**Case Report**

**Müllerianosis and endosalpingiosis of the urinary bladder: report of two cases with review of the literature**

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**Abstract:** Müllerianosis of the urinary bladder is an extremely rare benign condition, characterized by the presence of a mixture of at least two müllerian-derived components, and endosalpingiosis is also an extremely rare condition, characterized by the presence of tubal-type epithelium. In this report, we describe the 17th case of müllerianosis and 5th case of endosalpingiosis of the urinary bladder. A 39-year-old Japanese female presented with menstrual hematuria and was found to have a polypoid lesion in the posterior wall of the urinary bladder. Histopathological study demonstrated variably-sized dilated tubular glands in the lamina propria and muscularis propria. These dilated glands were covered by ciliated cuboidal cells, and some of them were covered by columnar cells with intracytoplasmic mucin. Moreover, a tiny focus of endometrial tissues was also present. Immunohistochemically, these glandular cells were positive for estrogen receptor. Accordingly, a diagnosis of müllerianosis was made. The second case was a 37-year-old Japanese female, who was found to have a polypoid lesion in the posterior wall of the bladder. Dilated tubular glands were covered by ciliated cells in the lamina propria and muscularis propria. Neither endocervical nor endometrial tissues were observed. Immunohistochemically, these ciliated cells were positive for estrogen receptor. Accordingly, a diagnosis of endosalpingiosis was made. Our analysis revealed that these two conditions mainly affect premenopausal females and occur exclusively in the posterior wall. Although the pathogenesis remains completely unresolved, a metaplastic theory is favored. The recognition of these two conditions is important because they can mimic invasive adenocarcinoma.

**Keywords:** Müllerianosis, endosalpingiosis, urinary bladder

**Introduction**

Müllerianosis of the urinary bladder is an extremely rare benign condition, first described by Young and Clement in 1996 [1]. This condition is characterized histopathologically by the presence of a mixture of at least two müllerian-derived components (endosalpinx, endometrium, and endocervix) in the lamina propria and muscularis propria of the urinary bladder [1]. Since the first reported cases, only 16 cases of müllerianosis of the urinary bladder have been reported in the English literature [2-14].

Endosalpingiosis of the urinary bladder is also an extremely rare condition characterized histopathologically by the sole presence of tubal-type epithelium without other müllerian components in the lamina propria and muscularis propria of the urinary bladder [15]. To the best of our knowledge, only 4 cases of endosalpingiosis of the urinary bladder have been documented in the English language literature [15-18].

In this report, we describe cases of müllerianosis and endosalpingiosis of the urinary bladder and review the clinicopathological features of these entities.

**Case reports**

**Case 1**

A 39-year-old Japanese female without history of Caesarean section or pelvic surgery present-
Müllerianosis of the urinary bladder

ed with menstrual dysuria. She had been under medical follow-up for uterine leiomyoma (no surgical procedure was performed), and then, an ultrasonography examination demonstrated a tumorous lesion in the urinary bladder. She was referred to our hospital where cystoscopic examination revealed a soft sessile polypoid lesion, measuring 25 mm in diameter, in the left posterior wall of the urinary bladder (Figure 1), and subsequently, transurethral resection of the tumor was performed.

Histopathological study revealed the presence of variably-sized dilated tubular glands in the lamina propria and muscularis propria (Figure 2A). The surface urothelial epithelium was without atypia, and no connection between the surface urothelial mucosa and dilated tubular glands was noted (Figure 2A). These dilated glands were covered by ciliated cuboidal cells containing small round nuclei without nucleolus (Figure 2A, inset), which corresponded to tubal-type epithelium. Some of the tubular glands were covered by columnar cells with intracytoplasmic mucin and small round nuclei (Figure 2B). These columnar cells resembled endocervical glandular cells. Moreover, a tiny focus of endometrial tissue, which was comprised of endometrial glandular and stromal cells, was also observed adjacent to the dilated tubal-type gland (Figure 2C). No mitotic figures were observed in these three components.

Immunohistochemical studies were performed using an autostainer (Ventana) by the same method as previously reported [19-23]. Estrogen receptor (ER) was expressed in the tubal-type epithelial cells, but not in the surface urothelial cells (Figure 2D). ER was also expressed in the endocervical glandular cells, and endometrial glandular and stromal cells (Figure 2E). Progesterone receptor (PgR) was also expressed in the tubal-type glandular cells, but not in the endocervical and endometrial glandular cells. CD10 was expressed only in the endometrial stromal cells (Figure 2F). Cytokeratin 7 was expressed in the surface urothelial cells, tubal, endocervical, and endometrial glands, but no cytokeratin 20-positive cells were noted. Only a few Ki-67-positive glandular cells were observed in these three components.

According to these histopathological and immunohistochemical results, an ultimate diagnosis of müllerianosis of the urinary bladder was made.

