

CASE REPORT

Müllerianosis of the urinary bladder: a rare case report and review of the literature

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Abstract

The aim of this paper is to report a very rare case of müllerianosis (endosalpinx, endometrium, and endocervix) in a post-menopausal woman. Müllerianosis of the bladder is a very rare disease, which affects mainly the women of the reproductive age group, but with a good prognosis if the transitional bladder carcinoma is resolved. We present the case of a 64-year-old woman complaining of left lower abdomen pain, repeated lower and upper tract urinary infections, emergency urinary incontinence and hematuria. The surgical history shows that she underwent a hysterectomy, caesarean section and appendectomy. The clinical examination emphasizes a normal abdomen, with a normal aspect of the post-operative scars and a second-degree cystocele. An abdominal computed tomography (CT) scan with contrast and a cystography were performed and showed a 16 mm lesion-like tumor on the left bladder wall respectively a third-degree vesicoureteral reflux. These investigations were followed by a cystoscopy and transurethral resection of the bladder tumor (TURBT). The histopathology report described three types of tissues: endometriosis, endocervicosis and endosalpingiosis. Sequent to these results, a partial cystectomy with the re-implantation of the left ureter was performed. Once again, the results of the specimen confirm the diagnosis of müllerianosis. The immediate post-operative outcomes were good, the patient having no pains and no more hematuria. Six month later, a tension-free vaginal tape obturator (TVT-O) operation was carried out for urinary incontinence and two years later, a correction for a post-surgical abdominal hernia was performed. Müllerianosis of the bladder is a very rare disease, which affects mainly the women at the procreation age, but with a good prognosis. The differential diagnosis with a malignant tumor is very important to be carefully made. Currently, there is no golden standard to treat this disease. The cystoscopy and the histopathological examination of the specimen are indispensable for the certainty diagnosis.

Keywords: müllerianosis, bladder carcinoma, partial cystectomy.

Introduction

Müllerianosis of the bladder was first described by Young & Clement, in 1996. This condition is histopathologically characterized by the presence of a mixture of at least two of three müllerian-derived components (endosalpinx, endometrium, and endocervix) in the lamina propria and muscularis propria of the urinary bladder [1]. Usually, this disease occurs in women at the reproductive group age. Clinical symptoms are quite varied, going from diffuse abdominal pain, dysuria, hematuria, up to recurring renal colics [2–4]. The implantative and metaplastic origins have been suggested in its pathogenesis, but there is still under discussion [5].

The aim of this paper is to report a very rare case of müllerianosis (endosalpinx, endometrium, and endocervix) in a post-menopausal woman.

Case presentation

We present the case of a 64-year-old woman complaining of left lower abdomen pain, recurring lower

and upper tract urinary infections, emergency urinary incontinence and hematuria. The surgical history shows that she underwent a hysterectomy, caesarean section and appendectomy.

The clinical examination emphasizes a normal abdomen, with a normal aspect of the post-operative scars and a second-degree cystocele. The rest of the vaginal examination was normal. The cytological exam shows no features.

Facing this situation, we have realized an abdominal computed tomography (CT) scan with contrast, which showed a 16 mm tumor in the left bladder wall, surrounding the left ureteral meatus (Figure 1).

To complete the imagistic investigation, we performed also a cystography in order to rule out any malformation, which can produce the urinary incontinence and repeated lower and upper urinary tract infections. The results showed a 3rd degree left vesicoureteral reflux, but no urethral anomalies and a normal bladder neck (Figure 2).

We decided to perform a cystoscopy, which discloses a non-polypoid tumor-like lesion, surrounding the left ureteral meatus, covered by a normal mucosa. The rest

of the aspect of the bladder shows no particularities. A transurethral resection of the bladder tumor (TURBT) of the non-polypoid tumor was undertaken and the macroscopically examination of the paraffin included specimen consisted in harvesting five tissues fragments between 4 and 8 mm in the large axis. The sections were first stained with Hematoxylin–Eosin (HE) and then the microscopic images were taken with a Nikon camera using a Nikon microscope. The histopathological examination revealed bladder fragments representing mucosa, sub-mucosa and muscularis propria. The mucosa is corresponding to an urothelial epithelium and glandular mucosa type. It consists from a uniform uni- or pseudo-pluristratified cylindrical epithelium, often with a tuboendometrial aspect and sometimes with an endocervical aspect, but free of any significant atypical tissue (Figure 3). At the level of the sub-mucosa and muscularis propria, the specimens there were described different forms and sizes of glandular structures with the same epithelium characteristics (Figures 4 and 5). The attention was drawn by the image of a gland with the same inner structures situated in the bladder serosa (Figure 6). In conclusion, the histological aspect of the specimens is compatible with müllerianosis.

