

Müllerian Remnant Embedded in Labia Majora

Peter Eskander, Zöe Baker, and Evalynn Vasquez



CASE PRESENTATION

A 15-year-old female presented to our Pediatric Urology Clinic complaining of inability to use tampons. She has a particularly complex medical history including Klippel-Feil syndrome, which is a congenital musculoskeletal condition characterized by the fusion of 2 vertebrae of the neck, bilateral microtia with aural atresia and conductive hearing loss, dysmorphic facial features and a cloacal malformation with a common urogenital sinus. Genetic testing revealed 46XX with a very small gain of material at 10q23.11. Surgical repair of the urogenital sinus was performed at 3 years of age at an outside hospital, which left her introitus partially obstructed. There was also redundant skin due to breakdown of her urogenital sinus repair which caused friction irritation against her clothing. She otherwise had the ability to void spontaneously. Upon further questioning, the patient disclosed that for the past year she has been bothered by the appearance of a suprapubic mass which could be seen through tight-fitting clothing. She reported occasional tenderness to palpation, but denied erythema, fevers, and drainage. She reported that the mass suddenly appeared and had been stable in size. She denied any trauma to the area. She denied any urinary symptoms including dysuria and incontinence. She was free of recent urinary tract infections. Menarche was reached at age 12 and regular cycles had been observed since. No pertinent family or social history was noted during the medical interview.

Physical examination performed in clinic revealed left-sided redundant labia minora, accompanied with tenderness to palpation in the suprapubic region consistent with a cystic mass. The mass measured approximately 3 cm in length and can be appreciated in Figure 1. Our patient presented with a satisfactory vaginal cavity but the introitus was obstructed by an anteriorly displaced fourchette.

DIFFERENTIAL DIAGNOSIS

Based on the history taken and the absence of swelling, redness, tenderness to palpation, and fever, an infection

of the affected area was unlikely. Patient also denied trauma ruling down the presence of a hematoma. Initial imaging and examination led us to believe that the mass may have been a retained corporal body. Prior to MRI, a renal ultrasound was performed which revealed healthy kidneys with interval growth without evidence of hydronephrosis. There were no abnormalities of the bladder noted and no pelvic masses were seen on ultrasound. Cystogram had been previously performed which showed normal capacity, smooth-walled bladder without evidence of vesicoureteral reflux or other abnormalities.

Palpation revealed that the mass felt cystic in nature and pelvic MRI revealed a cyst originating in the patient's mons pubis and tracking down to her labia majora. Centered within the body of the clitoris, the mass appeared as an isointense to hyperintense T2-weighted serpiginous lesion with possible vascular etiology measuring in its largest dimensions 5.0 cm × 2.3 cm × 5.0 cm (Fig. 2). On T1-weighted images, the lesion also appeared



Figure 1. Gross appearance of the suprapubic mass and the partially obstructed introitus (arrow) which was the patient's original chief concern. Clitoral hood (*), mass (**). (Color version available online.)

From the University of Missouri-Columbia School of Medicine; and the Children's Hospital of Los Angeles

Address correspondence to: Peter Eskander, B.S., 1008 S. College Ave APT 202 Columbia, MO 65201. E-mail: peb5m@health.missouri.edu

Submitted: August 12, 2019, accepted (with revisions): September 16, 2019



Figure 2. Sagittal, T2 weighted MRI showing the pubic bone (*), bladder (arrow), and a fluid-filled likely hematogenous mass (** seen in the superficial tissue and traveling toward the clitoris and urethra.

hyperintense and there was uniform homogeneous enhancement. The lesion extended inferiorly to the level of the urethra and vagina (Fig. 3) and superiorly and anteriorly to the level of the labia majora. No gross fistula was observed within the perineum and the patient's bladder maintained a spherical shape on MRI. The uterus, ovaries, and rectum were unremarkable. Intraoperatively, the cystic nature of the mass could be easily appreciated with its fluid filled core and well demarcated sac (Fig. 4). Other likely diagnoses included a Bartholin's duct cyst, cyst of the Canal of Nuck, or vulvar epithelial inclusion cyst. Proximity to the clitoris ruled down the likelihood of a Bartholin's duct cyst despite predilection for the labia majora.¹ The patient and her family elected for surgical intervention based on her symptoms and the bothersome location of the mass. Preoperative urinalysis was unremarkable and spontaneous urine output was recorded between

200 and 300 milliliters. Excision was uncomplicated and follow-up approximately a month and a half later revealed her labial incisions were healing well with a patent vaginal orifice.

