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Case report

A mixed Müllerian cystadenoma presenting as a paraurethral tumor

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1. Introduction

A mixed Müllerian cystadenoma presenting as a paraurethral tumor was diagnosed after paraurethral tumor excision in a 24-year-old woman. She became aware of the tumor after an external injury at 17 years of age, with no history of sexual intercourse. Seven years after the injury, she first visited the gynecologist, who diagnosed a paraurethral tumor. Then, 15 months later, the paraurethral tumor was excised. The tumor was histologically diagnosed as a mixed Müllerian cystadenoma.

Paraurethral cysts are rare benign lesions usually arising in adult women with a history of vaginal delivery. Since the cysts usually have no communication with the urethra and may bulge into the vagina or vulva, patients sometimes present to gynecologists. Clinically identified paraurethral tumors are mixed conditions including cases that are both congenital/acquired in etiology and non-neoplastic/neoplastic in nature. Although there are very few comprehensive studies of the pathological features of paraurethral cysts (Das, 1981), neoplastic cysts seem to be very rare, with an exceptional case report of an adenocarcinoma arising in a paraurethral cyst (Massari et al., 2014).

A case of a paraurethral cyst in a young adult female without a history of sexual intercourse is reported. The histological findings of the cyst resembled those of a mixed Müllerian cystadenoma of the ovary, and the cystic lesion was considered to be neoplastic in nature. This is the first case of mixed Müllerian cystadenoma of the paraurethral region. Its histogenesis is discussed, referring to its much more common ovarian and pelvic counterparts.

2. Case

A 24-year-old woman was seen at a gynecological outpatient department because she felt a vulvar mass. When she was 17 years old, with no history of sexual intercourse, she injured her external genitals in a fall from a bicycle. Since then, she had noted proptosis of the tumor only when she applied abdominal pressure. Seven years after the injury, she visited the hospital for the first time. On gynecological examination, a round, mobile tumor was found. The mass was approximately 1.5 cm (Fig. 1(a)), with a smooth surface. The mass arose from the anterior wall of the vagina. She felt discomfort, but no pain or difficulty on urination. A transvaginal ultrasound examination showed two normal ovaries and a normal uterus. Magnetic resonance imaging (MRI) showed a sharply defined tumor, slight high intensity on T1-weighted and high intensity on T2-weighted imaging, closely related to the vaginal vault. The tumor caused an impression on the urethra, but invasive growth was not suspected.

After a wait-and-see approach for 15 months, without change in tumor size, she requested surgical resection because of discomfort. Excision of the paraurethral tumor was carried out by urologists. At the beginning of the operation, cystoscopy was performed. There was no

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connection observed between the paraurethral tumor and the urethra. The operation was performed with the patient under spinal anesthesia. The mucosa was divided lengthwise, and the tumor was carefully dissected (Fig. 1(b)). During the dissection, the tumor ruptured, and yellowish fluid appeared (Fig. 2). A catheter was placed into the tumor through the ruptured hole, and 2 ml of distilled water were instilled. The tumor was dissected from the vaginal wall. The yellowish fluid was cultured, and no significant bacteria were identified. The patient was discharged two days after the operation without complications. There has been no recurrence at 6 months after the operation.

3. Pathological findings

Histologically, the cystic lesion was lined by a mixture of three different types of epithelium: ciliated columnar cells resembling those of the fallopian tubes; endocervical-like mucinous cells; and squamous cells (Fig. 3). The squamous cells merged gradually with immature reserve cells beneath the mucinous epithelium, as seen in the normal uterine cervical transitional zone. No atypia was noted in the epithelial component. There were several papillary projections with a broad fibrovascular core covered by ciliated epithelium. Neither endometriosis nor chronic inflammatory changes were seen around the cystic lesion. On immunohistochemical examination, all epithelial cells were positive for estrogen receptor (ER) and PAX8 (Fig. 4).

