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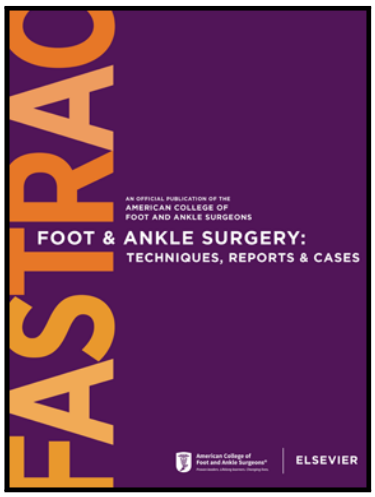

Title: A Rare Case of a Cutaneous Ciliated Cyst of Mullerian Origin Found in the Lower Extremity: A Case Report

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Title: Title: A Rare Case of a Cutaneous Ciliated Cyst of Mullerian Origin Found in the Lower Extremity: A Case Report

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Abstract:

Cutaneous Ciliated Cyst (CCC) of Mullerian origin are rare, benign, soft tissue tumors with less than 60 reported occurrences reported in literature, none in foot and ankle publications. Most of these lesions occur in the lower extremity of women of child-bearing age. We present a case involving a 33-year-old female who presented with a painful soft tissue mass to the right hindfoot. Physical examination demonstrated a well-circumscribed, adhered soft tissue lesion proximal to the 5th metatarsal base. Conservative treatment failed to relieve symptoms. MRI demonstrated a lobulated collection of fluid in the area of the soft tissue lesion. The mass was surgically excised

and sent to pathology. Histopathologic and immunohistochemical examination showed pseudostratified cuboidal to columnar epithelial lining with nuclear positivity for estrogen and progesterone receptors, a benign lesion with lineage from the Mullerian duct. The patient was followed for 14+ months and has subsequently recovered without complications or recurrence. We aim to illustrate characteristics that define these rare lesions and further educate foot and ankle surgeons on CCC management.

Introduction

Cutaneous ciliated cysts (CCC) of Mullerian origin are exceptionally rare, benign soft tissue tumors. These lesions are most often found in the lower extremity of adolescent females, however, there have been a few cases reported in the male population and in differing locations.[1] CCC was first encountered in 1850 by Hess and later in 1978 in a case study by Farmer and Helwig who described 11 such lesions identified in the lower extremities of women of reproductive age.[2]

There are a limited amount of reports discussing CCC. Roughly only 60 cases of CCC have been reported in the literature to date. The benign nature of these lesions is confirmed via histopathological and immunohistochemical examination which shows pseudostratified cuboidal to columnar epithelial lining with nuclear positivity for estrogen (ER), progesterone receptors (PR), PAX8, cytokeratins and negative for carcinoembryonic antigen (CEA).[3-5]

Herein, we present a rare case of a symptomatic CCC of Mullerian origin found on the foot of a young female patient, and describe subsequent clinical work-up and surgical management. The purpose of this case report is to describe the embryologic

origin and outline the appropriate components of surgical management when treating such uncommon and symptomatic lesions.

Case Presentation

A 33-year-old female with an unremarkable past medical history presented to the clinic with complaints of a painful, 3 centimeter (cm) solitary soft tissue mass to the right lateral hindfoot. This lesion was adjacent to the peroneal tendon course and superior to the glabrous junction. The mass was raised and freely mobile within the soft tissues with an intact overlying skin envelope. According to the patient, the mass had been present for three years and had gradually increased in size.

An MRI was obtained which demonstrated a 1.4 x 1.5 x 1.3 cm lobulated collection of near-fluid intensity within the subcutaneous tissues of the lateral hindfoot without osseous, tendinous or vascular involvement (**Figure 1-3**). Differential diagnoses described in the MRI read from the radiologist included a ganglion cyst versus epidermal inclusion cyst.

Operative Technique

The patient was placed on the operating room table in a supine position with a bump under the ipsilateral hip to provide optimal positioning. No tourniquet was utilized. After induction of anesthesia, a pre-operative regional block was administered to the right lateral foot using lidocaine without epinephrine. Attention was then directed to the 5th metatarsal base region, where a #15 scalpel was used to make a curvilinear incision overlying the soft tissue mass. Dissection was carried through skin and subcutaneous

tissues. The soft tissue mass was identified within the subcutaneous layer and noted to be well encapsulated with a fibrous layer. The mass itself was hyperpigmented and firm in nature with no appreciable fluid collection (**Figure 4-6**). The mass was meticulously excised from the surrounding tissue using sharp dissection and passed to the back table for histological examination. The excised soft tissue mass measured 3.5 x 2.2 x 1.5 cm. Intra-operatively it was confirmed the lesion had no apparent vascular, tendonous or osseous involvement, as found previously by MRI. There were no surrounding signs of infection present. Hemostasis was achieved and the surgical site was irrigated with copious amounts of sterile saline. Deep closure was performed with Vicryl suture, followed by layered closure of the subcutaneous layer with Vicryl and skin closure with Prolene.

Postoperative Course

The patient was placed in a well-padded posterior splint and was non-weight bearing for two weeks. Sutures were removed at two-week follow-up and she was then permitted to be weight-bearing as tolerated in a stiff-soled shoe with a transition to regular shoes gear at four weeks. The incision went on to heal in a benign fashion without complication. At the final follow-up at one year, she related no pain or discomfort to the operative site. There has been no evidence of lesion recurrence to date.