Case 2

A 37-year-old Japanese female with a history of surgical resection of ovarian cyst and rectal endometriosis was incidentally found to have a polypoid lesion in the urinary bladder by ultrasonography. Magnetic resonance imaging showed a well-circumscribed tumorous lesion, measuring in 20 mm in diameter, located in the posterior urinary bladder wall that extended to both the surface and external sides of the wall (Figure 3). Cystoscopic examination revealed a tumorous lesion in the posterior wall of the urinary bladder, thus, transurethral resection of the tumor was performed.

Histopathological study demonstrated variably-sized dilated tubular glands in the lamina propria and muscularis propria beneath the non-neoplastic urothelial epithelium (Figure 4A). These dilated glands were covered by ciliated cuboidal cells without atypia (Figure 4A, inset). No mitotic figures were noted. Neither endocervical nor endometrial tissues were observed.

Immunohistochemically, the ciliated cuboidal cells were diffusely positive for ER (Figure 4B). Some of the ciliated cells were also positive for PgR. Cytokeratin 7 was expressed in the surface urothelial and tubal-type cells, but no cytokeratin 20-positive cells were noted. Only a few Ki-67-positive glandular cells were observed.

Figure 1. Cystoscopic findings of Case 1 showing a soft sessile polypoid lesion in the posterior wall of the urinary bladder.
Accordingly, an ultimate diagnosis of endosalpingiosis of the urinary bladder was made.

**Discussion**

In this report, we described the 17th documented case of müllerianosis and 5th documented case of endosalpingiosis of the urinary bladder. **Table 1** summarizes the clinicopathological features of the previously reported cases of these two entities as well as the present ones. These conditions mainly affect premenopausal females (average age 44.6 years), however, a few cases occurring in postmenopausal females
Müllerianosis of the urinary bladder

have also been documented (Table 1). The most common complaint was hematuria or dysuria. Nine patients had history of uterus or urinary bladder surgery. These conditions occur exclusively in the posterior wall of the urinary bladder.

The histopathological hallmark of müllerianosis is the presence of a mixture of at least two of three müllerian-derived components [1]. Ten of 17 cases of müllerianosis of the urinary bladder including the present one had all three müllerian components. The tubal component was present in 16 cases, endometrial component in 15 cases, and endocervical component in 14 cases (Table 1).

The pathogenesis of müllerianosis and endosalpingiosis remains completely unresolved. However, some hypotheses have been proposed. The implantation theory by Young and 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 of müllerianosis have a frequent clinical history of Caesarean section or pelvic surgery (9/17 cases of müllerianosis) (Table 1). However, approximately half of the cases including Case 1 did not have any history of these procedures, and moreover, müllerianosis occurring in extraabdominal sites, such as the spine, has also been reported [24]. These cases do not support the implantation theory [13], and moreover, an implantation theory may be a valid explanation for single tissue ectopias [2].

Donne 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 [2]. Moreover, Koren et al. reported a case of müllerianosis of the urinary bladder which suggested a metaplastic origin [7]. They described a small focus of metaplastic ciliated epithelium of the tubal type in continuity with the urothelium in glandularis cystitis, and these metaplastic glandular cells were immunohistochemically positive for ER and PgR [7]. Therefore, they speculated that müllerianosis can arise through metaplasia of the urothelium in a setting of chronic inflammation [7]. Furthermore, Branca and Barresi speculated that peritoneal mesothelium, also referred to as the
### Table 1. Clinicopathological features of müllerianosis and endosalpingiosis of the urinary bladder

