Wolffian tumor (female adnexal tumor of Wolffian origin) presenting as a pelvic side wall mass: Report of a case

Claire Rosen1, Emily Reardon1, Susan Shyu2, Julia Terhune1, Paul Saats2, Olga Ioffe2 and Stephen Kavic1

Abstract
The Wolffian tumor, previously identified as “female adnexal tumor of probable Wolffian origin,” is a rare tumor first described in 1973. The tumor is usually benign and is characterized by diffuse and tubular patterns, accentuated by reticulum and periodic acid–Schiff stains. Immunohistochemistry is used to further identify and classify these tumors, which are positive for cytokeratins, vimentin, inhibin, calretinin, and CD10 and negative for cytokeratin 20, epithelial membrane antigen, estrogen receptor, progesterone receptor, 34betaE12, and glutathione S-transferase. We report the case of a 47-year-old female with Wolffian tumor arising from the pelvic sidewall, separate from all reproductive organs. This is the first reported case of Wolffian tumor in this location.

Keywords
Wolffian, female adnexal tumor of probable Wolffian origin, adnexal tumor, immunohistochemistry, reproduction

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Introduction
A rare tumor occurring in the adnexal region was originally described by Karminejad and Scully in 1973 as “female adnexal tumor of probable Wolffian origin (FATWO).”1 A variety of other names have been given to this tumor, including the current World Health Organization designation of Wolffian tumor.2 There have been less than 100 cases reported in the English literature, with fewer than 30 cases of malignant or recurrent disease.3,4 These tumors are solid or cystic and characterized by small, closely packed cells that are often described as “sieve-like” in appearance.5–8 Immunohistochemistry may be helpful in the diagnosis of these tumors.9–13 We report a case of an incidentally identified Wolffian tumor located on the pelvic sidewall, at a distance from the adnexa, in a 48-year-old female undergoing open repair of a recurrent ventral hernia. To our knowledge, this is the first reported case of Wolffian tumor arising in this location.

Case presentation
A 47-year-old female with past medical history of chronic obstructive pulmonary disease, asthma, diabetes mellitus, anxiety, hiatal hernia, obesity (body mass index 47.8), and sleep apnea presented to our hospital in 2017 for open repair of recurrent ventral hernia with incarceration. The operation consisted of extensive lysis of adhesions, removal of previously placed mesh, and excision of principal hernia sac. In the pelvis, the patient was incidentally noted to have a right pelvic wall mass, which appeared to be incarcerated fat, which was lateral to, and completely separate from, her right ovary and fallopian tube. There was no vascular pedicle. This was excised with electrocautery and sent for pathologic evaluation.

On pathologic review, the mass weighed 8 g and measured 3.5 × 2.5 × 2.3 cm. The surface was smooth and yellow-tan. The cut surface was white-tan, firm, and slightly rubbery with focal hemorrhage involving less than 2% of the...
Microscopic examination revealed epithelial cells arranged in solid sheets, elongate gland-like structures, and tubules. The cells contained monotonous, oval, hyperchromatic nuclei (Image 1). On immunohistochemical studies, the tumor cells were found to be positive for inhibin, calretinin, pancytokeratin, and CD10 and negative for PAX-8, CD34, actin, desmin, S100, EMA, and HMB45, supporting the diagnosis of Wolffian tumor (Image 2).

Her post-operative course was uneventful, with no immediate complications. She was seen in clinic for follow-up approximately 1 month after surgery, asymptomatic, and healing well. She was discharged from clinic and instructed to return as needed.

**Discussion**

The Wolffian tumor is a rare tumor first described 1973. It is characterized by diffuse and tubular patterns, accentuated by reticulum and periodic acid–Schiff (PAS) stains, and initially postulated as Wolffian in origin secondary to its microscopic appearance and common location within the adnexa. During embryologic development, hormones control the development of the Müllerian ductal system (which gives rise to the uterus, fallopian tubes, and upper part of the vagina) and the Wolffian ductal system (which gives rise of the epididymis, vas deferens, seminal vesicle, and ejaculatory duct). In the male fetus, anti-Müllerian hormone (AMH) induces the

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**Image 1.** Pelvic side wall mass (H&E stain). (a) The mass is well-circumscribed at scanning magnification. (b) Bland small epithelioid cells are arranged in predominantly diffuse pattern (medium magnification). (c) Numerous tubules are outlined by a well-defined basement membrane (medium magnification). Cells demonstrate oval hyperchromatic nuclei and finely granular chromatin with no atypia or mitotic activity.

**Image 2.** Immunohistochemistry. The cells also demonstrate strong positivity for (a) inhibin, (b) pancytokeratin, and (c) CD10. (d) They are negative for epithelial membrane antigen.
regression of the Müllerian ducts and testosterone induces the differentiation of the Wolffian ducts, while in the female fetus, the lack of AMH allows the Müllerian ducts to develop while the Wolffian ducts degenerate.14

In their initial description of the tumor, Karminejad and Scully note that a Müllerian origin of the FATWO was improbable, despite its common location within the Müllerian-derived organs, as the tumor does not closely resemble any neoplasm arising from a Müllerian duct derivative or surface epithelium of the ovary.1 They therefore proposed the term “FATWO.” The tumor has subsequently been referred to as Wolffian adnexal tumor, Wolffian adenoma, and reidentify Wolffian adenoma. The current preferred terminology, according to the World Health Organization Classification of Tumors, is Wolffian tumor.14

The removal of the “adnexal” part of the name in the current terminology is supported by the present case, in which the tumor occurred along the right pelvic sidewall, distant from the adnexa. We have not identified another case occurring in this location in the literature. The vast majority of Wolffian tumors occur within the broad ligament, fallopian tubes, mesosalpinx, or ovary.15 However, two cases have been described as retroperitoneal in location, one of which was reported prior to formal characterization in 1973.16

There have also been three reported cases of male Wolffian tumors, further supporting the abbreviated nomenclature.17

Age at diagnosis ranges from teenage to elderly, and the tumor generally is diagnosed secondary to local compressive symptoms or found incidentally on physical exam or imaging. Our described case was found incidentally during surgery. Although the majority of Wolffian tumors are benign, and they were initially characterized as such in 1973, some have been noted to be malignant with metastases throughout the pelvis and abdomen, and even to the chest.18 In a PubMed search of all papers with “Wolffian” and “Tumor*” in the title, 58 papers were found. Within these, there were 67 reported cases of FATWO, with 19 reported malignant incidences. While publication bias would be expected to amplify the proportion of malignant cases, the literature clearly supports a malignant potential for this tumor.

Overall, the literature supports the notion that approximately one-fifth of Wolffian tumors are diagnosed as malignant.5,4,19 However, it is important to consider that advances in immunohistochemistry have improved specificity in diagnosis of the Wolffian tumor in comparison to other tumors of reproductive origin, and that perhaps some of the reported incidences of malignant Wolffian tumors are misidentified well-differentiated carcinomas (especially endometrioid carcinoma).3,7–9 Although some case reports have suggested that specific markers may aid in differentiating malignant versus benign Wolffian tumors, the malignant potential of the Wolffian tumor has not been clearly established by molecular and immunohistochemical properties.20,21

Instead, the malignant diagnosis of the Wolffian tumor is determined by clinical recurrence or spread.19 Further reports with immunohistochemical classification of these tumors are necessary to aid in our predication of malignant potential.

From a histopathological standpoint, the FATWO demonstrates diffuse, solid, and sieve-like cystic areas, with occasional mitotic figures.5–8,15 Tubular patterns may be highlighted with PAS or reticulin stains.1,15 As the molecular composition of the Wolffian tumor can resemble other tumors of reproductive origin, immunohistochemistry is used to further identify and classify these tumors. Wolffian tumor cells are positive for cytokeratins, vimentin, inhibin, calretinin, and CD10 and negative for cytokeratin 20, epithelial membrane antigen (EMA), estrogen receptor (ER), progesterone receptor (PR), 34betaE12, and glutathione S-transferase.9–13,15 Proliferation index by Ki-67 is typically low. The absence of EMA is most helpful in distinguishing Wolffian tumors from epithelial neoplasms, and the presence of CD10 staining is most helpful in distinguishing it from sex cord-stromal tumors.

In differentiating Wolffian tumors from other tumors, that is, endometrioid adenocarcinomas and sex-cord stromal tumors, which may appear similar on microscopic analysis, immunohistochemistry plays an important role. In a study by Goyal et al.,13 looking at transcription factors for development of reproductive organs, it was found that paired box proteins (PAX), especially PAX-8, were found in endometrioid adenocarcinomas and steroidogenic factor-1 (SF-1) was found in all but one analyzed sex-cord stromal tumor. However, all analyzed Wolffian tumors were negative for these factors, as well as GATA binding protein 3 (GATA-3; another transcription factor involved in Wolffian duct morphogenesis). Unfortunately, the database used in this study looked at tumors from 1990 to 2014, and only eight Wolffian tumors were available for analysis. Further considering a larger volume of tumors, across multiple institutions, is necessary to better guide diagnosis.

**Conclusion**

Overall, this case adds to the literature the report of a rare tumor, including the immunohistochemistry used in diagnosis. To the best of our knowledge, this is the first reported case of Wolffian tumor arising from the pelvic sidewall, separate from all reproductive organs. It supports the current nomenclature of the Wolffian tumor by histological diagnosis. Further understanding and classification of the Wolffian tumor will likely rely heavily on immunohistochemical staining, and clinicians and scientists should utilize a wide array of staining to ensure appropriate diagnosis and add to the literature.

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ORCID iD

Claire Rosen https://orcid.org/0000-0002-1029-5522

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