Pathology

Histopathological examination revealed a cutaneous ciliated cyst consisting of benign fibro-adipose tissue with a central cystic structure lined by ciliated pseudostratified cuboidal to columnar epithelium, with focal squamous metaplasia. The

ciliated columnar cells were positive for ER, PR, and Ck7 compatible with a cutaneous ciliated cyst/cutaneous cyst of Mullerian origin. The stain was negative for CEA, further confirming the benign nature of this lesion. The case and report was discussed with the reviewing pathologist who confirmed this structure and staining is similar to what is expected to be found in the female fallopian tube lining and is benign in nature.

Discussion

Non-neoplastic or benign neoplasms make up the majority of soft-tissue masses encountered in the foot and ankle.[6] It is important for foot and ankle surgeons to understand defining clinical and radiographic soft tissue lesion characteristics for proper surgical management, especially when encountering rare types. CCC are exceptionally rare, benign cystic lesions that occur predominantly in young females, with less than 60 cases reported in the English literature to date.[1,3]

As these lesions are most often encountered in the lower extremity of females, theory suggests this to be the case secondary to the sites of “Mullerian rests” being immediately adjacent to lower limb buds during the early stages of gestation.[2] Portions of these “Mullerian rests” may detach from forming reproductive system and incorporate into the forming limb bud.[1,3] As previously mentioned, these lesions are found in the lower extremities of females of child-bearing age, however, there have been a small amount cases reported in other anatomic locations and in male cohorts.[1,7-11] The presence of CCC in male patients has led to a second theory involving a potential sweat gland origin. It has been theorized these lesions may arise secondary to metaplasia of sweat gland (eccrine) epithelium. It has been previously suggested that cutaneous

ciliated cysts with estrogen and progesterone receptor positivity are best termed cutaneous Mullerian cysts, while lesions negative for these receptors should be referred to as cutaneous eccrine cysts.[7] Debate still exists on the exact mechanism and origin of these particular lesions.

Clinically, CCC typically present as subcutaneous nodule with cystic features on physical examination. Typically there are fluctuant on palpation and may be freely movable or fixed to the overlying dermis. They are most commonly found on the lower extremity, but have been reported to present on a variety of different anatomic locations such as the fingertips, back, abdominal wall, and scalp[7-11]. They classically present as skin-toned, but have been described to have a bluish discoloration with overlying telangiectasias.[4] Typically these lesions are slow-growing and may be painful or painless depending on location and size.

Diagnosis of CCC is predominantly a clinical diagnosis based on physical exam characteristics, combined with confirmatory excisional biopsy. Plain film radiographs and CT scans are relatively non-specific diagnostic imaging tools when it comes to CCC. MRI should be obtained to identify the extent of the lesion and evaluate for possible malignant characteristics [1,7,8]. Needle aspiration is typically unsuccessful, therefore the authors recommend excisional biopsy with histopathological examination for proper diagnosis and determining further treatment strategy.

These lesions are defined histopathologically as having pseudostratified columnar ciliated epithelium which is commonly encountered in the fallopian tube epithelium.[3-5] CCC is frequently hormone-responsive, with immunohistochemical reactivity to ER and PR, often becoming symptomatic during menses or pregnancy. A

growth phase of these lesions has been described during pregnancy and or menses when there is elevated hormone activity. [1,12] The benign nature of these soft-tissue masses is further exhibited with negative immunostaining for CEA.

Additional immunohistochemical considerations for CCC include PAX-8 expression. PAX-8 is a paired box (PAX) marker which has been identified as a mediator for organogenesis in fetal development. The main functions of PAX-8 transcription include the development of organs in the central nervous system, thyroid, kidney, mesonephric, and Mullerian duct system. Expression of PAX-8 is often maintained in these organ systems and is used to help diagnose renal, thyroid, and ovarian carcinomas. PAX-8 is found in 90% of tumors originating from the Mullerian duct[13]. Positive staining for this marker helps to confirm the Mullerian origin of these lesions.

Conclusion

In conclusion, we report a case of CCC of Mullerian origin, an exceptionally rare, benign soft tissue tumor found in the lower extremity. To date, roughly 60 cases have been reported in the literature, none of which include foot and ankle publications. It is imperative for the foot and ankle surgeon to be familiar with both common and uncommon soft tissue lesions given the large number which can be encountered. We hope the case and information provided in this report can help clinicians and surgeons alike to properly assess these lesions and take well-founded steps in treatment, including surgical excision and pathologic examination.

Conflict of Interest Statement

The authors declare that they have no competing financial interests or personal relationships which would have influenced the results of this paper.

