CASE REPORT

Ureteral stenosis due to endometriosis

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Abstract

Endometriosis is characterized by the presence of endometrial tissue outside the uterine cavity, with potential to undergo malignant transformation. We report the case of a 36-year-old patient with a clinical and imagistic diagnosis of left vaginal pouch and left parametrium tumor. The patient presented lumbar and pelvic pain, dysuria and polakuryia. Ultrasound revealed changes in the left kidney confirmed by the CT scan, which also revealed the presence of a tumor in the left parametrium infiltrating the bladder, juxtavesical ureter, uterus and cervix. Laboratory tests were within normal limits. Surgery consisted of interadnexal hysterectomy, proximal colpectomy, left distal ureterectomy with ureterocystoneostomy. Pathological examination established the final diagnosis of infiltrative deep endometriosis involving the urinary tract. In the case of a young fertile patient with gynecological symptoms and morphofunctional changes of the urinary system, urinary tract endometriosis should always be a diagnostic option.

Keywords: endometriosis, ureterohydronephrosis, ureteral stenosis, tumor formation.

Introduction

Endometriosis is a chronic gynecological disorder characterized by the presence of endometrial tissue outside the uterine cavity [1]. The clinical consequences of endometriosis include pelvic pain exacerbated during certain periods of utero-ovarian cycle, dysmenorrhea and infertility. The incidence is between 6% and 10% of all genitaly active females and 35–50% of women with pelvic pain and infertility [2]. The disease most often affects the ovaries (up to 88% of all cases), uterine ligaments, fallopian tubes, rectum, cervical-vaginal region and urinary tract. Urinary tract involvement is rare accounting for around 1–2% of all cases [3], of which 84% are found in the bladder [4]. However, endometriosis can be encountered in other abdominal organs such as the liver, pancreas, intestinal tract, spleen [5], gallbladder [6], the abdominal wall and even the navel [7]. Distant locations, far from the abdominal cavity, were also mentioned, such as the nasal mucosa [8], or central nervous system [9]. Although considered a benign disease, recent data show that endometriosis, and especially cystic ovarian endometriosis, can undergo malignant degeneration [10].

We report the case of a 36-year-old patient with a clinical and imagistic diagnosis of tumor of the left vaginal pouch and left parametrium.

Patient, Methods and Results

Patient V.D.E., aged 36 years, presented with pelvic pain with moderate intensity, which started several years ago, associated with lower back pain. Since 2008, the intensity of the pelvic and back pain increased and were often associated with dysmenorrhea and polymenorrhea. To relieve the symptoms the patient received different painkillers and anti-inflammatory treatments, with partial results. From 2010, dysuria and polakuryia were added to the above-mentioned symptoms, and lumbar pain became mainly located in the left lumbar region, which caused the patient to refer to the specialists. General clinical examination revealed a normostenic patient with normal weight whose cardiovascular parameters were within normal limits. The left lumbar region was painful to touch and Giordano maneuver was intensely positive. Pelvic examination revealed the presence of a lesional cervix and a tumor involving the uterus, left vaginal pouch and parametrium. Abdominal and pelvic ultrasound revealed a left kidney with a slightly increased size, with a 117 mm cranio-caudal axis, a 55 mm transverse diameter, with a parenchymal index reduced to 7 mm, and significant pyelocaliceal (22 mm, polylobulated lower pelvis, 19 mm medial pelvis, and an 18 mm upper pelvis), and lumbar ureteral dilations (13 mm anteroposterior diameter) (Figure 1).

Computer-tomographic examination (CT) with contrast substance revealed the presence of left ureterohydrenephrosis with diminished secretion and excretion in the left kidney (Figures 2 and 3). The left ureteral dilation reached the juxtavesical region where it showed a significant stenosis, with thread-like appearance. The bladder was deformed, with left posteoro-lateral infiltration, and pseudotumor-like appearance. The uterus and cervix had increased size, with the presence of a tumor in the left parametrium infiltrating the bladder, juxtavesical ureter, uterus and cervix (Figure 4). Pelvic and lumbar aortic adenopathy were absent.
Laboratory tests (glucose, urea, creatinine, blood count, liver function tests) were within normal limits.

Under these circumstances, surgery was required to remove the tumor and treat the ureterohydronephrosis. The opening of the abdominal and pelvic cavity revealed the presence of a large uterus, with hard tumor appearance, infiltrated by a tumor developed in the left parametrium. The tumor partially infiltrated the bladder and encompassed the last 3–4 cm of the left ureter. Surgery consisted of interadnexal hysterectomy, proximal colpectomy, left distal ureterectomy with ureterocystoneostomy. Postoperative course was good, with urinary and pelvic symptoms disappearing. Ultrasound performed at 30 days after surgery revealed the return to normal size of the left kidney and the absence of ureterohydronephrosis.

For single immunohistochemistry, after antigen retrieval, sections were cooled down to room temperature and were incubated for 30 minutes in a 1% hydrogen peroxide solution. Sections were next washed in PBS, followed by a blocking step of 30 minutes in 2% skim milk. Next, the slides were incubated with primary antibodies overnight at 4°C. The signal was detected with 3,3′-diaminobenzidine (DAB) (Dako) and the slides were coverslipped in DPX (Fluka) after Hematoxylin counterstaining.

Sections were imaged with a Nikon Eclipse 55i microscope (Nikon, Apidrag, Romania) equipped with a 5-megapixel cooled CCD camera. Images were captured and archived using a Nikon frame grabber and the Image ProPlus 7 AMS software (Media Cybernetics Inc, Buckinghamshire, UK).

Pathological examination revealed:
- macroscopic examination: enlarged uterus, infiltrating and compressing the bladder.
- microscopic examination: large uterus, infiltrated by a tumor developed in the left parametrium, partially infiltrating the bladder and encompassing the last 3–4 cm of the left ureter. Surgery consisted of interadnexal hysterectomy, proximal colpectomy, left distal ureterectomy with ureterocystoneostomy. Postoperative course was good, with urinary and pelvic symptoms disappearing.

Table 1 – Antibodies used for the immunohistochemical study

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Manufacturer</th>
<th>Clone</th>
<th>Host/Target/Clonality</th>
<th>Antigen retrieval</th>
<th>Dilution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-CK7</td>
<td>Dako</td>
<td>OV-TL 12/30</td>
<td>Ms/Hu/Monoclonal</td>
<td>Sodium citrate, pH 6</td>
<td>1:50</td>
</tr>
<tr>
<td>Anti-CK8 LMW</td>
<td>Dako</td>
<td>35βH11</td>
<td>Ms/Hu/Monoclonal</td>
<td>EDTA, pH 9</td>
<td>Ready to use</td>
</tr>
<tr>
<td>Anti-CK18</td>
<td>Dako</td>
<td>DC 10</td>
<td>Ms/Hu/Monoclonal</td>
<td>EDTA, pH 9</td>
<td>1:25</td>
</tr>
<tr>
<td>Anti-CK20</td>
<td>Dako</td>
<td>K20.8</td>
<td>Ms/Hu/Monoclonal</td>
<td>Sodium citrate, pH 6</td>
<td>1:25</td>
</tr>
<tr>
<td>Anti-ERα</td>
<td>Dako</td>
<td>1D5</td>
<td>Ms/Hu/Monoclonal</td>
<td>EDTA, pH 9</td>
<td>1:50</td>
</tr>
<tr>
<td>Anti-PR</td>
<td>Dako</td>
<td>PgR 636</td>
<td>Ms/Hu/Monoclonal</td>
<td>EDTA, pH 9</td>
<td>1:50</td>
</tr>
<tr>
<td>Anti-CK HMW</td>
<td>Dako</td>
<td>34βE12</td>
<td>Ms/Hu/Monoclonal</td>
<td>Sodium citrate, pH 6</td>
<td>1:50</td>
</tr>
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After surgical excision, the biological material was immediately placed in 4% formaldehyde solution buffered to a pH of 7.2–7.4 with monosodium phosphate and processed using the usual technique for paraffin embedding. Four-μm thick serial sections were cut using a rotary microtome (Microm HM350) equipped with a waterfall based section transfer system (STS, Microm). Sections were stained using the HE technique as well as immunohistochemical (IHC) ones.

For the immunohistochemical study, sections were cut using the same equipment, but with a thickness of 3 μm. Sections were collected on poly-L-lysine coated slides, dried in a thermostat at 37°C for 24 hours, in order to obtain a perfect adhesion of the biological material to the surface of the histological slide, and then stained using different antibodies (Table 1).
Ureteral stenosis due to endometriosis

A 43-year-old woman presented with complaints of dysuria and gross hematuria. Examination revealed a palpable mass in the left lower quadrant. Abdominal ultrasound showed a pelvic mass with hydronephrosis. Cystoscopy revealed a left vesical diverticulum and right ureteral stenosis. An endoscopic biopsy of the diverticulum revealed endometrial hyperplasia. Given the clinical presentation, computed tomography (CT) and MRI were performed, which showed a 4 cm heterogeneous mass involving the left parametrium and extending into the left pelvic ureter. The patient underwent laparoscopic hysterectomy and left pelvic lymphadenectomy.

At the time of surgery, the tumor involved the left uterus and proximal cervix, hard, infiltrated left parametrium; the tumor comprises a 4 cm long segment of the pelvic ureter, with thread-like lumen, ant infiltration of the wall;

- microscopic examination: tumor fragments from the left vaginal pouch stained using usual stains revealed proliferative phase endometrial islands, with stroma and endometrial glands showing a heterogeneous pattern; hyperplasia of the endometrial layer, muscular layer hypertrophy and periureteral foci of endometriosis were seen in the left ureter (Figures 5 and 6).

Given the infiltrative macroscopic appearance of the tumor, positive and differential diagnosis required immunohistochemical examination. IHC study revealed an intense reaction to anti-progesterone receptor antibody in stromal cells and glands of ectopic endometrial tissue (Figure 7) and the absence of response in ureteric mucosa (Figure 8). Instead, the estrogen receptor immunohistochemical reaction was weakly positive in ectopic foci and negative in ureteral mucosa (Figures 9 and 10). CK7 and CK18 reaction was intense in both the epithelium of endometrial glands and the urothelium (Figures 11–14); however, CK8 reaction was moderate within the urothelium and absent in endometrial cells.

Figure 5—Endometrial glands and stroma disseminating within the connective tissue of the left parametrium (HE stain, ×100).

Figure 6—Endometrial islands within the adventitia and muscular layer of the left ureter, juxtavesical (HE stain, ×100).

Figure 7—Intense positive reaction to anti-PR antibody in cells within endometriosis foci (Anti-PR immunostaining, ×100).

Figure 8—Ureteral mucosa with negative reaction to anti-PR antibody (Anti-PR immunostaining, ×100).

Figure 9—Weak positive reaction to anti-ER antibody within cells of endometrial glands and stroma (Anti-ER immunostaining, ×200).

Figure 10—Ureteral mucosa showing negative reaction to anti-ER antibody (Anti-ER immunostaining, ×100).
Discussion

According to some authors, endometriosis is a controversial and enigmatic disease [11] because the pathological mechanisms underlying its development and progression are still unknown. Over time, several hypotheses were formulated regarding the development of ectopic endometrium.

A first hypothesis is that of retrograde menstruation, which states that endometrial tissue reaches the peritoneal cavity via the Fallopian tubes by retrograde menstruation [12].

A second theory is that of coelomic metaplasia. This theory postulates that endometriosis develops by metaplasia of cells from the visceral and abdominal peritoneum. Thus, some stimuli (yet unspecified) would induce metaplastic changes in serous peritoneal cells, resulting in endometrial implants [13].

The embryonic residue theory argues that the presence of residual embryonic cells of Müller ducts into the peritoneal cavity could lead to endometrial tissue formation when subjected to appropriate stimuli [14].

Another theory, that of lympho-vascular metastases, suggests that endometrial cells may spread into ectopic sites via lymphatic and blood vessels. This theory could explain distant locations of endometriosis, away from the abdominal cavity.

In our case, the development of a tumor in the left vaginal pouch and left parametrium may be the result of insemination (implantation) of this area with endometrial tissue by retrograde menstruation, or via blood vessels.

It should be noted that in adult women, the endometrium is a very dynamic tissue that undergoes proliferative processes and ovarian regression with each cycle. Within this tissue, adult progenitor stem cells were demonstrated which are likely responsible for this remarkable regenerating capacity. According to some authors [15], these progenitor stem cells may have an increased capacity to generate endometriosis, if they get in other places in the body.

Depending on location and morphological appearance three types of endometriosis were described: superficial peritoneal, ovarian and deep infiltrative endometriosis. The deep infiltrative form usually affects the uterosacral ligaments, rectovaginal space, the upper third of the posterior wall of the vagina, the bowel and urinary tract [16]. The infiltrative form of the urinary tract can be seen in up to 6% of women who have pelvic endometriosis [17]. Our case was a typical case of deep infiltrative endometriosis affecting the urinary tract, causing distal left ureteral stenosis with secondary left ureterohydronephrosis. The peculiarity of our case was represented by the non-specific symptoms, psuedotumoral development and the impossibility to establish a preoperative etiologic diagnosis.
According to some authors [18, 19], ureteral lesions are extensions of retrocervical endometriosis. Depending on the degree of infiltration of the ureteral wall there are two types of ureteral endometriosis: the intrinsic type (infiltration of muscular mucosa of the urothelium), and the extrinsic type (when endometriosis is found only on the ureteral adventitia and is surrounded by connective tissue) [20]. Our case falls within the extrinsic ureteral endometriosis, as the muscle layer and tunica adventitia of the left ureter were affected.

As other authors also state [21], we believe that urinary tract endometriosis, especially that affecting the ureter, is quite serious because its evolution generates secondary hydroureteronephrosis and destruction of the renal parenchyma.

Our therapeutic approach, namely tumor excision by ureteroneocystostomy, led to favorable results, with rapid extinction of symptoms after surgery. Although some authors [19, 22–24] have proposed various surgical treatments depending on the type of extrinsic or intrinsic ureteral endometriosis in patients with ureteral stenosis located close to the ureter–bladder junction and secondary hydroureteronephrosis, the recommended surgical procedure is ureteroneocystostomy [24, 25].

Conclusions

In the case of a patient of childbearing age, with gynecological symptoms and morphofunctional changes of the urinary system, one should always consider the possibility of urinary tract endometriosis.

References


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