In general, transurethral resection is the treatment of choice in superficial and focal lesions, but because of the location, of the infiltration of the bladder muscle, of the

size and of the effects of the tumor over the surrounding structures (3rd degree vesicoureteral reflux), we have chosen to perform a partial cystectomy with left ureteral reimplantation in a second surgical time.

After the surgery, the macroscopically histological examination described a 3 cm specimen with a thickened multinodular and microcystic wall. The microscopic examination studied the muscle which appears hyperplasic with neuroid hyperplasia. It contains benign glandular structures lined by an endocervical epithelium and tubo-endometrial epithelium. These glandular structures are not surrounded by stroma. The surface of the urothelial epithelium was without atypia, and no connection between the surface of the urothelial mucosa and the dilated tubular glands was noted. The conclusion of the histological report was bladder müllerianosis with no atypia or malignancy sings.

As the diagnosis was obvious after the histopathological examination of the specimens, no immunohistochemistry examination was performed.

The immediate post-operative outcomes were good, the patient having no pains, no more urinary infections and no more hematuria. Six months later, a tension-free vaginal tape obturator (TVT-O) operation was carried out for urinary incontinence and two years later, a correction for a post-surgical abdominal hernia was performed.

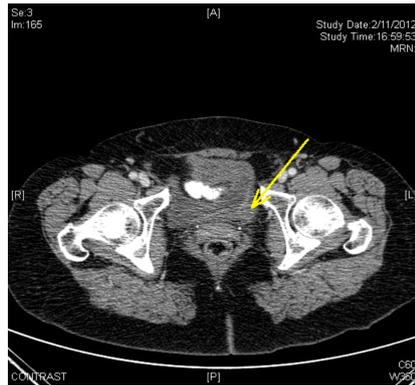


Figure 1 – Abdominal CT scan with contrast. Yellow arrow showing a 16 mm tumor in the posterolateral bladder wall, surrounding the left ureteral meatus.

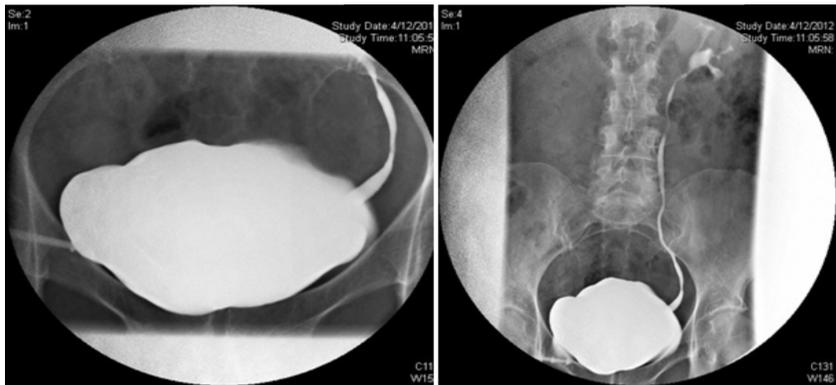


Figure 2 – Per-voiding cystography showing a 3rd degree left vesicoureteral reflux, but no urethral anomalies and a normal bladder neck.

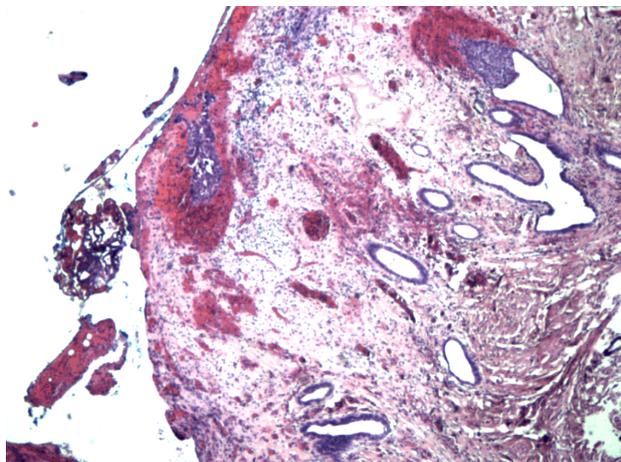


Figure 3 – Urothelial epithelium and glandular mucosa type. Uniform uni- or pseudo-pluristratified cylindrical epithelium often with a tubo-endometrial aspect and sometimes with an endocervical aspect. HE staining, ×40.

