Update on Urinary Tract Endometriosis

a report by

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Endometriosis is defined as the presence of active (i.e. responsive to hormone stimulation) endometrial tissue outside the uterine cavity. Three pathogenic theories have been suggested to explain the presence of active endometrium in ectopic sites: the embryonic theory postulates its development from embryonic remnants of the Wolffian or Müllerian ducts; the metaplastic theory postulates the transformation of tissues originating from the celomic mesothelium in endometrial tissue if stimulated by hormonal or inflammatory factors; and the migratory or metastatic theory postulates the migration of endometrial cells through lymphatic or blood flow and their diffusion through retrograde menstruation from the tubes into the peritoneal cavity, by direct extension from the uterine wall by contiguity or after surgical procedures that open the uterine cavity (i.e. Caesarean section). There is some experimental proof of the migration/metastatic theory.[1,2]

Endometriosis generally affects pre-menopausal women and is one of the main causes of hospitalisation in female patients between 15 and 44 years of age,[3] with a prevalence of around 10%,[4,5] although reported figures vary widely depending on the population under study. It has also been reported rarely in post-menopausal women receiving substitutive oestrogenic hormone treatment or affected by ovarian or adrenal tumours with increased secretion of endogenous oestrogens. Recent clinical data suggest that low parity and heavy menstrual cycles are risk factors; however, previous hormone therapies, gynaecological surgery or Caesarean section must also be taken into account as possible risk factors, supporting the menstrual reflux aetiopathogenetic hypothesis.[5] The disease is characterised by high local aggressiveness and risk of recurrence and requires both surgical and hormonal treatment, which is mainly based on luteinising-hormone-releasing hormone (LHRH) analogues, danazol or oestroprogestins. Therefore, although biologically benign, endometriosis may be viewed as a true neoplastic process that can invade and damage all of the pelvic structures, and exceptionally can also migrate outside the pelvis to the skin or the lungs.[6] Moreover, it must be noted that the malignant degeneration of endometriosis in endometriocarcinoma is well recognised.

Although endometriosis can spread in almost any site, and despite the gradual increase in the number of diagnoses over the last few years following the diffusion of explorative laparoscopy, urinary tract involvement is still uncommon (1–5% of all cases of endometriosis) and mainly concerns the bladder and ureter according to a 8:1 ratio.[7,8] There is only anecdotal evidence of kidney or urethral endometriosis. The involvement of the urinary tract shares many features with gynaecological presentations but, at the same time, it has its own peculiar clinical and therapeutic characteristics and requires dedicated urological management.

Bladder and ureteral endometriosis are distinct clinical entities in terms of aetiopathogenesis, symptomatology and possible consequences for renal functionality. This affects the choice of diagnostic and therapeutic approach, which in both conditions should aim to relieve the symptoms and preserve renal function within acceptable morbidity levels. Treatment is still controversial and based on expert opinions because the rarity of this condition makes randomised studies almost unfeasible.

Bladder involvement should be regarded as a typical feature of deeply infiltrating endometriosis, a particular form of endometriosis that penetrates >5mm under the peritoneal surface,[9] since only the cases in which the detrusor is colonised are clinically significant. In contrast, superficial endometriosis of the supravesical peritoneum is usually only an intraoperative finding with no clinical impact. The presenting symptoms of bladder endometriosis are lower urinary tract symptoms (LUTS: frequency, tenesmus, painful micturition) and haematuria, but these characteristics can vary considerably depending on the size and location of the lesion. They are often confused with symptoms of urinary tract infections, which are extremely frequent in young women, as a mean delay to correct diagnosis of up to four to five years confirms.[10] Diagnostic doubts should arise based on the common evidence that symptoms are exacerbated in the pre-menstrual period and in cases of positive medical history for endometriosis or pelvic surgery. In such cases, cystoscopy is highly advisable, especially during the menstrual period, because evidence of a bluish submucosal polycyclic lesion located in the trigone, posterior wall or dome is pathognomonic. A biopsy is required only for doubtful cases. Before explorative laparoscopy, pelvic transvaginal ultrasonography, computed tomography (CT) or nuclear magnetic resonance (NMR) is advisable because

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these imaging techniques can contribute to halting the local spread of the disease and ascertaining the potential involvement of the vesico-uterine septum, which has specific surgical implications.[11]

Hormonal treatment is supported by some authors[12] because it leads to prompt relief of the symptoms, but relapses are common at therapy discontinuation. Moreover, it does not permit pregnancy and the side effects of long-term treatment are heavy. Therefore, the removal of the lesion is generally regarded as necessary to cure the disease. Since transurethral operative endoscopy cannot be radical due to the extramucosal nature of endometriosis,[12–14] the preferred option is surgical resection by partial cystectomy. This fully removes the disease, allowing durable recovery from the symptoms with acceptable morbidity, especially when carried out laparoscopically.[8,11] The technical complexity of the procedure is low for dome locations, which are often isolated and easily identifiable via transperitoneal access. Conversely, as recently reported in a large surgical series,[11] the base location can penetrate the vesico-uterine septum and the procedure thus has to be radical, involving partial resection of the anterior uterine wall. Moreover, such locations are frequently associated with severe, diffuse pelvic endometriosis; in these cases laparotomy access can be preferable because a number of additional (gynaecological or intestinal) procedures could be necessary.[11,14] Nevertheless, over the last few years the potential of laparoscopy has certainly increased and its indications are becoming wider, as the data published by referral institutions show.[15]

Ureteral locations are thought to develop from severe ovarian endometriosis[16] and are much more frequently associated with other pelvic foci than with bladder locations.[14] The pelvic ureteral tract is constantly affected, even though a single case of upper ureteral involvement is reported in the literature;[17] therefore, endometriosis should be included in the differential diagnosis of ureteral strictures in young women. The left side is most frequently affected, which may be ascribed to the sigma creating favourable local conditions for cell seeding retrogradely from the uterine cavity.[18] However, bilateral involvement is not infrequent and is reported in 5–23% of cases.[19] Ureteral endometriosis can take either an extrinsic form (70–80% of cases), affecting the external ureteral tunics through adherence to the surrounding structures or organs, or an intrinsic form (20–30% of cases), when the endometriosic tissue subverts the muscular layer or the ureteral mucosa, sometimes with an intraluminal projection. The response of the ectopic endometrial tissue to hormone stimulation results in cyclical bleeding of the lesion and its subsequent desquamation, necrosis and fibrosis, all of which contribute significantly to the development of ureteral stenosis.

Intrinsic endometriosis may be associated with lateralised pathognomonic macrohaematuria synchronised with the menstrual cycle, but such a presentation is rarely found in daily clinical practice. Indeed, the presentation is often silent (in up to 30% of cases), especially when the prejudice to the upper urinary tract is higher and renal insufficiency or hydronephrotic atrophy is diagnosed. Otherwise, symptoms are aspecifically related to the obstruction of the ureter (renal colic or pyelonephritis; 70% of cases[19]) with no radiological pathognomonic signs, and only in a minority of cases to the menstrual cycle. However, a positive medical history for endometriosis (around 60% of cases[19]) can really help to improve the diagnosis. The difficulties associated with diagnosing ureteral endometriosis are indirectly confirmed by the rate of kidney loss, which is high in historical series (23–47%) and lower but still significant in contemporary ones (10%).[19–21] Therefore, upper urinary tract evaluation by ultrasonography, CT, NMR or urography is always highly advisable during the diagnosis and follow-up of patients suffering from mild to severe pelvic endometriosis.

Medical treatment has been recommended by some authors,[21] sometimes in combination with ureteral stenting, but it is generally considered ineffective since fibrosis, which follows the response of endometriosis to hormone stimulation, contributes significantly to the development of stenosis and consequential loss of responsiveness to hormone stimulation: medical hormone suppression should therefore be regarded as an adjuvant therapy to surgery or as a preventative therapy for relapses when total hysterectomy with bilateral adnexectomy is not performed. Indeed, the need for new surgery following a relapse falls from 27% of cases treated solely by medical therapy to 3% of cases treated by hysterectomy with bilateral adnexectomy.[22] The young age of the patients, who often wish to have children, means that this option is not always easy to accept.

The degree of recovery of renal function through urinary drainage (nephrostomy or ureteral stenting), if necessary, can help to indicate reconstructive surgery versus nephrectomy. Elective laparoscopic ureterolysis should be chosen only for minimal, extrinsic and non-obstructive ureteral involvement because it is not sufficiently radical in cases of wider involvement of the ureter or intrinsic endometriosis, which is hard to determine without histological examination.[23,24] Conversely, when the urinary flow is obstructed and a dilation of the upper urinary tract is evident, surgical resection represents a more suitable option because it removes both the disease and the surrounding fibrosis. Urinary tract continuity can be restored by ureteral termino-terminal anastomosis only when the distal ureteral tract shows no signs of endometriosis. In our opinion, the safest way to restore urinary continuity is by ureteroneocystostomy, which does not use the ureteral tract distal to the site of endometriosis – which is marked by a higher risk of recurrence – and warrants tension- and disease-free anastomosis. Moreover, this is the preferred procedure in cases of relapse of ureteral endometriosis.[19] Due to the complexity of the operation and the frequent necessity of performing additional gynaecological or intestinal procedures, laparotomic access may be the best though not the easiest option, even though the feasibility of laparoscopy is known.[25] ■

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