4. Discussion

The current patient presented with a paraurethral cyst. There have been very few studies of the detailed pathological findings of paraurethral cysts except for that of Das in 1981 (Das, 1981). He classified the cysts into Müllerian, mesonephric, and urothelial cysts based on the embryologic component from which the cyst might have originated. A Müllerian cyst is lined by endocervical-type mucinous epithelium and occasional squamous cells. A mesonephric cyst is lined by non-mucinous cuboidal or low columnar epithelium. An urothelial cyst is lined by transitional epithelium. Although the present case was most similar to a Müllerian cyst, the papillary projection into the lumen and the presence of ciliated tubal-type epithelium are not the features of Müllerian cysts described by Das. Instead, the present case would be similar to seromucinous cystadenoma (Müllerian cystadenoma of mixed cell types) of the ovary in terms of a cystic neoplasm lined by a variable admixture of Müllerian-type epithelial cells (WHO classification 2020). Expression of ER and PAX8 in lining epithelial cells also supports the Müllerian origin. However, in the present case, there was no associated endometriosis characteristic of seromucinous cystadenoma. In the ovary and other extraovarian sites, endometriosis is considered a possible origin of seromucinous (Müllerian mixed epithelial) tumors.

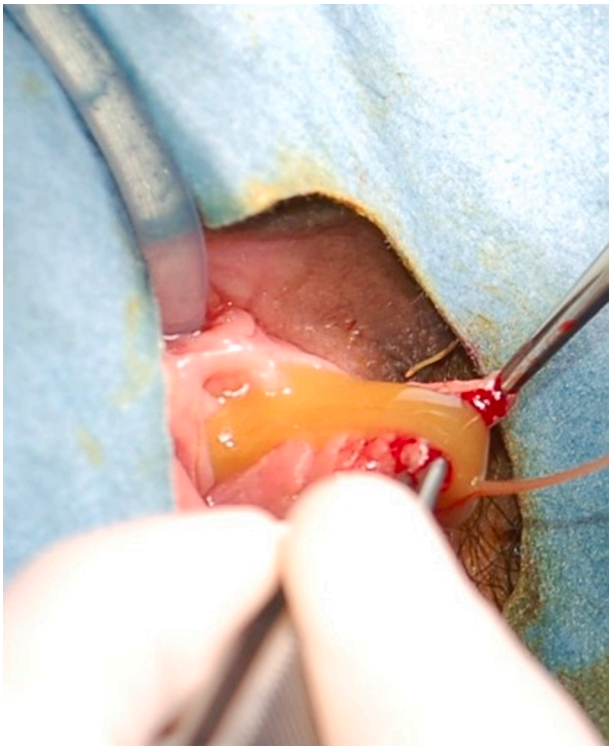

Fig. 2. The content is yellowish fluid.

Although the exact origin of the present tumor was difficult to identify, the lesion was described as a Müllerian cystadenoma of mixed cell types based on its histological characteristics.

Some possible mechanisms of occurrence can be assumed in this case. The most likely cause is a Müllerian cyst, which is the most common variety of vaginal cyst next to inclusion cysts. They are more commonly located paraurethrally in the anterior or anterolateral vaginal wall, and their obstruction or cystic degeneration of the various embryologic ductal and glandular systems could give rise to distinct varieties of cysts. A Müllerian cyst might have developed neoplastic change within the cyst during the 7 years since the patient first noticed tumor prolapse. However, whether the Müllerian cyst was congenital and prolapsed after the injury or the cyst was formed by the injury is unclear.

