CEOG Clinical and Experimental Obstetrics & Gynecology

Endometriosis of the ureteral stump: an entity with severe manifestations

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Summary

A 50-year-old woman on continuous oral estroprogestin therapy and with a history of endometriosis presented with gross hematuria and right reno-ureteral colic pain. Fifteen years before she had undergone total nephrectomy for loss of function of her right kidney due to an ureteral endometriotic nodule resulting in ureteral obstruction. The ureter had not been removed. For the following 15 years-period she had not manifested symptoms or signs of endometriosis. Although imaging investigations allowed to suspect endometriosis of the ureteral stump, urothelial cancer or carcinoma arising in endometriosis nodule could not be excluded. A laparoscopic hysterosalpingo-oophorectomy with the residual ureteral stump removal was performed. Some endometriotic implants on the ureteral stump wall were histologically detected. Proximal ureterectomy should be recommended in patients affected by ureteral endometriosis with a non-functioning kidney since long-term severe complications could derive from the residual stump. A continuous estroprogestin therapy does not totally prevent these complications.

Key words: Endometriosis; Estroprogestins; Nephrectomy; Ureteral stump; Ureterectomy.

Introduction

Urological endometriosis affects women most commonly in the 25-40-year-old age group. In the majority, the bladder is involved, and this accounts for 85% of urological endometriosis [1]. Ureteral endometriosis only accounts for 0.1−0.4% of all cases. This involvement is often limited to one ureter, commonly the left, and can potentially lead to urinary tract obstruction, ureterohydronephrosis, and loss of renal function [2]. Indeed, endometriosis involvement of the overlying peritoneum, uterosacral ligament, or ovary may result in compression of the ureteral wall. Less commonly, endometriosis is intrinsic resulting in a thickened ureteral wall with fibrosis and proliferation of the ureteric muscolaris [3]. At time of diagnosis, about 30% of women with ureteral endometriosis will have 25−50% loss of nephrons and when there is less than 15−20% of total function, a decision for nephrectomy may be indicated [1-3]. In these cases, the benefit of total nephroureterectomy versus total nephrectomy has not been examined. Excision of the entire ureter during nephrectomy for endometriosis is not routinely performed. Specifically, no publication exists addressing risks associated with a retained ureteral stump that has somehow contributed to the pathogenesis of the underlying disease.

The authors present an extreme rare case of ureteral endometriosis of the ureteral stump manifested with a serious symptomatology in a premenopausal woman 15 years after nephrectomy, and the recommendation behind this significant but avoidable complication. Other similar severe cases are also described.

Case Report

A 50-year-old woman with a history of endometriosis presented twice to the emergency department (ED) during a two weeks period with gross hematuria and a right reno-ureteral colic pain. Fifteen years before she had undergone total nephrectomy for complete loss of function of her right kidney due to a ureteral endometriotic nodule resulting in ureteral obstruction in the absence of previous relevant symptomatology for endometriosis. Following surgery, she had been treated with continuous oral estroprogestin therapy and for the following 15 years-period she had not manifested symptoms or signs of endometriosis.

After the first ED visit, she was dismissed with a diagnosis of lower urinary tract infection. During the second ED visit, she was referred to the urologic and gynecologic departments. Standard blood exams revealed a normal residual kidney function and renal ultrasound showed a normal left kidney morphology. Ovaries and uterus on ultrasound showed a regular morphology and an endometrial pattern compatible with a long term use of oral estroprogestin therapy. Magnetic resonance imaging showed a fibrotic tissue involving the back of the uterus and vaginal fornix for 180°, as well as the right uterosacral ligaments. A 2-cm nodule of hemorrhagic endometriosis was visible in the context of this area, demonstrating increased enhancement after contrast medium injection. Ovaries were not involved by endometriosis. The left ureter demonstrated a regular ureteral calibre and course. The right ureter course was shown to be entrapped in the fibrotic area without any other signs. No signs of vegetative masses or irregular borders were also demonstrated in the bladder (Figure 1). Cystoscopy could verify the presence of blood clots on the right ureteral orifice

Revised manuscript accepted for publication April 28, 2016

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLIV, n. 4, 2017
doi: 10.12891/ceog3700.2017

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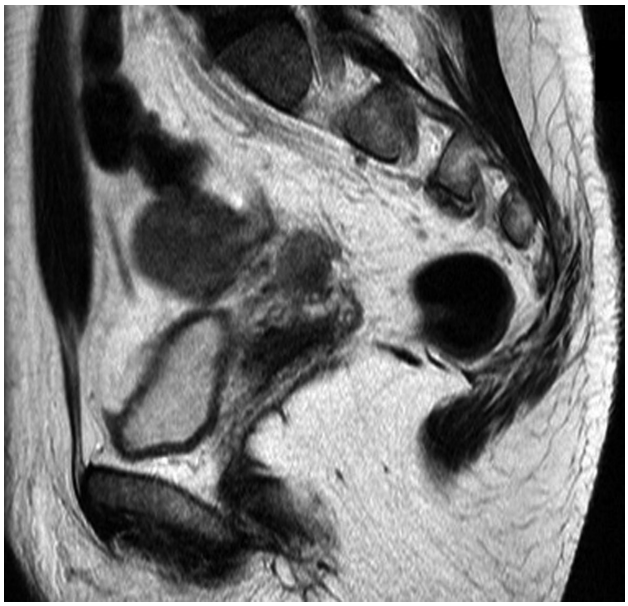

Figure 1. — Sagittal T2-weighted MRI showing a low-signal-intensity area correlated with endometriosis parametrial involvement.

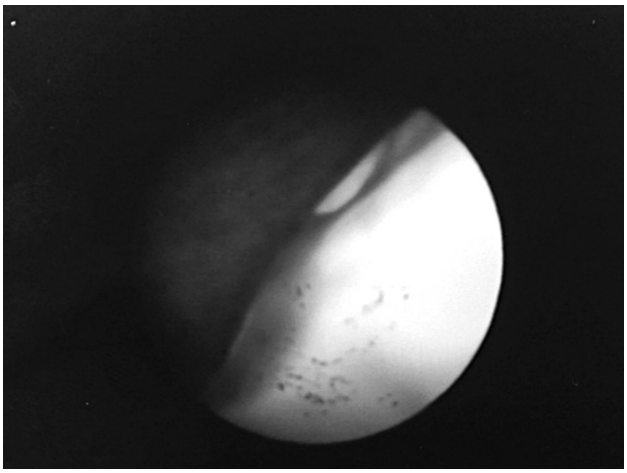

Figure 2. — At cystoscopy, blood is evident on the right ureteral orifice.

thus supporting the ureteral origin of the hematuria (Figure 2). Urine cytology was negative for presence of malignant cells [4]. Although endometriosis of the residual ureteral stump was suspected, differential diagnosis of urothelial cancer or carcinoma arising in the intrinsic endometriosis nodule could not be totally excluded [5]. Given the severe symptomatology, the patient was recommended to stop the estroprogestin therapy and to commence a GnRH-agonist treatment (leuprorelin acetate, 3.75 mg/month). The therapy was also intended to be useful for the diagnostic dilemma since the GnRH-agonist represents an effective treatment for endometriosis but not for non estrogen-dependent affections [5]. During the initial GnRH analog flare-up effect when the symptomatology was still present, the patient was also informed that a definitive diagnosis could be done only by the surgical removal of the right ureter. Indeed, the potential benefit derived from a GnRH analog therapy could represent only an indirect demonstration of endometriosis presence. A shared decision was taken for the surgical approach even if, after 12 days of therapy, hematuria and pain completely disappeared. A laparoscopic hysterectomy and salpingo-oophorectomy with the removal of the residual ureteral stump and of the endometriotic lesion was performed. The patient was discharged after four days without complications. Histologic examination demonstrated the presence of some endometriotic implants on the ureteral stump wall (Figure 3) and no other relevant histopathologic features in the other tissues removed. The woman is now asymptomatic at six months of follow-up with no right flank pain. The patient gave informed written consent to the publication of her data with guarantees of confidentiality. As requested by the local Institutional Review Board (IRB), a notification for the submission of the case to the Journal with the signed informed consent has been sent to the IRB.

Discussion

Due to the rarity of the event, whether ureteral stump left after nephrectomy for endometriosis represents a source of complications, is still to be established [5]. Other severe

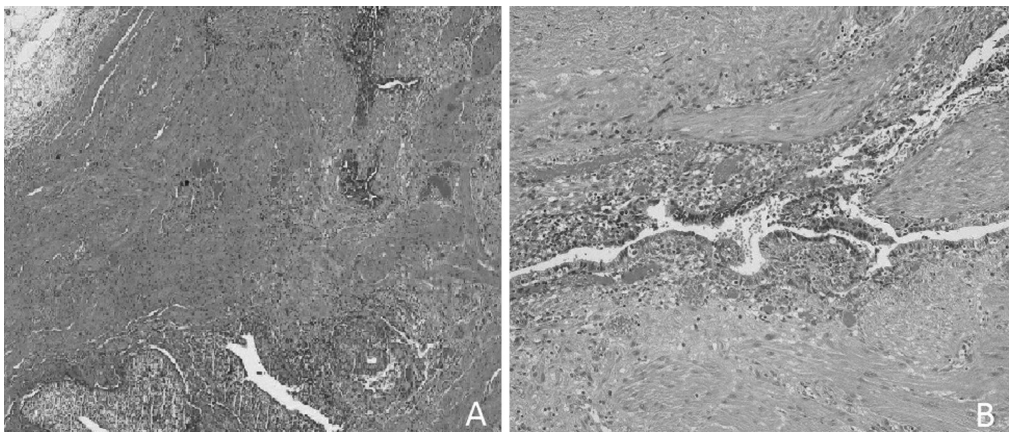

Figure 3. — Typical endometrial type glands and stroma in the ureteral wall at low (A, ×62.5) and high magnification (B, ×125).

manifestations have been described. A case of endometriotic tumor in the ureteral stump has been described in a 49-year-old patient after nephrectomy for endometriosis [6]. A ureter remnant characterized by glandular structures consistent with endometriosis and resulting in hematoureter was found in a 17-year-old woman with a history of nephrectomy as an infant [7]. An incidence of 2.51% has been reported for primary ureteral stump tumors after nephrectomy for benign diseases and this risk increased to 12.5% for long-standing inflammatory diseases [8]. Inflammation represents a typical feature of endometriosis, as the presence of tissue in ectopic sites determines the overproduction of prostaglandins, cytokines, and chemokines [9]. The macrophage NF-κB-dependent pathway is also engaged, with transactivation of responsive gene elements controlling angiogenesis and tissue remodelling [9]. Thus, based on the inflammatory nature of endometriosis, the possibility that the inflammatory environment might represent a constant trigger for risk of transformation of transitional cells cannot be ruled out.

Of note, the patient described in the present report was under a continuous estroprogestin therapy and consequently she has not been menstruating for several years. The reason for which the ectopic endometrium under estroprogestins started to menstruate after 15 years of inactivity is completely unknown. Certainly, the fact that the eutopic endometrium was hypotrophic while the ectopic endometrium was functionally active strongly supports the idea that patterns of estrogen and progesterone receptors were different in the two tissues [10]. Whether receptor changes were consequent to some tissue modifications occurring during the peri-menopausal period is as well completely unknown. In any case, it is important to underline that a continuous estroprogestin therapy, even administered for many years, cannot prevent this severe complication, requiring a reparative surgery and consequently, proximal ureterectomy is advisable in patients affected by ureteral endometriosis with a non-functioning kidney.

In conclusion, in rare cases of endometriosis, the residual stump is symptomatic and its excision is curative. Proximal ureterectomy should be recommended as the standard procedure for patients affected by ureteral endometriosis with a non-functioning kidney. A continuous estroprogestin therapy administered for over ten years does not totally prevent severe complications deriving from the presence of the ureteral stump.

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