CASE REPORT

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# Müllerianosis of cervix. Case report

# Müllerianosis de cuello uterino. Reporte de caso

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**ABSTRACT**

Müllerianosis is an embryonal disease of the müllerian or paramesonephric ducts, consists in the mixture of two or more types of tissues and results in the formation of adenomyosis, endometriosis, endosalpingiosis, and endocervicosis. It most often affects the urinary bladder in women of childbearing age. Müllerianosis of the cervix is a very rare benign condition, with few reported cases. The exact pathogenesis remains a matter of debate. There are several theories on its etiology; the main two are the implantation and metaplastic theories. Symptoms range from absent to pelvic pain and dysmenorrhea. It generally appears as a cystic tumor with glands of different sizes lined by endometrial, endocervical, or tubal epithelium. This lesion could be confused with other benign, premalignant, or even malignant lesions, and histopathological confirmation is necessary. Because it is a benign disease, no additional treatment is required after surgical resection. A case of müllerianosis of cervix is presented.

Key words: Uterine cervical neoplasms, Müllerianosis.

**RESUMEN**

La müllerianosis es una enfermedad embrionaria de los conductos de Müller o paramesonéfricos, que consiste en la mezcla de dos o más tipos de tejidos y que da como resultado la formación de adenomiosis, endometriosis, endosalpingiosis y endocervicosis. Con mayor frecuencia afecta la vejiga urinaria de las mujeres en edad fértil. La müllerianosis del cuello uterino es una afección benigna muy rara, con pocos casos reportados. La patogenia exacta sigue siendo tema de debate. Existen varias teorías sobre su etiología; las dos principales son la teoría de implantación y la metaplásica. Los síntomas varían desde su ausencia hasta dolor pélvico y dismenorrea. Generalmente aparece como tumor quístico con glándulas de diferentes tamaños revestidas por epitelio endometrial, endocervical o tubárico. Esta lesión podría confundirse con otras lesiones benignas, premalignas o malignas y es necesario la confirmación histopatológica. Debido a que es una enfermedad benigna, no necesita tratamiento adicional luego de la resección quirúrgica. Se presenta un caso de müllerianosis del cuello uterino.

Palabras clave. Neoplasias del cuello uterino, Müllerianosis.

## Introduction

Müllerianosis is a disease in which, during organogenesis, cells derived from Müllerian tissue remain outside their final locations, resulting in four conditions: adenomyosis, endometriosis, endosalpingiosis, and endocervicosis[(1)]. This condition has been documented in different anatomical sites and is characterized by the presence of two or more types of Müllerian origin tissue in women of childbearing age[(2)]. Müllerianosis of cervix has been rarely described, but its clinical, cytological and histological characteristics can mimic other benign or malignant cervical lesions[(3)]. A case of müllerianosis of the cervix is presented.

## Clinical case

A 50-year-old patient with V gravida, V para consulted for mild hypogastric pain of approximately two months of evolution. She referred menarche at 17 years-old, with irregular (duration of 35 to 60 days and bleeding of 7 to 9 days) and painful menstrual cycles since age 41 years and increased genital bleeding in the last two months. She denied dysuria, hematuria, and urinary pressure. In addition, she reported a history of uterine leiomyomata and ovarian cysts resection 15 years earlier. She denied any other important personal or family history.

On physical examination, the patient was in fair condition, afebrile but tachycardic (100 heart beats per minute) and blood pressure 121/78 mmHg. Abdomen presented slight muscular defense, without signs of peritoneal irritation, slightly painful on palpation of hypogastrium, with negative Blumberg and McBurney signs. On vaginal examination, the cervix was enlarged, edematous, and soft, with no adnexal involvement. No blood, flow, or tissue was observed in the cervical canal. Laboratory values were: leukocytes 8 900 cells/mL, neutrophils 71%, C-reactive protein 10 mg/L and fibrinogen 290 mg/dL.

Pelvic ultrasound showed endometrial thickness of 11 millimeters, with well-defined endometrial-myometrial junction area. Cervix measured 12 x 7 centimeters with a multicystic tumor in the posterior portion of cervix, the largest cyst measuring 3 centimeters and presenting echogenic patterns (Figure 1). The tumor altered the cervical anatomy, but not the corpus uteri or exocervix. Both adnexa were normal and there was no evidence of free fluid in the pelvic cavity. Doppler ultrasound showed moderate vascularization, with increased resistance index in the tumor septa.