Ethical Approval

Not applicable

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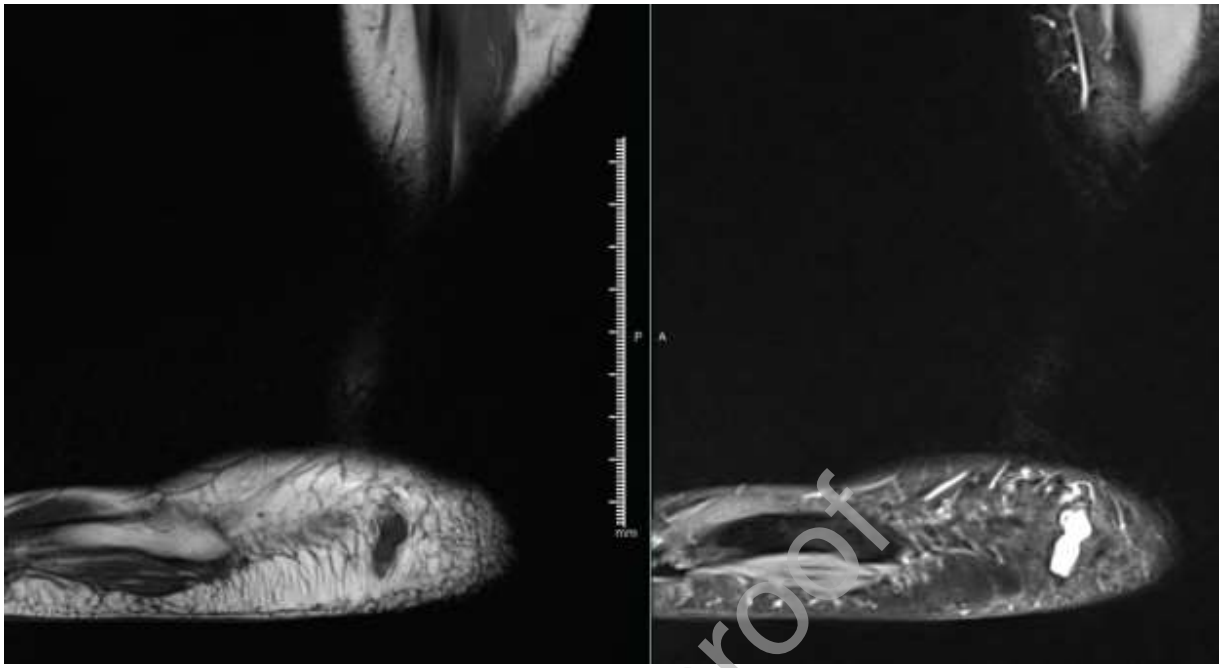
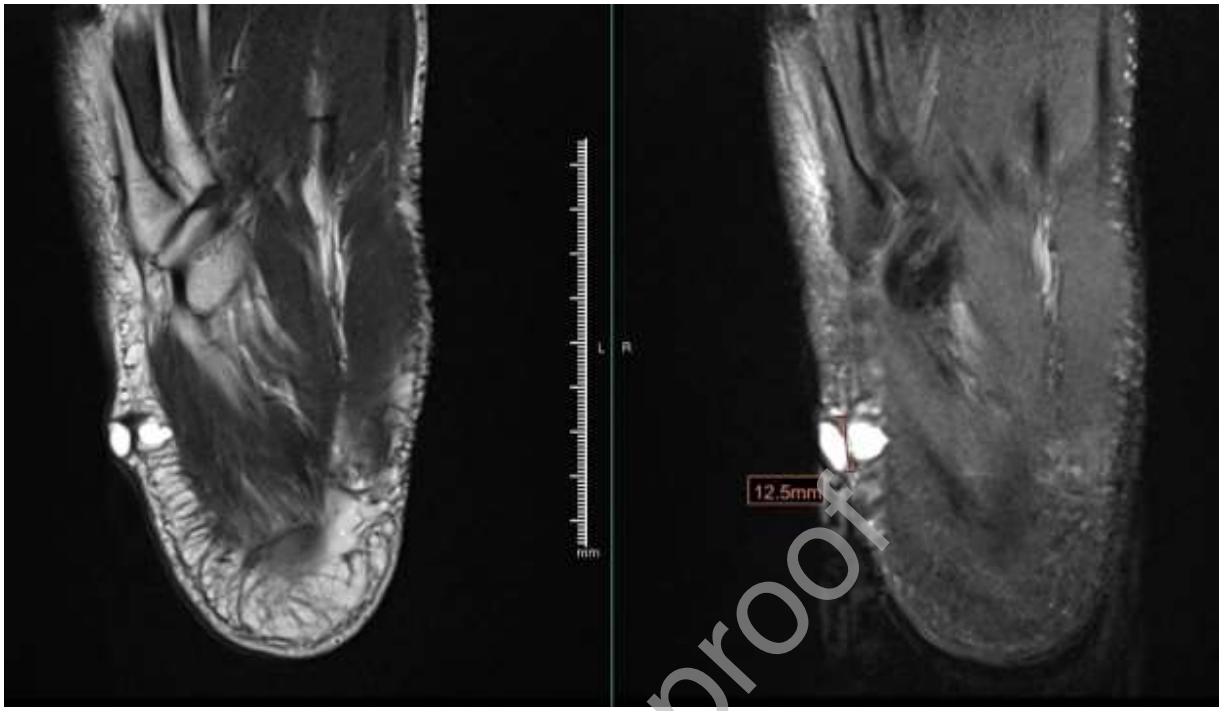
Figures

Figure 1:



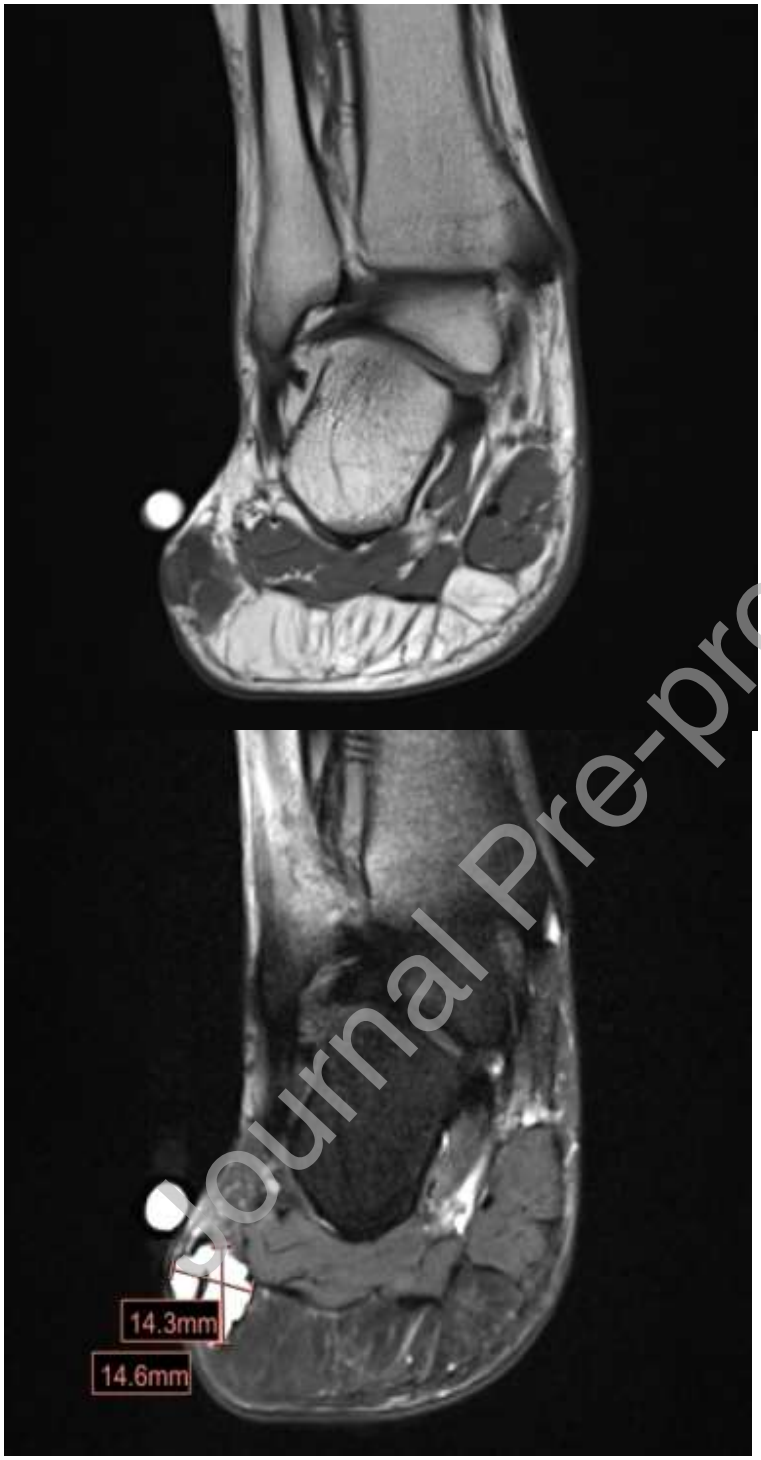
Sagittal MRI T1 (left) and T2 (right) images of 1.4 x 1.5 x 1.3 lobulated collection of near fluid signal intensity in subcutaneous tissues.

Figure 2:



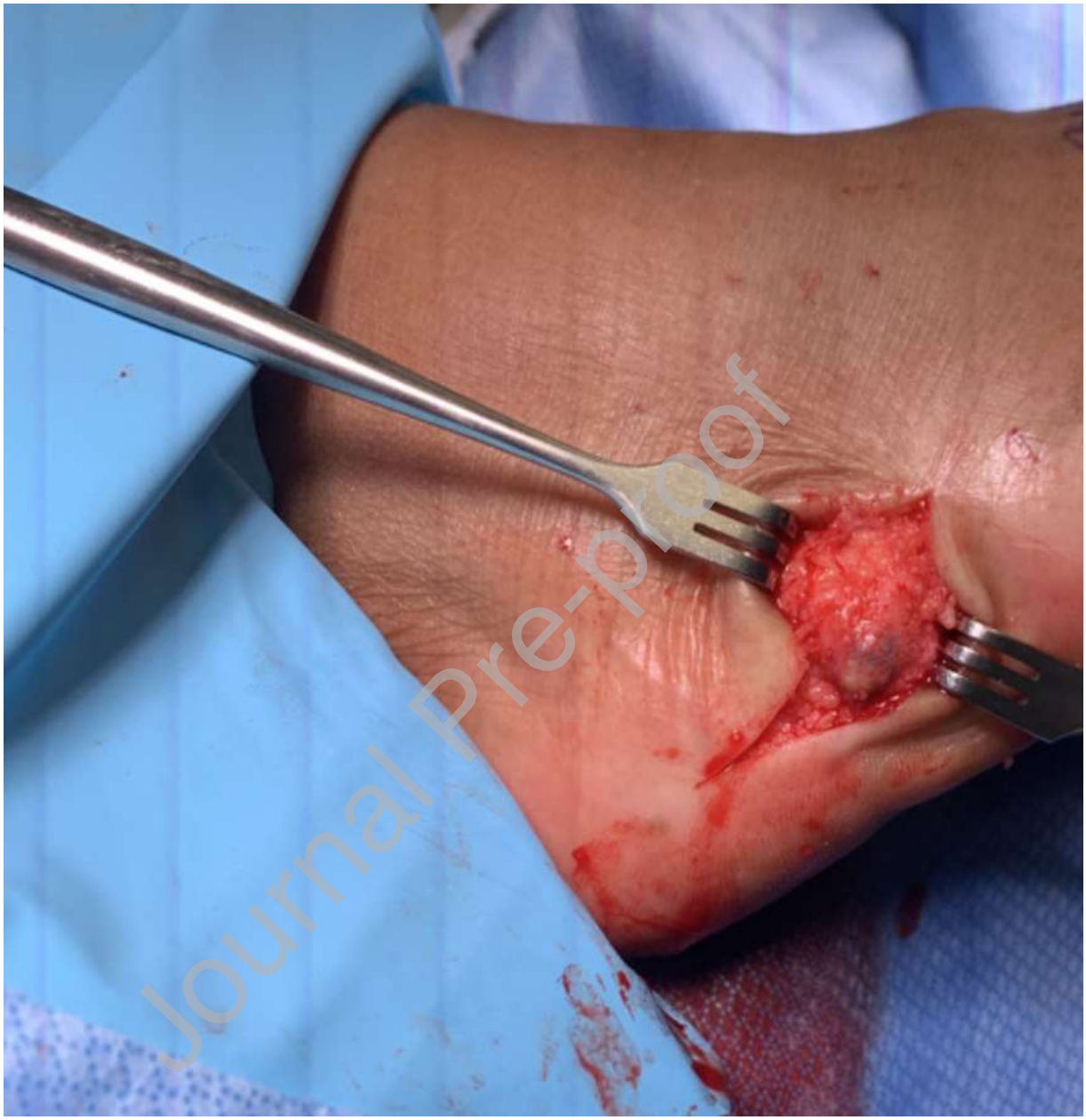
Axial MRI T1 (left) and T2 (right) images of 1.4 x 1.5 x 1.3 lobulated collection of near fluid signal intensity in subcutaneous tissues.

Figure 3:



Coronal MRI T1 (left) and T2 (right) images of 1.4 x 1.5 x 1.3 lobulated collection of near fluid signal intensity in subcutaneous tissues

Figure 4:



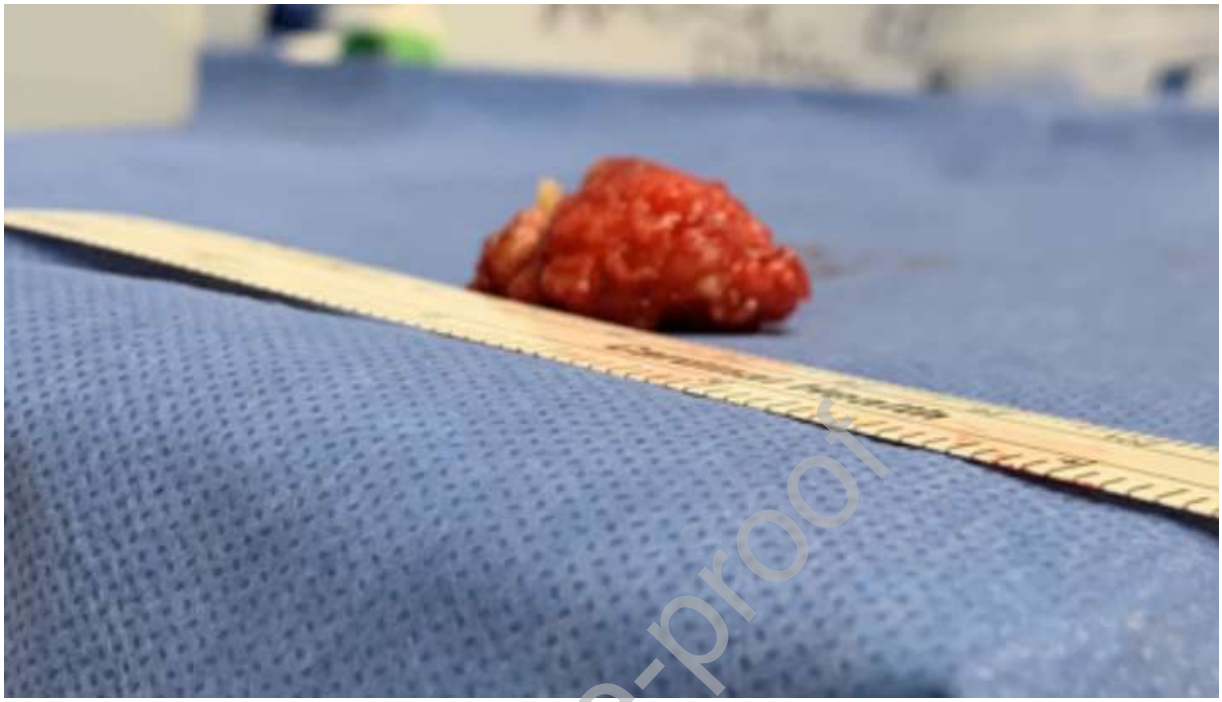
Intra-operative view of identified lesion