HISTOPATHOLOGY

The unlikely finding of Müllerian tissue within the patient's labia majora led to intense histopathologic scrutiny. The specimen was labeled a "suprapubic mass" and grossly consisted of a tan, fluctuant, intact cyst measuring 7.5 × 2.3 × 2.5 cm with a cyst wall composed of a tan brown, soft material that averaged 0.15 cm in thickness. Microscopically, sections contained a large cystic structure with an internal lining mostly denuded and replaced by chronically inflamed granulation tissue. The focally preserved area is lined by ciliated columnar epithelial cells, which is consistent with typical Müllerian duct epithelium, although cuboidal or squamous cells may also be appreciated.^{4,12} The lumen contained degenerated peripheral blood elements and there was no evidence of malignancy identified. A mucicarmine stain was not performed in order to differentiate Müllerian (mucinous) from mesonephric (nonmucinous) origin.⁴ It is worth noting that these histopathologic findings bear no resemblance to other parts of our differential found more commonly within the labia majora such as a cyst of the Canal of Nuck and retained corporal tissue, which are characterized by simple cuboidal mesothelial cells and sponge-like tissue containing sinusoid blood-filled spaces lined by endothelium and separated by septa formed from the tunica albuginea, respectively.^{4,14}

DISCUSSION (CONTRIBUTING SENIOR AUTHOR – EVALYNN VASQUEZ, MD-MBA)

The most fascinating component of this case lies in the embryologic origins of the female reproductive system and the extremely rare finding of a Müllerian cyst outside of the vaginal canal. Evidence of prolapsed Müllerian cysts originating in the vaginal canal has been well documented,^{6,15,16}

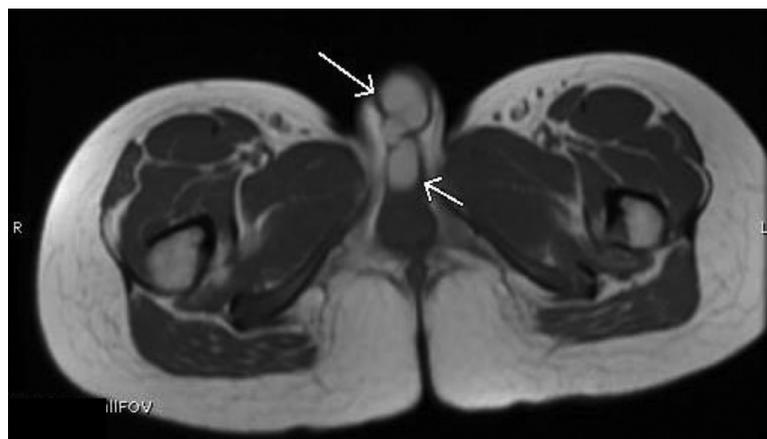


Figure 3. Axial, T2 weighted MRI imaging showing the serpiginous mass traveling medially toward the clitoris and urethra.

