, Rm. 3173, Boston MA 02115, United States.
E-mail address: soleung@bwh.harvard.edu (S.O.A. Leung).

https://doi.org/10.1016/j.gore.2020.100612
Received 13 June 2020; Received in revised form 12 July 2020; Accepted 14 July 2020
Available online 21 July 2020

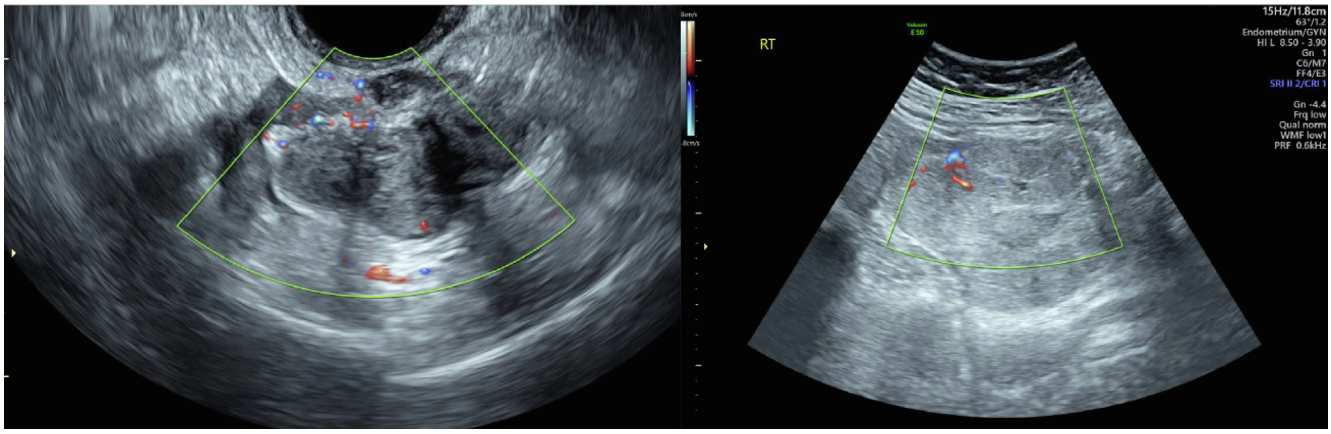

Fig. 1. Pelvic ultrasound of Case A (left) and Case B (right).

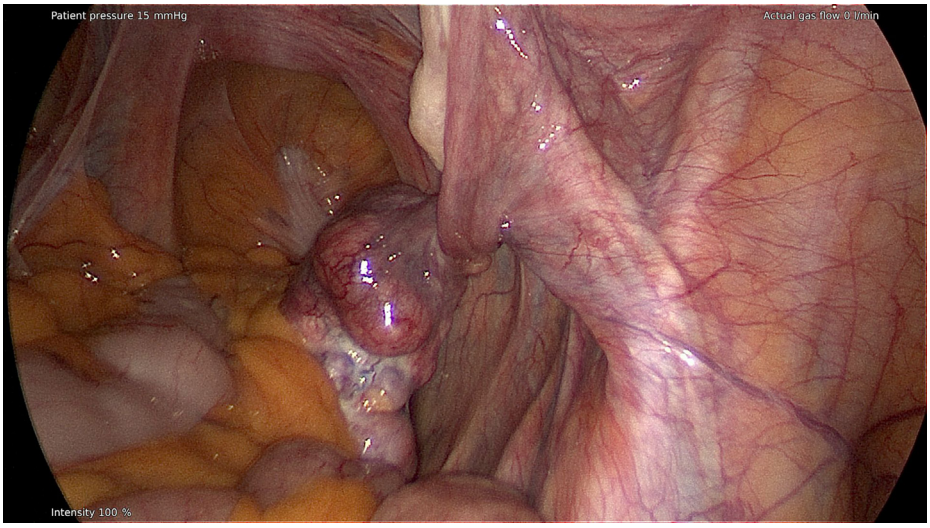

Fig. 2. Intra-operative findings of Case A.