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Chief complaint</th>
<th>History of surgery</th>
<th>Location</th>
<th>Size (mm)</th>
<th>Histopathology</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Müllerianosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>37</td>
<td>Not available</td>
<td></td>
<td>Posterior wall</td>
<td>30-40</td>
<td>S (3/3 cases)</td>
<td>[1]</td>
</tr>
<tr>
<td>2</td>
<td>44</td>
<td>Lower quadrant discomfort</td>
<td>CS (1/3 case)</td>
<td>Posterior wall</td>
<td>20-30</td>
<td>M (2/3 cases)</td>
<td>[1]</td>
</tr>
<tr>
<td>3</td>
<td>46</td>
<td>Irregular menses</td>
<td></td>
<td>Posterior wall</td>
<td>20</td>
<td>C (3/3 cases)</td>
<td>[1]</td>
</tr>
<tr>
<td>4</td>
<td>27</td>
<td>Dysmenorrhea, menstrual dysuria</td>
<td>None</td>
<td>Posterior wall</td>
<td>45 x 40</td>
<td>S, M, C</td>
<td>[2]</td>
</tr>
<tr>
<td>5</td>
<td>38</td>
<td>Pelvic discomfort, dysuria</td>
<td>Hysterectomy</td>
<td>Not available</td>
<td>Not available</td>
<td>S, M</td>
<td>[3]</td>
</tr>
<tr>
<td>6</td>
<td>48</td>
<td>Abdominal pain, dysuria, hematuria</td>
<td>Hysterectomy</td>
<td>Not available</td>
<td>2</td>
<td>S, C</td>
<td>[4]</td>
</tr>
<tr>
<td>7</td>
<td>37</td>
<td>Vaginal discharge, iliac fossa pain</td>
<td>CS, salpingo-oophorectomy</td>
<td>Posterior wall</td>
<td>30 x 20</td>
<td>S, M, C</td>
<td>[5]</td>
</tr>
<tr>
<td>8</td>
<td>53</td>
<td>Hematuria</td>
<td>Not available</td>
<td>Posterior wall</td>
<td>10</td>
<td>S, M, C + endometrioid adenocarcinoma</td>
<td>[6]</td>
</tr>
<tr>
<td>9</td>
<td>41</td>
<td>Dysuria, pelvic pain, hematuria</td>
<td>None</td>
<td>Posterior wall</td>
<td>Not available</td>
<td>S, M, C</td>
<td>[7]</td>
</tr>
<tr>
<td>10</td>
<td>70</td>
<td>Vaginal bleeding</td>
<td>Hysterectomy, salpingo-oophorectomy</td>
<td>Trigone</td>
<td>Not available</td>
<td>S, M</td>
<td>[8]</td>
</tr>
<tr>
<td>11</td>
<td>45</td>
<td>Pelvic pain, dysuria, hematuria</td>
<td>CS</td>
<td>Posterior wall</td>
<td>23 x 21 x 17</td>
<td>S, M, C</td>
<td>[9]</td>
</tr>
<tr>
<td>12</td>
<td>32</td>
<td>Dysuria</td>
<td>Not available</td>
<td>Lateral wall</td>
<td>40</td>
<td>S, M, C</td>
<td>[10]</td>
</tr>
<tr>
<td>13</td>
<td>28</td>
<td>Hematuria</td>
<td>None</td>
<td>Dome, lateral wall</td>
<td>40</td>
<td>M, C</td>
<td>[11]</td>
</tr>
<tr>
<td>14</td>
<td>61</td>
<td>Dysuria, frequent urination</td>
<td>CS</td>
<td>Posterior wall</td>
<td>28 x 22</td>
<td>S, M, C</td>
<td>[12]</td>
</tr>
<tr>
<td>15</td>
<td>50</td>
<td>Hematuria, dysuria</td>
<td>None</td>
<td>Posterior wall</td>
<td>Not available</td>
<td>S, M, C</td>
<td>[13]</td>
</tr>
<tr>
<td>16</td>
<td>30</td>
<td>Iliac fossa pain</td>
<td>None</td>
<td>Posterior wall</td>
<td>39 x 37 x 32</td>
<td>S, M</td>
<td>[14]</td>
</tr>
<tr>
<td><strong>Present Case 1</strong></td>
<td>39</td>
<td>Menstrual dysuria</td>
<td>None</td>
<td>Posterior wall</td>
<td>25</td>
<td>S, M, C</td>
<td></td>
</tr>
<tr>
<td><strong>Endosalpingiosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>67</td>
<td>Suprapubic pain</td>
<td>CS, hysterectomy</td>
<td>Dome</td>
<td>20</td>
<td>S</td>
<td>[15]</td>
</tr>
<tr>
<td>2</td>
<td>48</td>
<td>Uterine bleeding</td>
<td>None</td>
<td>Posterior wall</td>
<td>10</td>
<td>S</td>
<td>[16]</td>
</tr>
<tr>
<td>3</td>
<td>54</td>
<td>Dysuria</td>
<td>Traumatic bladder injury</td>
<td>Posterior wall</td>
<td>25</td>
<td>S</td>
<td>[17]</td>
</tr>
<tr>
<td>4</td>
<td>49</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
<td>S</td>
<td>[18]</td>
</tr>
<tr>
<td><strong>Present Case 2</strong></td>
<td>37</td>
<td>None</td>
<td>Ovarian cyst, rectal endometriosis</td>
<td>Posterior wall</td>
<td>20</td>
<td>S</td>
<td></td>
</tr>
</tbody>
</table>

C, Endocervix; CS, Caesarean section; M, Endometrium; S, Endosalpinx.
secondary müllerian system, may retain the potential to differentiate into tubal, endometrial, and endocervical tissues in the adult [13]. According to these findings, a metaplastic theory is favored.

The histopathological diagnosis is essential for the diagnosis of müllerianosis and endosalpingiosis of the urinary bladder. However, only two reports regarding the cytological features of müllerianosis of the urinary bladder have been documented [3, 11]. According to the report by Guan et al., only endometrioid-type glandular cells were present in the voided urine specimen [11]. The urine specimen had cohesive, three-dimensional aggregates of glandular cells with scant cytoplasm and slightly irregular nuclei [9]. Moreover, Jimenez-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 [3]. The cytdiagnosis of müllerianosis may be impossible according to these cytological features.

The histopathological diagnostic considerations of müllerianosis and endosalpingiosis of the urinary bladder include several benign conditions, such as cystitic glandularis, urachal remnant, nephrogenic adenoma, and adenocarcinoma [13]. In particular, the differentiation from invasive adenocarcinoma is very important. Müllerianosis and endosalpingiosis 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 [6]. Therefore, albeit extremely rare conditions, the recognition of müllerianosis and endosalpingiosis and the detailed histopathological analyses are important for the correct diagnosis.

Disclosure of conflict of interest

None.

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References

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