Figure

5:

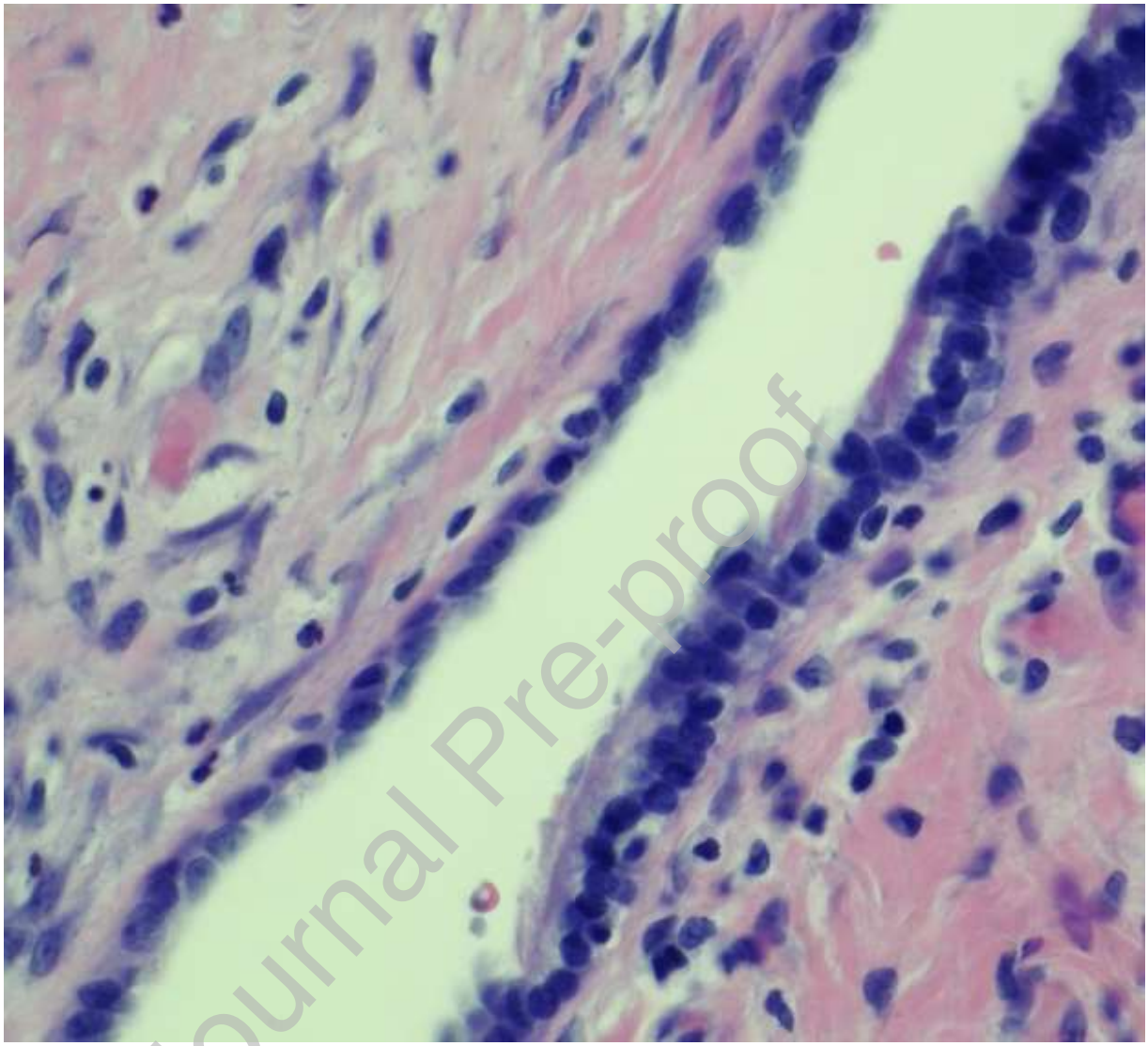
Intra-operative view of the lesion following surgical excision

Figure 6:



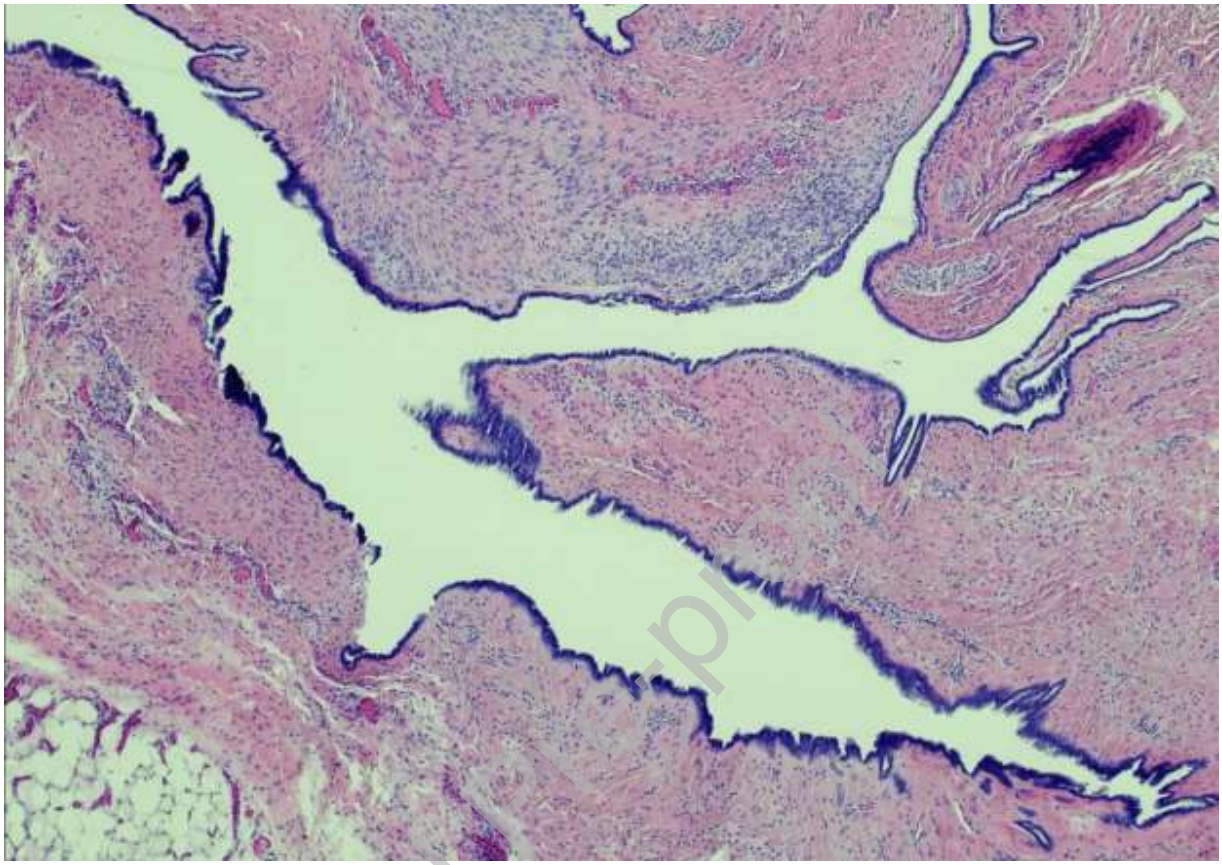
Intra-operative view of the lesion following surgical excision

Figure 7a:



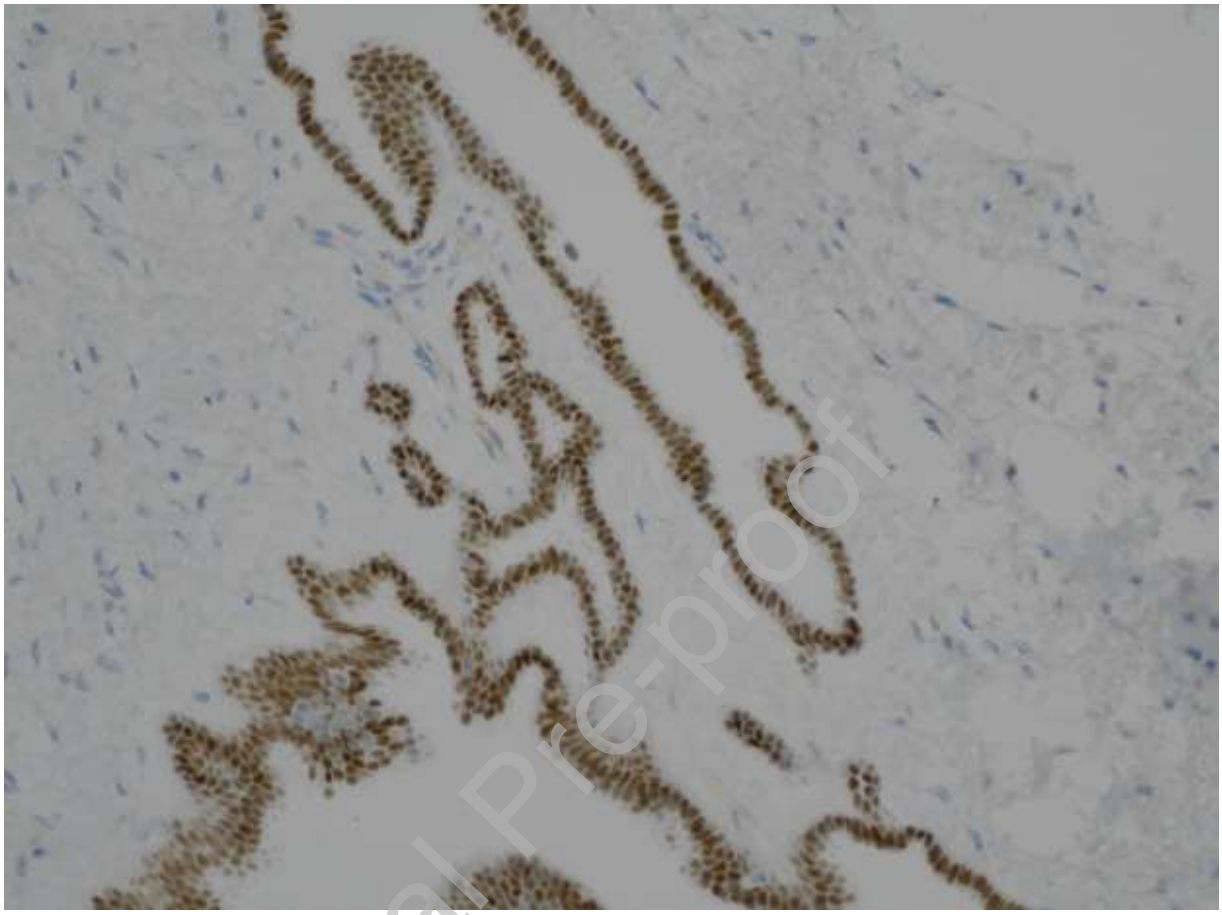
Low power photomicrograph demonstrating a uniloculated cystic structure lined by pseudostratified columnar epithelium. H&E. Magnification 40x.