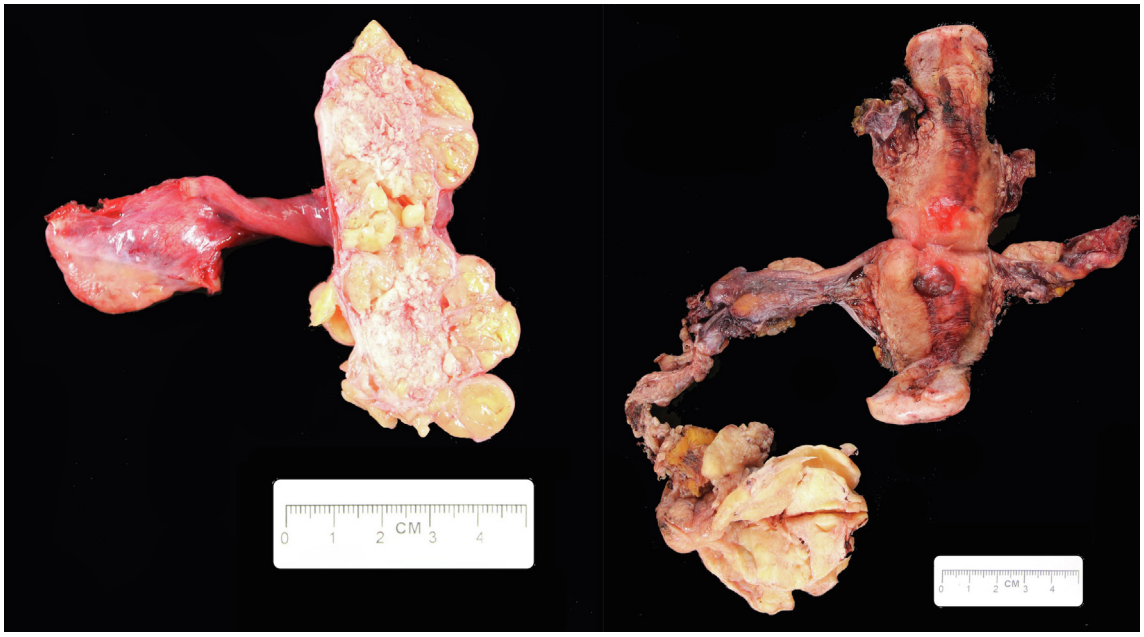

Fig. 3. Gross pathology of Case A (left) and Case B (right).

10U/mL, CEA 1.6 ng/mL, and CA 19–9 was 7U/mL. Two weeks after presentation she underwent a diagnostic laparoscopy. Upon initial survey of the abdomen, the right adnexa was noted to contain a heterogeneous, partially calcified mass adjacent to the right fallopian tube, which was torsed on itself (Fig. 2). A right salpingo-oophorectomy was performed and the specimen, tube, and ovary were extracted through a mini-Pfannenstiel incision. Intra-op frozen section revealed a "lobulated paratubal mass, favor female adnexal tumor of Wolffian origin." Upper abdominal survey, uterus, left tube and ovary were unremarkable. Pelvic washings were submitted, but given no visible intraabdominal metastatic lesions and low concern for high grade neoplasm, no further surgical staging was performed. Final pathology revealed a 6.8 cm female adnexal tumor of probable Wolffian origin. IHC staining was positive for SF1, AE1/3 (focal) and calretinin; while negative for GATA3, ER, PAX8, CD10, and EMA. Gross pathology is presented in Fig. 3. The patient recovered well post-operatively, was discharged home the same day. Given the low malignant potential of this lesion, the patient was referred back to her general gynecologist for routine follow-up.

2.2. Case B

A 57-year-old post-menopausal G2P2 Armenian woman with a past medical history of hypothyroidism presented to her gynecologist with blood-tinged vaginal discharge and, as part of her workup, had a pelvic ultrasound notable for an "irregular solid mass in the right adnexa measuring 8.2 × 8.7 × 6.9 cm with moderate color flow. Endometrial thickness noted at 4.1 mm." (Fig. 1) She had no complaints other than vaginal discharge and denied any abdominal pain. An endometrial biopsy showed superficial fragments of weakly proliferative endometrium with no hyperplasia or malignancy. Her CA-125 was 10U/mL

The patient was taken to the OR the following week in the setting of ultrasonographic evidence of an adnexal mass, and intraoperative findings revealed a fleshy, necrotic mass in the right adnexa, densely adherent along the anterior cul-de-sac, clearly separate from fallopian tube and ovary. No other abnormalities were visible on survey of upper and lower abdomen. Frozen section revealed "*peri*-adnexal mass, apparently not attached to ovary and tube, possibilities include FATWO, solitary fibrous tumor or carcinoma with sex-cord like differentiation." The patient underwent a laparoscopic hysterectomy, bilateral salpingo-oophorectomy, omentectomy and pelvic peritoneal biopsy. Permanent pathology revealed a 9.5 cm FATWO. Immunohistochemistry staining was positive for WT-1, inhibin (multifocal), calretinin (multifocal), SF-1 (focal) and negative for STAT6 and CK7. The patient recovered well post-operatively and was discharged home the same day. Routine follow-up with her general gynecologist was recommended.