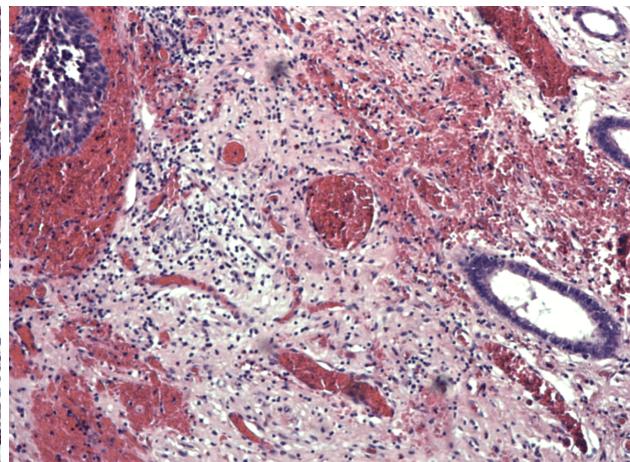


Figure 4 – Different forms and sizes of glandular structures with the same uni- or pseudo-pluristratified cylindrical epithelium often with a tubo-endometrial aspect and sometimes with an endocervical aspect. HE staining, ×100.

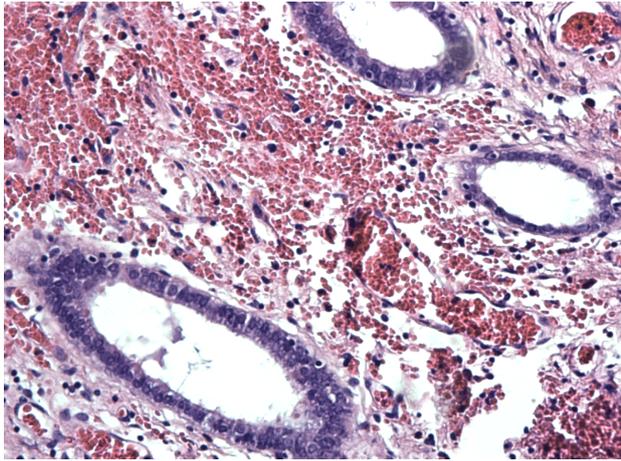


Figure 5 – Glands in the bladder wall lined by mucinous tall columnar epithelium with basal nuclei. HE staining, $\times 200$.

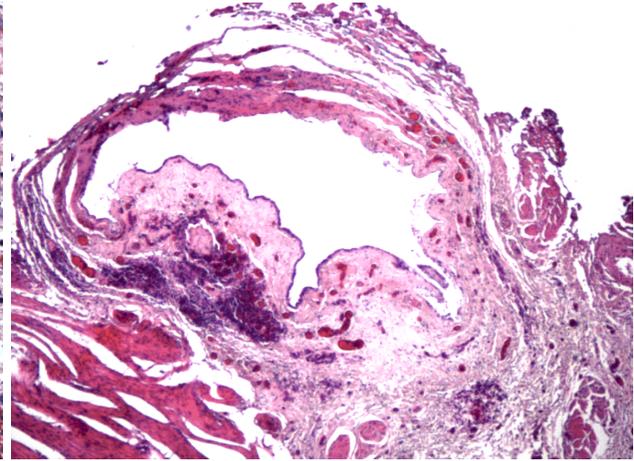


Figure 6 – Gland with the same inner characteristics in the bladder serosa. HE staining, $\times 40$.

Discussion

Müllerianosis of the bladder represents the presence of the three related benign müllerian glandular epithelial proliferations – endosalpinx, endometrium, and endocervix – in the bladder wall. Since the first reported cases, only 17 cases of müllerianosis of the urinary bladder have been reported in the English literature [5–16], for which the real incidence and classification is difficult to assess.

In this report, we described the 18th documented case of müllerianosis and the 8th which contains the three müllerian-derived components. Furthermore, it is the 2nd case in the literature described in a post-menopause patient.

The disease occurs only in women and mainly in women of the reproductive age group. The pathogenesis of müllerianosis and endosalpingiosis remains completely unresolved. However, some hypotheses have been proposed. The implantation theory by Young & Clement proposes that müllerian tissue implants in the urinary bladder wall during caesarean section or pelvic surgery [1]. This theory is supported by the fact that patients with müllerianosis have a frequent clinical history of caesarean section or pelvic surgery [17]. However, approximately half of the cases did not have any history of these procedures, and moreover, müllerianosis occurring in extra-abdominal sites, such as the spine, has also been reported [18]. These cases do not support the implantation theory [17], and moreover, an implantation theory may be a valid explanation for single tissue ectopias [5].