Figure 7b:



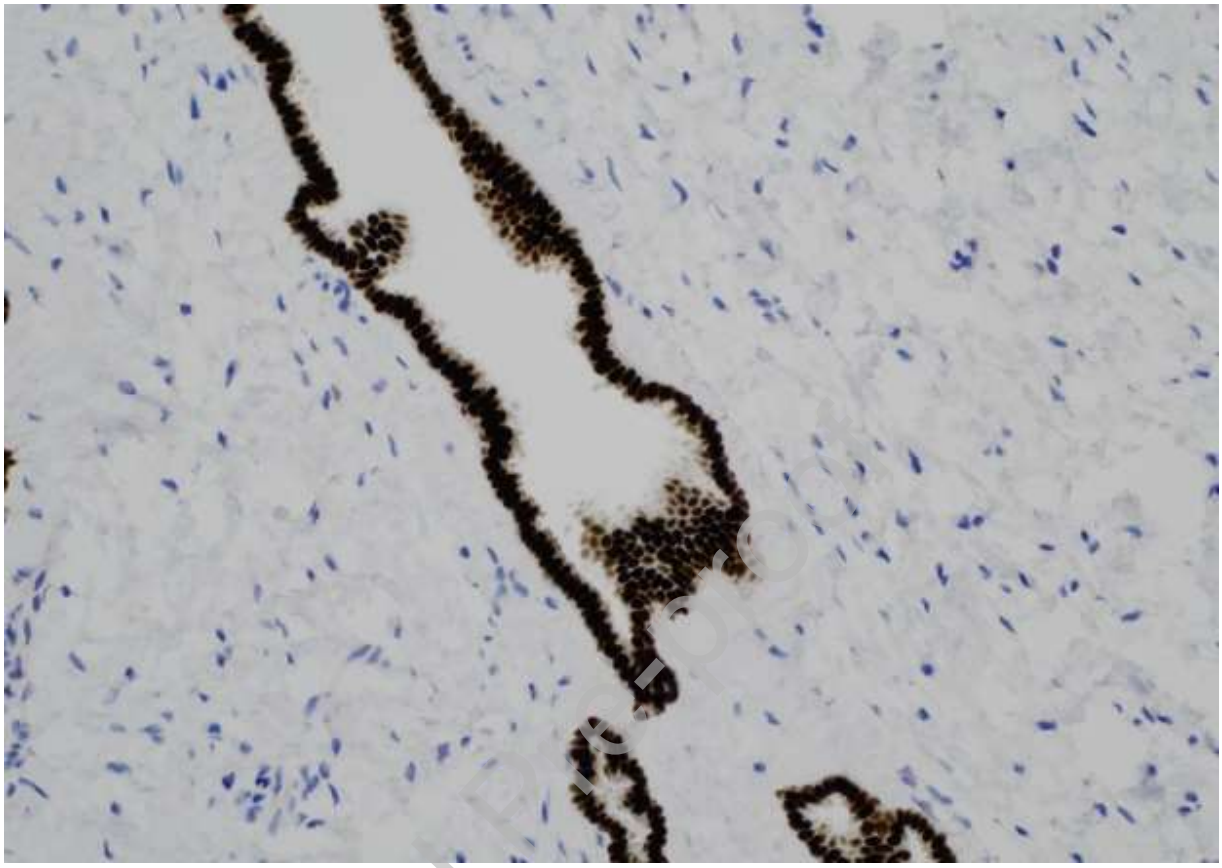
High power photomicrograph. The resemblance to the fallopian tubal epithelium is apparent. The luminal aspect of the ciliated cells is lined by a terminal bar with cilia. H&E. Magnification 400x.

Figure 8a:



Lesional cells stain positive for ER and PR immunohistochemistry. Magnification, 200x.

Figure 8b:



Lesional cells stain positive for ER and PR immunohistochemistry. Magnification, 200x.

Informed Patient Consent

☒ Complete informed consent was obtained from the patient for the publication of this study and accompanying images.

☐The authors declare that informed patient consent was not provided for the following reason:

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: