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Case report

# Müllerianosis of the urinary bladder may simulate a bladder cancer: a case report

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**Abstract.** Müllerianosis is an extremely rare entity consisting of an admixture of 2 or more müllerian tissues. We report the case of a 61 years old woman who came to our attention with hypogastric pain and dysuria. She was in menopause and had a previous history of cesarean section. Ultrasound and CT-scan of the abdomen showed a proliferative bladder lesion close to the left ureteric orifice. Transurethral resection of the bladder (TUR-B) was performed. Histopathological examination of the specimens was negative for bladder cancer and revealed the presence of endosalpingeal tissue. Postoperative course was unremarkable as well as follow up at 12 months. A proper knowledge and awareness of this disease, even if rare, is necessary for an accurate differential diagnosis and to perform an appropriate treatment. (www.actabiomedica.it)

**Key words:** Müllerianosis, Bladder lesion, Transurethral resection

## Introduction

Müllerianosis is a rare entity consisting of an admixture of 2 or more of the following ectopic tissues: cervical (1), tubaric or endometrial epithelium within the lamina propria and the muscular layer of the urinary bladder. It is a benign disease, most commonly affecting the urinary bladder of women of fertile age. The most common site of the urinary tract affected by endometriosis, endocervicosis and endosalpingiosis is the urinary bladder. Macroscopically, müllerianosis presents as a polypoid mass in the dome or posterior wall of the bladder. The simultaneous presence of at least two types of these tissues was referred to as müllerianosis by Young and Clement, in 1996 (1). The clinical manifestations of the disease may include dysuria, pelvic pain, hematuria, non-specific symptoms that are related to the responsiveness of müllerian glands to a hormonal stimulus. A few patients present with catamenial exacerbation or dyspareunia.

In some cases, the diagnosis is an incidental finding at imaging or cystoscopy. The features of this lesion clinically, cytologically, and histologically tend to mimic other benign and malignant lesions of the bladder. Bladder lesions can be detected after the finding of an echogenic nodule on ultrasound, or a low signal intensity lesion on T1-weighted images and a high signal intensity lesions on T2-weighted sequences on Magnetic Resonance (MR) (2). Cystoscopy and transurethral resection of the mass is fundamental for the differential diagnosis (3). The clinical context and the identification of periglandular endometrial stroma at histologic examination, as well as the immunohistochemical demonstration of estrogen and progesterone receptors in the glands are of the utmost importance in the differential diagnosis. Correct and prompt diagnosis is crucial for appropriate management, as patients may benefit from transurethral resection or hormonal therapy and avoid radical surgery.

## Case Report

A 61-year-old woman presented with hypogastric pain and dysuria. She was a smoker (20 sigarettes/day) and denied gross haematuria. She was in menopause. Previous history was consistent with chronic gastritis, tonsillectomy, appendicectomy and caesarean section. Abdominal and speculum examination were normal. An ultrasound of the urinary tract was performed, showing an echogenic mass close to the left ureteric orifice. CT-scan of the abdomen confirmed the presence of a periostial urinary bladder lesion 18 x 12 mm diameter without ipsilateral hydronephrosis. Urinary cytology did not show atypical or tumoral cells. Urine culture showed no evidence of infection. Blood tests were normal, also. Cystoscopy showed a red and bubbled area around the left ureteric orifice consistent with the lesion detected on ultrasound and CT scan.

Transurethral resection of lesion with concomitant cold biopsies was performed. Post-operative time was unremarkable and the patient was discharged on 1 day after surgery.

Histopathological examination of the specimens was negative for bladder cancer and revealed the presence of endosalpingeal tissues within the lamina propria and muscolaris consisting of tubular glands covered by ciliated epithelium. Solid von Brunn's nests were found, also.

At 12-month follow-up, the patient was free from recurrence and referred not to have urinary symptoms.

## Discussion

Müllerianosis of the bladder is a very rare benign condition characterized by the presence of a mixture of bladder wall components and at least two of these müllerian-derived tissues: endosalpinx, endometrium and endocervix (1). In some cases, however, it may present as an endosalpingiosis, that consists of the sole presence of nondescript glands lined with tubal type epithelium without any other müllerian tissue (4).

The exact pathogenesis of müllerianosis it still subject of discussion. The main theories reported in the literature are the implantation and the metaplastic theory.

The first one advocates the migration of müllerian-derived tissue cells caused by previous pelvic surgery.

This theory was described by Young &Clement and is supported by the history of pelvis surgery or caesarian section in the vast majority of patients presenting with the disease (1).

However, the implantation theory cannot explain the pathogenesis of müllerianosis in patients who did not undergo any previous surgical procedure. In such patients, the metaplastic theory may be advocated, suggesting that the presence of müllerian-derived tissue could be related to the potential of differentiation of peritoneal cells in response to hormonal stimuli. According with this theory, Branca and Barresi have hypothesized that peritoneal mesothelium, also referred to as secondary müllerian system may retain the potential to differentiate into müllerian-derived tissue in adults. Reportedly, the invariable location of the lesion are the posterior wall and the dome of the bladder, the only part of the bladder covered by the peritoneum (5), suggesting that the origin of the disease is in the process of differentiation of the mesothelial cell. In favor of the metaplastic theory, Koren et al. described a case of a 41-year-old woman with no previous history of caesarian section, diagnosed with müllerianosis of the posterior bladder wall. Koren et al. speculated that the mesothelial cells of the peritoneal layer may differentiate in tubal, endometrial or endocervical phenotype, due to its receptivity to female hormones (6). Donne C et al. support this this theory (7). Even if this seems to be in line with our pathologic findings, as in our case the immunohistochemical study revealed the cuboidal cells were diffusely positive for estrogen and progesterone receptors, we cannot suppose that in our case metaplasia occurred in response to female hormones, as our patient was neither in reproductive age or on hormonal replacement therapy.

Data reported in the literature are still controversial and we regret to admit that the pathogenesis of müllerianosis remains unresolved. Although not completely understood by the pathogenetic point of view, müllerianosis is a rare entity whose clinical manifestations should be very well known as a misdiagnosis may have detrimental effects on the patients.

Our case presented with dysuria, pelvic pain and haematuria, that is not different from the majority of the cases reported in the literature. However, a more atypical presentation is reported, like irregular menses, dysmenorrheal or vaginal bleeding (8). These symptoms are related to hormonal responsiveness of müllerian tissue cells and may be present in females in reproductive age.

Interestingly, in some cases the symptoms are very aspecific and may delay the diagnosis. Maeda K et al report that lower quadrant discomfort, or non-specific abdominal pain may be the only symptoms, thus making the differential diagnosis much more difficult (8).

Our patient referred abdominal pain associated with "a sensation of stinging and burning during urination", that made us focus our attention on the urinary system. Cystoscopy revealed to be crucial for the diagnosis, as it led to the direct endoscopic finding of the bladder lesion.

Urinary cytology is generally not conclusive. To our best knowledge, only two cases have been reported in which cytologic features showed to be of interest in the diagnostic process. Jimenez-Heffernan JA et al in 2000 and Guan et al in 2012 described a case of müllerianosis in which endometrial-type glandular cells were present in the voided urine specimen (9,10). In this respect, Amir RAR et al argued that urinary cytology may have a role in the diagnostic process, as it helps rule out neoplastic lesions (11).

Radiologically, on both CT-scan or MRI the lesion presents as a polypoid mass of the bladder.

Even if rare and benign, müllerianosis can be confused with other rare and malignant entities. Infiltrating primary or metastatic adenocarcinoma of the bladder may arise from the bladder or from the urachal remnant. Urachal adenocarcinoma is preferentially located on the dome of the badder as well as müllerianosis, thus making the differential diagnosis more difficult. Primary adenocarcinoma of the bladder is recognized by its histological feature, showing a neplastic epithelium. In addition, the presence of endometrial glands at histology is in favor of müllerianosis. Also an endocervical adenocarcinoma secondarily involving the bladder may mimic müllerianosis. In this respect, radiologic investigations, such as CT-scan and MRI may be of help in showing the primary site of the disease (5).

Last but not least, nephrogenic adenoma is a benign process involving the urinary bladder. This disease, however, does not involve the muscolaris propria of the bladder and is positive for racemase (5,12).

If malignant transformation of endometriosis is well known, malignant transformation of extragonadal müllerianosis is extremely rare. Garavan F et al described the only case reported in the literature (13).

A proper understanding of vesical mullerianosis is of the utmost importance for an appropriate management of the patient. Surgery is the gold standard for the treatment of this disease and consists of Trans-Urethral Resection of the Bladder lesion (TUR-B). When partial cystectomy is required, it may be performed with open or laparoscopy approach. In case of deep infiltration of the muscolaris propria of the baldder with involvement of uterus, hysterectomy with partial cystectomy may be necessary (10).

## Conclusion

Müllerianosis is rare benign disease affecting the urinary bladder of women of reproductive age. Clinical manifestation is aspecific, ranging from abdominal pain to dysuria and haematuria. Radiological investigation may reveal a polypoid mass of the dome of the bladder that may resemble a bladder tumor. Cystoscopy with transurethral resection of the mass shows müllerian-derived epithelium.

Müllerianosis can mimic many benign or malignant disorders of the lower urinary tract and enters the differential diagnosis with infiltrating primary or metastatic adenocarcinoma of the bladder, urachal adenocarcinoma and nephrogenic adenoma.

A proper understanding of this disease and a full awareness of the differential diagnosis is crucial for avoiding a delayed diagnosis and to perform an appropriate treatment rather than radical surgery.

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## References


1. Young RH, Clement PB. Müllerianosis of the urinary bladder. Mod Pathol 1996; 9: 731-737.
2. Eskridge MR, Rovner ES, Payne KD, et al. MRI of endocervicosis: An unusual cause of clustered periurethral cystic masses involving the bladder. AJR Am J Roentgenol. 2007;188:W147–149
3. McSorley S, Kochman A, DeSouza J. Müllerianosis of the urinary bladder in a postmenopausal woman. Urology 2013;81:488-490
4. Edmondson JD, Vogeley KJ, Howell JD, et al. Endosalpingiosis of bladder. J Urol 2002; 167:1401-1402
5. Branca G, Barresi V. Müllerianosis of the urinary bladder: a rare tumor like lesion. Arch Pathol Lab Med. 2014;138:432-6
6. Koren J, Mensikova J, Mukensnabl P, et al. Müllerianosis of the urinary bladder: report of a case with suggested metaplastic origin. Virchows Arch 2006;449:268-271
7. Donne C, Vidal M, Buttin X, et al. Mullerianosis of the urinary bladder: clinical and immunohistochemical findings. Histopathology 1998;33:290-292
8. Maeda K, Kojima F, Ishida M, et al. Müllerianosis and endosalpingiosis of the urinary bladder: report of two cases with review of the literature. Int J Clin Exp Pathol 2014; 7:4408-4414
9. Jimenez-Heffernan JA, Sanchez-Piedra D, Bernaldo de Quiros L, et al. Endosalpingiosis (müllerianosis) of the bladder: a potential source of error in urinary cytology. Cytopathology 2000;11:348-353
10. Guan H, Rosenthal DL, Erozan YS. Mullerianosis of the urinary bladder: report of a case with diagnosis suggested in urine cytology and review of literature. Diagn Cytopathol2012;40:997-1001
11. Amir RAR, Taheini KM, Sheikh SS. Mullerianosis of the Urinary Bladder: A case report. Case Rep Oncol 2018;11:206–211
12. Skinnider BF, Oliva E, Young RH, et al. Expression of alpha-methylacyl-CoA racemase (S) in nephrogenic adenoma: a significant immunohistochemical pitfall compounding the differential diagnosis with prostatic adenocarcinoma. Am J Surg Pathol 2004; 28:701-705
13. Garavan F, Grainger R, Jeffers M. Endometrioid carcinoma of the urinary bladder complicating vescicalMullerianosis: A case report and review of the literature. Virchows Arch 2004;444:587-589
14. Ogah K, Hartis R, Hilton P. Mullerianosis involving the urinary bladder. Int Urogynecol J 2012;23:123-125


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