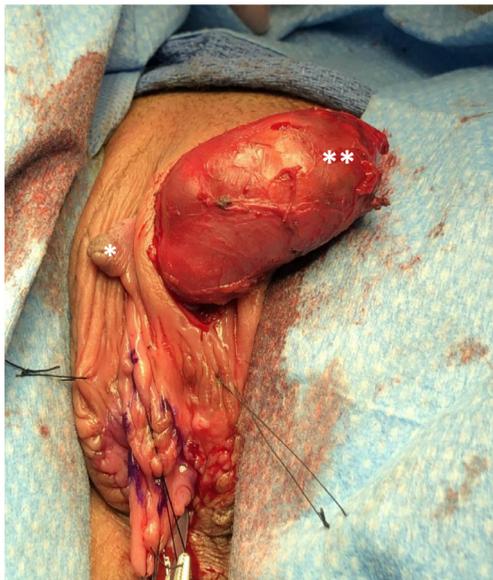


Figure 4. Intraoperative view of cystic mass within labia majora. Clitoral hood (*), mass (**). (Color version available online.)

which strengthens the call to work up any protruding vaginal masses for embryologic remnants, but very little, if any, literature exists describing Müllerian remnants actually originating in the external genitalia (Fig. 3). At birth, the patient was already exposed to atypical differentiation of her external genitalia in the form of her cloacal malformation. Prior to the seventh week of gestation, the fetal hindgut and urogenital sinus open into the cloaca.³ At this point, mesenchymal tissue, or the urorectal septum, separates the gastrointestinal from the genitourinary system, which lays the foundation for the development of external genitalia via the urogenital sinus, genital tubercle, urogenital folds, and labioscrotal swellings.²⁻⁵ Differentiation of the female's external genitalia is governed by the absence of sex-determining region Y, as well as, the presence of its antagonist, wingless-related MMTV integration site 4 (WNT4).³ On the other hand, the Müllerian duct is strictly responsible for the development of the female internal reproductive system in conjunction with estrogen. Specifically, the structures included are the uterine tubes, uterus, and proximal portions of the vagina; the distal vagina originates from the urogenital sinus.¹³ The staunch differences between the embryologic origins of the internal and external female reproductive tissue explains why the most common location for Müllerian cysts is anywhere within the vaginal walls, with the highest occurrence along the anterolateral aspect of the vagina.^{4,6}

When considering embryologic origins, the development of the round ligament offers an interesting addition to the differential diagnosis—a cyst of the Canal of Nuck. The role of the female gubernaculum remains debated, but traditionally, the round ligament is thought to be a direct product from the caudal end of the gubernaculum which invaginates through the tunica vaginalis and anchors in

the posterior wall of the labia majora.^{4,5,7-9} A persistent tunica vaginalis leads to a cyst of the Canal of Nuck, but histopathology rules this diagnosis out despite the regional specificity. One small detail in the role of the gubernaculum may, however, explain how Müllerian tissue arrived in the unlikely location of our patient's labia majora. Although the ends of the gubernaculum (in the form of the round ligament) do not originate from the Wolffian or Müllerian ducts, it does attach to the Müllerian ducts on the lateral aspects of the developing uterus. This connection is hypothesized to allow or induce the adequate development of the uterus and provides a possible mode of transmission of Müllerian tissue.⁷ Damage or malformation here has historically been associated with perineal anomalies and may have been one of the precipitating factors leading to our patient's congenital defects.^{7,10,11} Regionally, both the Bartholin and Skene glands are appropriate to consider, however, the mass' lack of infectious symptoms ruled down the likely etiology of these types of cysts. Gartner cysts may also be considered, but they are less common than their Müllerian counterparts (10%), characterized by abnormalities in the metanephric urinary system, and are almost always confined to the lateral walls of the vagina⁶—all components working against that diagnosis in this case. Despite these distinctions, our case proves that embryologic cysts are not always limited to the vaginal canal and completing the mucicarmine stain from earlier may have helped identify a Gartner cyst, had the lining epithelium not been as indicative of Müllerian origin. Müllerian cysts have the highest incidence of all vaginal cysts (40%-44%),^{4,6} but the presentation and location of our patient's mass highlights why this was truly a rare case.