3. Discussion

The diagnosis of FATWO is a challenging one and making an accurate diagnosis of this predominantly benign lesion can affect the planned surgical procedure. There are, to our knowledge, no serum biomarkers directly associated with FATWOs, thereby limiting preoperative clinical suspicion (Shalaby and Shenoy, 2020). Radiologically, FATWO is also a challenging diagnosis. On MRI imaging, FATWOs are described as slightly hyperintense adnexal masses with cystic degeneration—difficult to differentiate from subserosal leiomyomas and other ovarian tumors such as thecomas (Matsuki et al., 1999). CT demonstrates lesions that can be cystic or solid with heterogeneous enhancement, while ultrasound reveals similar findings with typically well-vascularized flow. FATWOs are commonly described as having some calcified component, visualized on both radiologic and gross examination (Matsuki et al., 1999; Kahyaoglu et al., 2012).

Based on clinical presentation, intra-operative examination, and pathological analysis, the differential diagnosis for a FATWO includes endometrioid adenocarcinomas and sex cord stromal tumors such as Sertoli-Leydig cell tumor and granulosa cell tumor. The location of the tumor is an important factor in supporting the diagnosis of a FATWO. FATWOs typically do not involve the fallopian tube or ovary and most commonly arise in the broad ligament, whereas Sertioli-Leydig tumors have not been identified in the paratubal area or broad ligament. Endometrioid adenocarcinomas that mimic FATWOs typically involve the fallopian tube or ovarian parenchyma (Goyal et al., 2016).

Grossly, FATWOs are solid to cystic with a grey-yellow cut surface. Microscopically, FATWOs can show a variety of morphologies including sieve-like, tubular, sheet-like, and trabecular patterns (Kahyaoglu et al., 2012). The tumors can be a mixture of the patterns with uniform, low-grade nuclei. Sertoli-Leydig tumors can have similar histologic findings, but the presence of Leydig cells can help differentiate them from FATWOs. Additionally, on clinical presentation, patients with Sertoli-Leydig cell tumors may exhibit endocrine symptoms, which are not features of FATWOs. Histopathology from Case A is presented in supplementary materials (supplementary figure 2).

In general, FATWOs are considered benign lesions, with a few case reports of aggressive behavior including cases of metastases and recurrence (Heatley, 2009). The available case reports are, no doubt, enriched with FATWOs that behave aggressively as benign lesions are most often clinically silent, incidentally found, and thus underdiagnosed. Within the available literature, there are no specific clinical or histopathologic findings that correlate with aggressiveness of a FATWO aside from metastases noted at the time of initial resection; it has been proposed that on pathologic examination the presence of necrosis, capsular invasion, cellular pleomorphism, and a high number of mitoses, as in most lesions, correlate with an aggressive FATWO subtype (Shalaby and Shenoy, 2020). If metastases occur, they are most commonly in the liver and lung (Shalaby and Shenoy, 2020).

Given the small number of FATWOs diagnosed to date, there are a variety of management options described. Complete surgical resection of the lesion is, in most cases, curative, and depending on the menopausal and childbearing status of the patient, hysterectomy and/or oophorectomy is a reasonable approach. While there is a lack of literature related to reproductive outcomes after management of a FATWO, one case report notes recurrence of FATWO after pregnancy, postulating the potential for a degree of hormone dependence (Atallah et al., 2004). Chemotherapy has an unclear role in the management of recurrent FATWOs, which are most often managed with repeat surgical resection or debulking. In cases in which chemotherapy is utilized, most commonly carboplatin/paclitaxel is used (Shalaby and Shenoy, 2020; Kwon et al., 2016). Upon review of available literature, however, data regarding any significant impacts of chemotherapy intervention on time to subsequent recurrence, progression free survival and/or the benefit vs associated morbidities of systemic therapy in the management of recurrent FATWO is limited. There are no current guidelines on routine imaging or physical examination follow up for women with a FATWO diagnosis, though most cases report routine gynecologic follow up.