Donné *et al.* proposed the metaplastic theory because the presence of multiple müllerian components may reflect the lesion's capacity of differentiation, and the location of müllerianosis is exclusively restricted to the posterior wall of the urinary bladder, an area that topographically corresponds to its peritoneal covering and that may be particularly receptive to female hormones [5].

Moreover, Koren *et al.* reported a case of müllerianosis of the urinary bladder, which suggested a metaplastic origin [10]. They described a small focus of metaplastic ciliated epithelium of the tubal type in continuity with the urothelium in cystitis glandularis, and these metaplastic glandular cells were immunohistochemically positive for

estrogen (ER) and progesterone (PgR) receptors [10]. Therefore, they speculated that müllerianosis can arise through metaplasia of the urothelium in a setting of chronic inflammation [10]. Furthermore, Branca & Barresi speculated that peritoneal mesothelium, also referred to as the secondary müllerian system, may retain the potential to differentiate into tubal, endometrial, and endocervical tissues in the adult [15]. According to these findings, a metaplastic theory is favored.

The clinical frequent presentations were abdominal/pelvic pain and dysuria/hematuria, which may or may not be associated with menstruation. The radiological study revealed polypoid, mass-like lesion, predominantly involving the dome or posterior wall of the bladder [13].

The histopathological diagnosis is essential for the diagnosis of the müllerianosis of the urinary bladder [18]. However, only two reports regarding the cytological features of müllerianosis of the urinary bladder have been documented [6, 13]. According to the report by Guan *et al.*, only endometrial-type glandular cells were present in the voided urine specimen [13]. The urine specimen had cohesive, three-dimensional aggregates of glandular cells with scant cytoplasm and slightly irregular nuclei [13]. Moreover, Jiménez-Heffernan *et al.* described the cytological features of a urine specimen, which had large monolayered epithelial cell aggregates with slightly irregular nuclei and scant cytoplasm [6]. The cytodiagnosis of müllerianosis may be impossible according to these cytological features.

The differential diagnosis of müllerianosis should be made, first of all, with bladder cancer [5]. In particular, the differentiation from invasive adenocarcinoma is very important. Müllerianosis can be distinguished from adenocarcinoma and various non-neoplastic glandular lesions of the urinary bladder based on a variety of architectural and cytological features [1].

Müllerianosis can mimic invasive adenocarcinoma because the lesion of these two conditions is present in the lamina propria and muscularis propria. Moreover, one case of endometrioid adenocarcinoma arising concurrently with müllerianosis of the urinary bladder has been reported [9]. Once the bladder cancer suspicion was excluded, we have to think of benign lesions like cystitis cystica and cystitis glandularis that can mimic müllerianosis,

but they do not show deeply situated glands as in müllerianosis [15]. The others pathology that can mimic müllerianosis are the endometriosis, the nephrogenic adenoma and urachal remnants in the bladder, which can also show tubular structures lined by mucinous epithelium, but they are usually incidental findings observed near the dome of the bladder and it is usually surrounded by a loose peritubular fibromuscular tissue.

There are two types of treatment, the conservatory medical one and the surgical one.

The conservatory medical treatment is based on LH-RH (luteinizing hormone-releasing hormone) agonist who reduces the tumor volume, by inhibition of pituitary and gonadal function and direct effects on various hormone sensitive tumors. The criteria for patient inclusion in this treatment are small tumors (<1 cm), metaplastic way of implantation, tumors which do not alter the local anatomy.

The surgical treatment consists in TURBT during the biopsy and frozen section when the entire tumor is resected and partial or total cystectomy if the TURBT was insufficient, if there is a big tumor or if the lesion alters the local anatomy with repercussion on the surrounding tissue and organs.

The prognosis is good, but a case of transitional bladder adenocarcinoma was reported in a patient with bladder endometriosis [19].

☒ Conclusions

Müllerianosis of the bladder is a very rare disease, which affects mainly the women of the reproductive age group, but with a good prognosis. It is very important that the differential diagnosis with a malignant tumor should be carefully made. Currently, there is no golden standard to treat this disease. Cystoscopy and the pathological examination of the resected tissue are indispensable for the certainty diagnosis.

Conflict of interests

The authors declare that they do not have any conflict of interests.

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