Acknowledgments. Elizabeth A. Malm-Buatsi, MD

References

1. Temkin SM, Gregory T, Kohn EC, Duska L. Gynecology. In: Brunicaardi F, Andersen DK, Billiar TR, Dunn DL, Kao LS, Hunter JG, Matthews JB, Pollock RE. eds. *Schwartz's Principles of Surgery*, 11th ed New York, NY: McGraw-Hill; <http://accessmedicine.mhmedical.com.proxy.mul.missouri.edu/content.aspx?bookid=2576§ionid=216211905>. Accessed June 02, 2019.
2. DeUgarte CM. Embryology of the urogenital system & congenital anomalies of the genital tract. In: DeCherney AH, Nathan L, Laufer N, Roman AS. eds. *CURRENT Diagnosis & Treatment: Obstetrics & Gynecology*, 12th ed New York, NY: McGraw-Hill; <http://accessmedicine.mhmedical.com.proxy.mul.missouri.edu/content.aspx?bookid=2559§ionid=206957031>. Accessed June 02, 2019.
3. Crum C, Nucci M, Haefner H, Peters W. *Diagnostic Gynecologic And Obstetric Pathology*. 3rd ed; 2018.
4. Anderson S. Benign vulvovaginal cysts. *Diagn Histopathol*. 2010;16:495-499. <https://doi.org/10.1016/j.mpdhp.2010.08.004>.
5. Tanagho EA, Nguyen HT. Chapter 2. Embryology of the genitourinary system. In: McAninch JW, Lue TF, eds. *Smith and Tanagho's General Urology*. 18th ed New York, NY: McGraw-Hill; 2013. <http://accessmedicine.mhmedical.com.proxy.mul.missouri.edu/content.aspx?bookid=508§ionid=41088079>. Accessed 3 June 2019.
6. Töz E, Sancı M, Cumurcu S, Özcan A. Müllerian cyst of the vagina masquerading as a cystocele. *Case Rep Obstet Gynecol*. 2015;2015:1-3. <https://doi.org/10.1155/2015/376834>.

7. Ación P, Sánchez del Campo F, Mayol M, Ación M. The female gubernaculum: role in the embryology and development of the genital tract and in the possible genesis of malformations. *Eur J Obstet Gynecol Reprod Biol.* 2011;159:426–432. <https://doi.org/10.1016/j.ejogrb.2011.07.040>.
8. Cross S, Manek S. *Underwood's Pathology*. 7th ed Elsevier Inc.; 2019:438–464.
9. Standring S. *Gray's Anatomy*. 1st ed Elsevier Limited; 2016:1288–1313.
10. Elumalai G, Deosaran K. "Gubernaculum anomalies"- embryological basis and its clinical significance. *Elixir Embryol.* 2017;103:45645–45651.
11. Ación Pedro, Ación Maribel I. The history of female genital tract malformation classifications and proposal of an updated system. *Human Reprod Update*. September-October 2011;17(5):693–705. IssuePages; <https://doi.org/10.1093/humupd/dmr021>.
12. Ye L, Mayberry R, Lo CY, et al. Generation of human female reproductive tract epithelium from human embryonic stem cells. *PLoS One.*;6:e21136. doi:10.1371/journal.pone.0021136.
13. Kurita T. Developmental origin of vaginal epithelium. *Differentiation.* 2010;80:99–105. <https://doi.org/10.1016/j.diff.2010.06.007>.
14. Chen Kuo-Liang, Eberli Daniel, Yoo James J, Atala Anthony. Bio-engineered corporal tissue for structural and functional restoration of the penis. *Proc Natl Acad Sci.* 2010;107:3346–3350. <https://doi.org/10.1073/pnas.0909367106>.
15. Kresowik J, Kennedy CM, Wing S, Galask RP. Prolapsing vaginal cyst a case report. *J Reprod Med Obstet Gynecol.* 2007;52:852–854.
16. Dilbaz B, Şengül Ö, Dede S, Yerebasmaz N, Akkurt O. Prolapsing vaginal Mullerian cyst with cervical elongation mimicking cystocele. *J Obstet Gynaecol.* 2014:212–213. <https://doi.org/10.3109/01443615.2013.856389>.