4. Conclusion

Female adnexal tumor of probable Wolffian origin (FATWO) is a rare pathologic diagnosis most typically made in the workup of an imaging-identified adnexal mass without biomarker abnormalities. It is a lesion that exhibits an overall favorable prognosis with benign behavior. FATWOs can present a challenge, particularly on frozen section, of clear identification to guide the surgeon in appropriate intraoperative procedure and management. The cases we describe provide examples of both a pre- and post-menopausal diagnosis of FATWO, which had different presentations both clinically and on imaging as well as varied surgical management given the patients age, associated symptoms, and clinical status. In case A, the indolent nature of FATWO is demonstrated as the patient had the lesion noted on ultrasound 9 years prior. An uncommon complication of FATWO was demonstrated

with torsion prompting surgical intervention. In this case, conservative management was utilized with preservation of the uterus. Given a normal contralateral ovary and desire for permanent sterilization, the tube and ovary on the affected side were removed, though given the distinct location of FATWO from the tube and ovary, an argument for ovarian preservation can be made. More cases of FATWO and follow up of those diagnosed will be needed to better characterize the behavior of these lesions and clarify the most appropriate management strategy.

Ethics approval and consent to participate and consent for publication

Written informed consent was obtained from the patients.

Author contribution

MB wrote the main manuscript body. PP was involved in the pathologic interpretation including images and written content. AL, BD, MM, and NH were involved in the care of the patients. All authors were involved in the editing and approval of the manuscript.

Declaration of Competing Interest

The authors declare no conflicts of interest

Acknowledgements

Thank you to Bradley Quade, MD PhD for reviewing the manuscript. Thank you to Chih-Ping Mao, MD, PhD for his preparation of the gross pathology photo for Case B and Annacarolina da Silva, MD, MSc for her preparation of the histology photo for Case A.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gore.2020.100612.

References

Shalaby, A., Shenoy, V., 2020. Female Adnexal Tumor of Probable Wolffian Origin: A Review. Arch. Pathol. Lab. Med. 144 (1), 24–28.
Liu, L., Fang, Q., Xing, Y., 2018. Female adnexal tumor of probable Wolffian origin arising from mesosalpinx: A case report and review: FATWO, a rare neoplasm. J Obstet Gynaecol Res. 44 (9), 1859–1863.
Cossu, A., Casula, M., Paliogiannis, P., Tanda, F., Palomba, G., Sini, M.C., et al., 2017. Female Adnexal Tumors of Probable Wolffian Origin (FATWO): A Case Series With Next-Generation Sequencing Mutation Analysis. Int. J. Gynecol. Pathol. 36 (6), 575–581.
Matsuki, M., Kaji, Y., Matsuo, M., 1999. Female adnexal tumour of probable Wolffian origin: MR findings. Br J Radiol. 72 (861), 911–913.
Kahyaoglu, S., Kahyaoglu, I., Sirvan, L., Sengul, I., Timur, H., Mollamahmutoglu, L., 2012. Female Adnexial Tumor of Probable Wolffian Origin (FATWO) without Ki-67 Expression Reflecting Low Malignant Potential in a 55-Year-Old Woman. Eurasian J Med. 44 (3), 172–175.
Goyal, A., Masand, R.P., Roma, A.A., 2016 Mar. Value of PAX-8 and SF-1 Immunohistochemistry in the Distinction Between Female Adnexal Tumor of Probable Wolffian Origin and its Mimics. Int J Gynecol Pathol. 35 (2), 167–175.
Heatley, M.K., 2009. Is female adnexal tumour of probable wolffian origin a benign lesion? A systematic review of the English literature. Pathology. 41 (7), 645–648.
Atallah, D., Rouzier, R., Voutsadakis, I., Sader-Ghorra, C., Azoury, J., Camatte, S., et al., 2004. Malignant female adnexal tumor of probable wolffian origin relapsing after pregnancy. Gynecol Oncol. 95 (2), 402–404.
Kwon, M.J., Yun, M.J., Kim, M.K., 2016. A female adnexal tumor of probable Wolffian origin showing positive O-6-methylguanine-DNA methyltransferase methylation. Obstet Gynecol Sci. 59 (4), 328–332.