One of the possible origins of the present tumor is Müllerianosis, which is rare ectopic benign glandular tissue seen in various pelvic

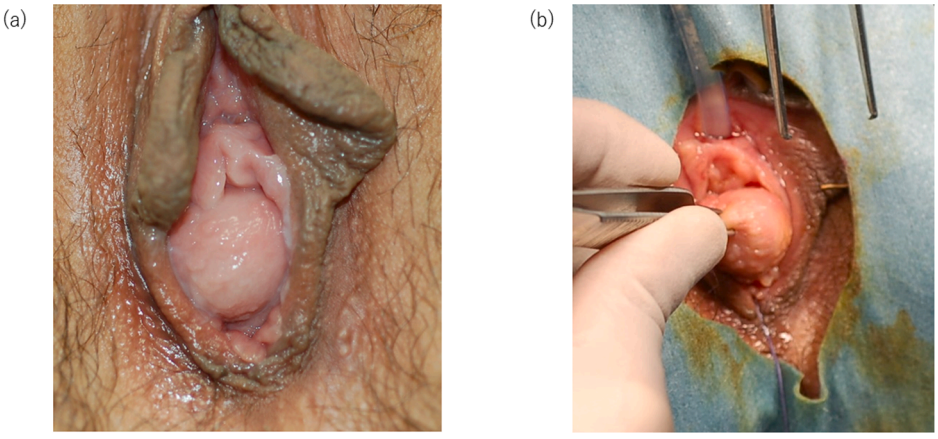

Fig. 1. (a) A round, mobile tumor, about 1.5 cm in size, with a smooth surface is seen. The mass arises from the anterior wall of the vagina. (b) The tumor is tugged and carefully dissected.

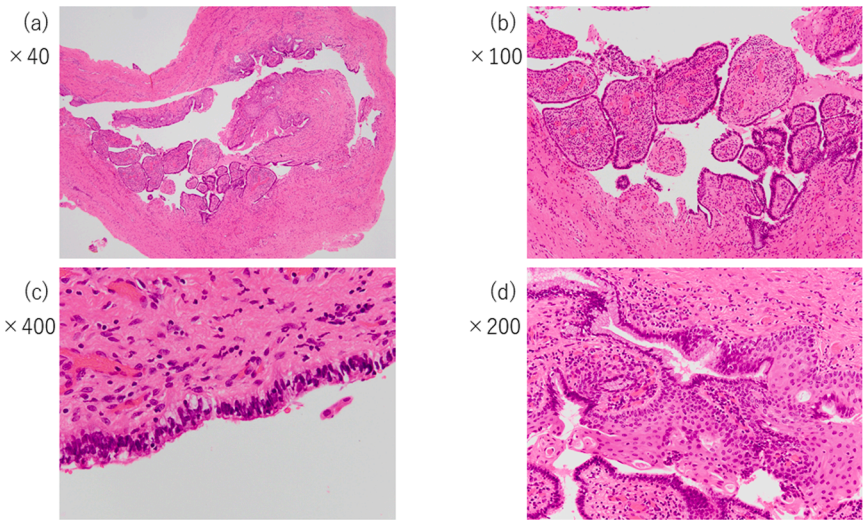

Fig. 3. The cystic lesion is unilocular and lined by a mixture of three different types of epithelium: ciliated columnar cells resembling those of the fallopian tube; endocervical-like mucinous cells; and squamous cells. There are several papillary projections into the lumen. Higher magnification image of the ciliated columnar cells resembling those of the fallopian tube. Squamous epithelium abuts the endocervical-type mucinous epithelium.

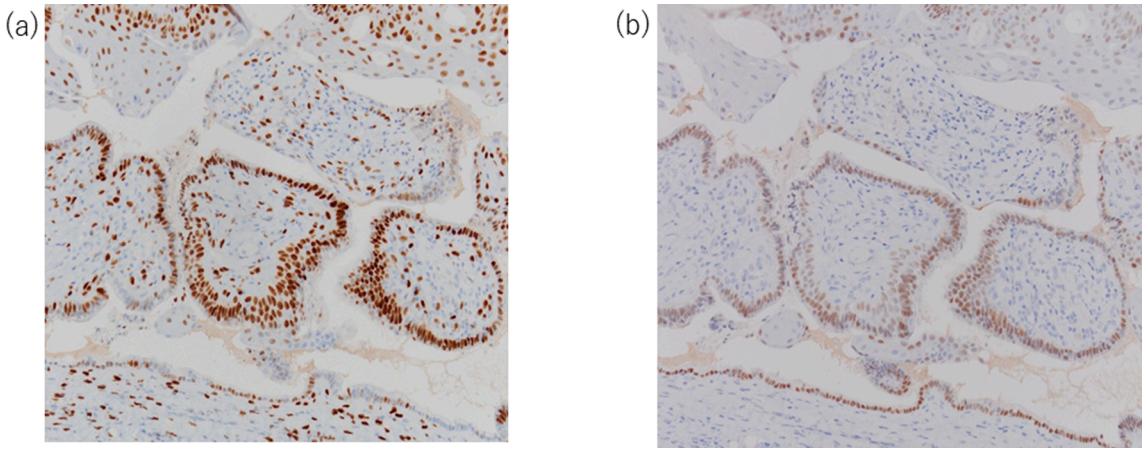

Fig. 4. Immunohistochemically, all epithelial cells are positive for estrogen receptor (ER). All lining epithelial cells are also positive for PAX8.

organs including the urinary bladder, peritoneum, and lymph nodes, consisting of a variable admixture of different types of Müllerian epithelium (Mahul and Tickoo, 2016; Amir et al., 2018). Neoplastic transformation of Müllerianosis is far less common than that of endometriosis.

Another possibility is a remnant of a Müllerian duct (Lee et al., 1998). Embryologically, at about 6 weeks of embryogenesis, the Müllerian or paramesonephric ducts appear lateral to the mesonephric duct. As they grow caudally, their distal ends fuse in the midline and reach the urogenital sinus as Müller's tubercle. The opening of a Müllerian duct into the coelomic cavity represents the ostium of the fallopian tube and the fimbria. During the normal development of the tube and fimbria, an aberration may occur and result in a paraovarian cyst. Similarly, paraurethral tissue may have an aberrant Müllerian duct remnant. Moreover, there is the possibility of an association between endometriosis and Müllerian carcinosarcoma (Agito et al., 2012; Melilli et al., 2001). It is an extremely rare pathological finding, but it has been documented in the ovaries and sigmoid colon. In the current case, there were no findings of endometriosis in the vaginal wall or pelvic cavity on ultrasound and MRI examinations.

The most common histological type of paraurethral tumor is reported to be leiomyoma (Perugia et al., 2012; Adams-Piper et al., 2015; Aydogmus et al., 2017; Braga et al., 2020). A Müllerian cystadenoma presenting as a paraurethral tumor has not been reported. However, it has been reported that a Müllerian cystadenoma developed from the ovary (WHO Classification, 2020), retroperitoneum (Sabarwal et al., 2017), and pancreas (Levy et al., 2005). A case of adenocarcinoma of the paraurethral glands was reported, which showed pelvic recurrence one month after tumor resection (Massari et al., 2014). Adenocarcinoma was considered in the differential diagnosis of this case.

This is the first reported case of a Müllerian cystadenoma that developed from a paraurethral lesion. The mechanisms of occurrence might be neoplastic change of a Müllerian cyst, Müllerianosis, or a remnant of a Müllerian duct. Since most paraurethral cysts are non-neoplastic, conservative treatment such as marsupialization can be effective (Sharifiaghdas et al., 2014). However, complete surgical excision with pathological evaluation may identify a rare neoplastic lesion, especially when the etiology is unusual.

5. Authors' contributions

Akie Takebayashi performed physical examination and wrote the initial draft of the manuscript. Suzuko Moritani performed pathological diagnosis and critically revised the manuscript for important intellectual content. Yuri Suzuki and Yuji Sakano operated and assisted in preparation of the manuscript. Yuji Tanaka: performed physical examination

and assisted in preparation of the manuscript. Yutaka Yoneoka, Mari Nakata and Akiko Ishiko assisted in preparation of the manuscript. Takashi Murakami critically revised the manuscript for important intellectual content. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of Competing Interest

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.

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