Computed tomography showed presence of a tumor located in the upper portion of the cervix, measuring approximately 10 centimeters, heterogeneous with hypo and hyperdense areas. There was no omental thickening or abdominopelvic lymphadenopathy. Colposcopy, cervical cytology and endometrial biopsy were normal and showed no evidence of premalignant or malignant lesions. Renal, hepatic, urinalysis, electrolyte and coagulation tests did not show alterations. Tumor marker values (carcinoembryonic antigen, alpha-fetoprotein, and CA-125) were within normal limits. In view of the findings, the possibility of cervical leiomyomatosis was considered.

During the exploratory laparotomy, a tumor that deformed cervix was observed (Figure 2), for which a total hysterectomy plus bilateral oophorosalpingectomy and infracolic omentectomy were performed. No alterations were found. Patient was discharged after three days, without additional treatment. After 18 months of surgery, the patient has not presented recurrences of the condition and follow-up ultrasound evaluations have not shown alterations.

Macroscopic evaluation of the tumor showed a multilocular cystic lesion filled with grayish mucinous fluid, measuring approximately 8 × 7 × 6 centimeters, occupying the posterior wall of the cervix and deforming the anterior wall, without affecting the endocervix. Histological examination revealed glandular structures of variable size lined by columnar epithelium, similar to endocervical glands within the mucin-filled cystic spaces, which in most of the studied areas were ciliated, compatible with endosalpingiosis, and in other more scarce, mucinous, compatible with endocervicosis, sometimes even in the

Figure 1. Sagittal ultrasound view of the cystic tumor infiltrating the cervix.

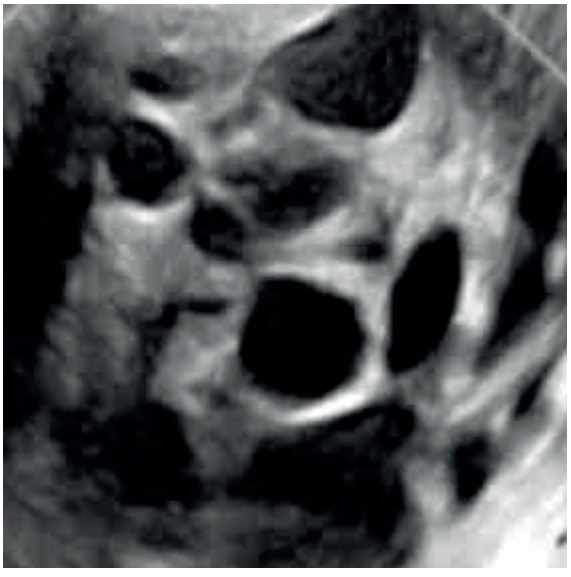
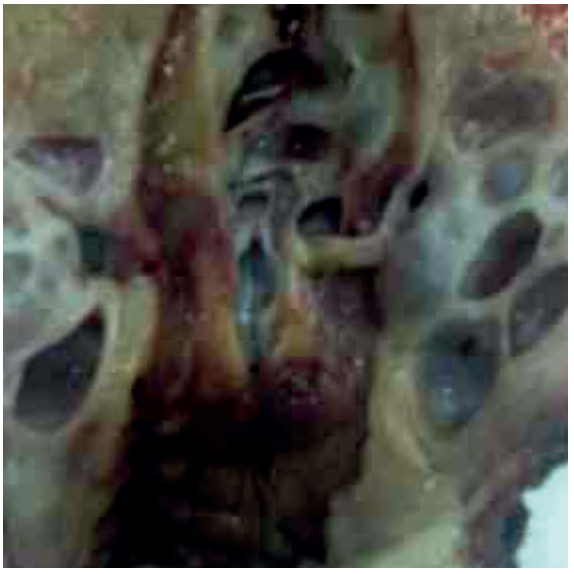


Figure 2. Müllerianosis of cervix characterized by the presence of multiple cystic cavities.



same gland. The cystic wall was covered by a single, high layer of mucinous columnar epithelium, with nuclei oriented towards the basement membrane, without abnormal pleomorphisms or mitoses. The endometrial-like stroma was absent, ruling out the presence of concomitant endometriosis. On immunohistochemical staining, cystic gland cells were weakly positive for estrogen, progesterone and cytokeratin 7 receptors and negative for carcinoembryonic antigen, MUC6, P53 and P16, with low Ki-67 (Figure 3). The presence of these benign cystic glandular structures deep within the tissue and lined by variable epithelial cells was consistent with müllerianosis of cervix. No evidence of neoplastic alterations was found in the uterus, adnexa and omentum.

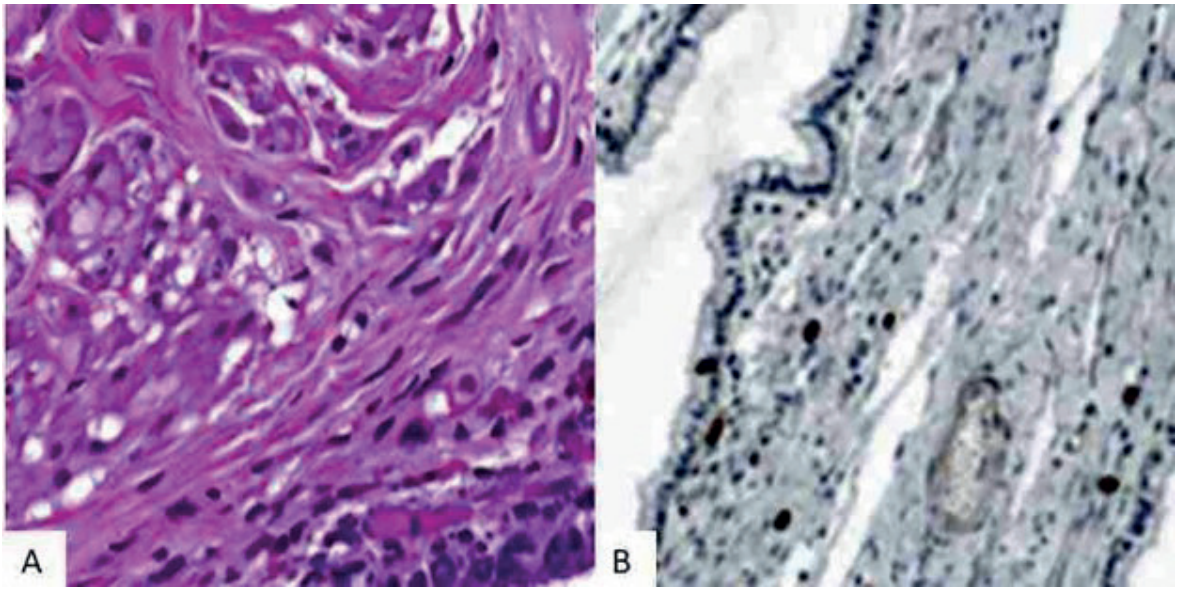
## Discussion

Müllerianosis is a mixture of two or more Müllerian tissues (endometrial, cervical, or tubal). Cervical müllerianosis is the rarest and apparently originates from the pelvic peritoneum or retroperitoneum[1]. Its main characteristic consists of pseudoneoplastic glandular lesions, with an uneven arrangement of the glands lined by benign mucinous endocervical epithelium, often dilated, in the cervix and which can extend to the paracervical tissue[2]. Unlike endometriosis, it appears within the affected organ rather than on the outer surface of the organ. There are few documented cases, so its true prevalence is difficult to determine. The most common affected sites are bladder and it has rarely been found in cervix, spinal cord, inguinal and axillary lymph nodes, ureters, rectum, and mesosalpinx[4-6].

The exact cause and pathogenesis of müllerianosis remains unknown. There are several theories, but the main ones are implantation and metaplastic. Implantation theory suggests that Müllerian tissues can develop within the tissue during some surgical procedure. However, it does not clarify those cases in patients with no surgical history or in distant sites. Metaplastic theory explains the presence of various types of tissue as a potential result of the differentiation of the Müllerian epithelium into endometrial, endocervical and tubal types. Peritoneal mesothelium, having undifferentiated or poorly differentiated cells that retain the ability to differentiate into various cell types, can be transformed directly into other tissue[7]. In general, most authorities favor the metaplastic theory over the implantation theory. Consequently, müllerianosis can be defined as a special type of choristoma composed of endometrial, endosalpingeal and endocervical tissues, either individually or in combination[8].

When a müllerian tissue is identified, it can be classified correctly and with a high degree of precision as the following criteria are met: a) no history of surgery in reproductive organs; b) absence of evidence of pelvic endometriosis during

Figure 3. Histological findings of müllerianosis of cervix. A) Cystic structures delimited by a layer of mucinous columnar epithelium (hematoxylin-eosin staining, 200X). B) Cells of cystic structures with diffuse immunostaining to cytokeratin 7 (20X).



laparoscopy, laparotomy or necropsy; and, c) be physically separated from the primary Müllerian system[8].

Cervical müllerianosis is usually an accidental finding and presents with a variable spectrum of symptoms, depending on the affected site. The most common symptoms include dysmenorrhea, pelvic, lower abdominal and / or lumbar pain, dyspareunia, irregular vaginal bleeding, and infertility, and its severity is related to the extent of the clinical picture. The age range is 28 to 55 years[7]. There are no case reports in male patients. Definitive diagnosis must be made based on the histological findings[9].

Imaging studies, such as magnetic resonance, can be helpful in establishing the extent of the disease[10]. Cervical müllerianosis generally does not affect cervical stroma in depth and has no solid components on T2 MRI images. In contrast, multicystic lesions that deeply invade cervical stroma and contain solid portions may indicate malignant tumors, such as carcinoma of cervix, which generally shows high signal intensity on T2 and low signal intensity of cervical stroma on T2 images[10,11]. Furthermore, müllerianosis can be similar to malignant adenoma. However, there are no pathognomonic radiological elements that allow differentiating both entities[11].

Preoperative diagnosis of this condition is important, since it mimics neoplastic lesions from a clinical and histological point of view. However, there are no precise preoperative diagnostic tools and many pseudo-neoplastic / neoplastic glandular lesions must be excluded. In the initial diagnosis of pseudo-neoplastic glandular lesions of the cervix, benign diseases, such as adenomyoma, premalignant lesions, or malignant ones, including malignant adenoma and carcinoma of cervix, should also be considered. When müllerianosis affects the entire cervical wall, it may be accompanied by normal endocervical glands; it is the cytological characteristics of the glands that allow their differentiation. In addition, glands in müllerianosis are cystic, irregular in shape and size, and filled with mucus, while endometrial glands are surrounded by endometrial-like stroma. Lesions are generally benign and lack signs of malignancy, such as atypia or increased number of mitoses[2,12].

On immunohistochemical evaluation, the estrogen and progesterone receptors are positive, making it hormone sensitive. The glandular component can also stain for CA-125, while the endometrial stromal tissue is positive for CD10[7]. Additionally, CD10-positive staining may be helpful in confirming the absence of this endometrial stroma. The finding of positivity to calretinin and D2-40 generally confirms the diagnosis. In contrast to malignant adenoma, the glands in müllerianosis express, in addition to hormone receptors, cytokeratin 7, but are negative for carcinoembryonic antigen and P53, while the expression of Ki 67 is usually low[13].

Because cervical müllerianosis is a benign disease, it does not require additional treatment after surgical resection[12]. However, medical treatment can be considered in those cases where there are risks associated with surgery. Treatment in cases of pelvic pain is similar for patients diagnosed with endometriosis. When there is associated infertility, therapeutic behavior is similar to that of patients with endosalpingiosis. However, gynecologic laparotomy and hysterectomy may be necessary for unusually large and deep cervical tumors in patients in whom malignant neoplasms cannot be excluded[14,15].

In conclusion, müllerianosis of cervix is a recently described rare benign lesion. This condition is characterized by glands covered by different elements of Müllerian tissue. It can often mimic other benign and malignant lesions clinically and histologically, so it is important to differentiate it from these neoplasms. It is difficult to diagnose during the preoperative period due to the clinical and radiological findings. Magnetic resonance imaging can be helpful in diagnosis, but histopathological confirmation is necessary.

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