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GYNAECOLOGICAL PATHOLOGY

Mesonephric proliferations of the female genital tract

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Summary

The mesonephric (Wolffian) duct regresses in females during embryological development. Remnants of this duct may persist typically along the lateral walls of the cervix, vagina, adnexa, and uterine corpus. These mesonephric epithelia may expand into hyperplastic proliferations and rarely form neoplasms. The spectrum of morphology, immunophenotype, clinical presentation, and molecular characteristics of mesonephric lesions is reviewed, with attention to distinction from entities in the differential diagnosis.

Key words: Mesonephric; Wolffian; mesonephric remnants; mesonephric hyperplasia; mesonephric carcinoma; mesonephric-like adenocarcinoma; female adnexal tumour of probably Wolffian origin.

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1. ORIGIN OF MESONEPHRIC PROLIFERATIONS (EMBRYOLOGY)

Mesonephric remnants are vestiges of the Wolffian (or 'mesonephric') ducts which regress during normal female development. The term 'Wolffian' has its origin from the name of the man who first described the embryology of the kidney (mesonephros) and its excretory ducts, Caspar Friedrich Wolff. Early in embryological development, a pair of Wolffian ducts exist adjacent to the Müllerian (or 'paramesonephric') ducts and connect the primitive kidney to the cloaca. During female development, in the absence of anti-Müllerian hormone (AMH; also known as Müllerian inhibiting substance or MIS) secreted by Sertoli cells of the developing testis, the mesonephric ducts regress while the fused Müllerian ducts continue to develop into the fallopian tubes, uterus, and vaginal wall. In males, the Wolffian ducts give rise to the seminal vesicles, epididymis, vas deferens, and efferent ducts of the testis, while the mullerian duct regresses, leaving only the vestige appendix epididymis in the paratestis.

It is worthy to point out that many tumours referred to as 'mesonephroma' or 'mesonephric carcinoma' of the ovary and other gynecological organs in older literature were actually referring to what is now currently considered clear cell carcinoma, because they resembled clear cell carcinomas of the kidney ('mesonephros'). This review focuses on those mesonephric remnants and proliferations related to the Wolffian/mesonephric duct, and does not further consider those tumours now considered clear cell carcinoma.

2. MESONEPHRIC REMNANTS AND CYSTS

2.1. Clinical features

Mesonephric remnants are typically identified in asymptomatic women, most commonly in the lateral wall of the cervix (3 and 9 o'clock) in up to one-third of normal cervices,[1,2] but also may be present within the wall of the uterine corpus and vagina as well as the ovarian hilum (rete ovarii) and mesosalpinx.

The Gartner duct, which is also derived from the mesonephric duct, may become obstructed resulting in a Gartner duct cyst.[3] Gartner cysts are uncommon (<1% of women[4]) and are typically located in the anterior or lateral walls of the vagina.[5] They may also be associated with renal and ureteral anomalies in the setting of congenital abnormalities of the mesonephric duct. Treatment for Gartner duct cyst is generally complete excision, for definitive diagnosis and relief of symptoms.

Mesonephric remnants and cysts are not associated with increased risk for malignancy; thus, they do not require treatment or follow-up unless associated with clinical symptoms.

2.2. Pathological features

2.2.1. Gross characteristics

In general, mesonephric remnants are non-mass forming and thus are not clinically or grossly apparent. Given that they are most likely to occur laterally, the location of routine cervical sampling will affect the frequency of encountering mesonephric remnants. Gartner duct cysts present similarly to other vaginal cysts.

2.2.2. Microscopic/morphological features

Histologically, mesonephric remnants are usually located deep in the cervical stroma but occasionally are identified immediately subjacent to endocervical or squamous mucosa. They are composed of clusters or linear arrays of small to medium-sized tubules lined by bland cuboidal cells with scant cytoplasm lacking ciliation, mucin, or squamous differentiation. The tubule lumens often contain a densely eosinophilic secretion that is periodic acid-Schiff (PAS) positive (Fig. 1A).[6,7] The nuclei in mesonephric remnants are uniform and lack hyperchromasia, but may show nuclear irregularity and grooves. Variations of mesonephric remnants include the ductal type (Fig. 1B),[6,8] where instead of small tubules there is a larger diameter duct that lacks intraluminal secretions, with or without associated tubules

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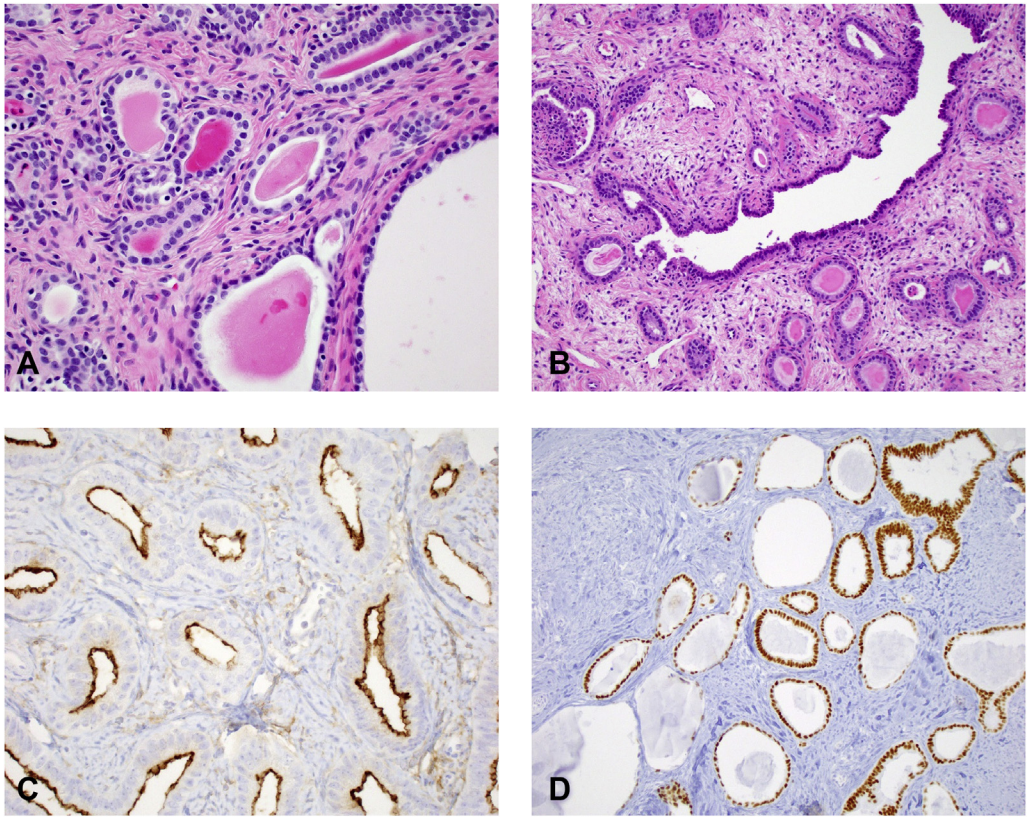

Fig. 1 (A) Mesonephric remnants are characterised by tubules lined by bland cuboidal or attenuated cells and often have colloid-like luminal secretions. (B) A ductal variant of mesonephric remnants in which the tubules are arranged around a large, sometimes cystically dilated duct structure. (C) CD10 immunohistochemistry in mesonephric remnants demonstrates apical or luminal staining. (D) GATA3 immunohistochemistry is strongly positive in cervical mesonephric remnants.

at the periphery. Mitotic activity is rarely if ever encountered.[9]

Gartner duct cysts are characterised by bland, cuboidal to low columnar non-mucinous epithelia. The cytoplasm is typically eosinophilic but may also have a vacuolated appearance. Mitotic activity is inconspicuous.

2.2.3. *Immunohistochemical features*

Immunohistochemically, mesonephric derived epithelia have a unique staining pattern allowing for distinction from endocervical and endometrial epithelium. CD10 typically highlights the apical (luminal) aspect of the cells (Fig. 1C),[10,11] and calretinin, GATA3 (Fig. 1D), and PAX8 are also frequently positive. Interestingly, mesonephric remnants in the adnexa are less likely to be GATA3 positive, and more likely to be inhibin positive,[12,13] for unclear reasons. Both p16 and p53 are negative or weak/patchy in benign mesonephric remnants.[14] For a complete summary of immunohistochemical features see Table 1 as well as discussion of differential diagnoses in subsequent sections.

2.2.4. *Molecular features*

No studies have evaluated molecular alterations in mesonephric remnants.

2.2.5. *Differential diagnosis*

Gartner duct cyst: Definitive diagnosis and distinction from other vaginal cysts can only be made by histological examination. Müllerian cysts and Bartholin duct cysts may also occur in the lateral walls of the vagina (as well as posteriorly) but are characterised by mucinous epithelium.

Cervical mesonephric remnants: One of the primary considerations with mesonephric proliferations is the distinction between remnants and mesonephric hyperplasia. In the first large series of mesonephric lesions reported by Ferry and Scully, the distinction between remnants and hyperplasia was somewhat arbitrary, but all remnants were orderly and well-circumscribed, with the largest being 6 mm.[7] Thus, a size cut-off of 6 mm has since been invoked to aid in distinguishing mesonephric remnants from hyperplasia. Cervical

Table 1 Immunohistochemistry of mesonephric lesions in the female genital tract

	MR/MH	MCA	MLA
PAX8	100%	88–100%	100%
GATA3	100%	95% (variable extent and intensity)	27%
CD10	73–83%	67%	78%
Calretinin	10%	67–88%	50%
TTF-1	ND	38%	92%
ER/PR	0%	0–25% (focal)	0%
p16 diffuse	0%	0%	0%
p53 abnormal	0%	ND	0%

MCA, mesonephric carcinoma; MH, mesonephric hyperplasia; MLA, mesonephric-like adenocarcinoma; MR, mesonephric remnants; ND, not done.

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