Urinary Tract Endometriosis: A Review of Literature

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Abstract

Objective: Deep endometriosis (DE) is the most severe form of endometriosis. Bowel and urinary tract are the most common sites of intrapelvic DE. Urinary tract endometriosis (UTE) mainly involves the bladder and the ureters. The two mostly accepted theories explaining the pathophysiology of UTE are the “Retrograde Menstruation Theory” and the “Müllerian Remnants Theory”. The purpose of this paper is to provide a review of literature on the UTE, a rare form, affecting only 1–6% of patients with endometriosis. Mechanism: A literature review was conducted using keywords specific to UTE and DE to identify peer-reviewed, original research articles published between 1996 and 2024. Findings in Brief: When the bladder is involved, the patient presents lower urinary tract symptoms. Ureteral endometriosis is usually asymptomatic, thus delaying early diagnosis and efficient treatment leading to cases of chronic ureteral stricture. Clinical history and examination as well as questionnaires play an important role in guiding the clinician. Diagnostic modalities include conventional imaging such as ultrasonography and magnetic resonance imaging (MRI) as well as invasive techniques such as cystoscopy. As for all endometriotic lesions, definitive diagnosis should be confirmed by histopathology. Treatment modalities include medical hormonal treatments or surgical treatment. There are a multitude of surgical techniques that are more or less invasive depending on the location and the extent of the lesion. Conclusions: UTE, an underdiagnosed form of endometriosis, and specialists should be aware of this important entity, due to the serious health implications for women.

Keywords: urinary endometriosis; deep infiltrating endometriosis; urinary symptoms; surgical treatment; medical treatment

1. Introduction

Endometriosis is a debilitating gynecological condition characterized by the presence of endometrial-like tissue outside the uterus, leading to significant clinical challenges. Although commonly found within the pelvic cavity, endometriosis can also manifest in extrapolvic sites such as the diaphragm [1] and more rarely, the umbilical region, inguinal area, and around nerves and organs like the sciatic nerve, liver, and pancreas [2]. The condition can be categorized based on lesion localization and depth of infiltration into three types: superficial, ovarian, and deep endometriosis (DE) [3]. DE, specifically, involves the endometrial-like tissue on or under the peritoneal surface [4], with a contentious definition that has been termed adenomyosis externa by Gordts et al. [5], characterized by large, often solitary lesions.

Urinary tract endometriosis (UTE), a subtype of DE, includes bladder endometriosis (BE) and ureteral endometriosis (UE), both associated with severe pelvic pain and significantly impaired quality of life [6]. BE is defined by the infiltration of the bladder’s detrusor muscle by endometrial glands and stroma, typically multifocal and affecting the bladder’s trigone and dome [7]. UE involves either direct endometriotic invasion of the ureters or indirect compression by associated fibrosis, potentially leading to intrinsic or extrinsic ureteral obstruction [8].

Diagnosing UTE poses significant difficulties due to its often-subtle symptoms and the complex nature of its presentation, which can mimic other urological conditions. Standard imaging techniques may fail to detect the extent of the disease or differentiate it from other pelvic pathologies, necessitating more invasive procedures like laparoscopy for definitive diagnosis. Treatment of UTE is equally challenging; it requires a multidisciplinary approach that balances surgical intervention with the preservation of renal function and fertility. Surgical treatment, particularly for ureteral endometriosis, involves risks of significant complications and recurrence of the disease.

This review will explore the diagnostic complexities and therapeutic challenges in managing UTE, emphasizing the need for improved diagnostic tools and more effective, less invasive treatment options. It will examine the latest advancements in imaging and surgical techniques, and discuss the emerging research on medical management strategies that could offer alternatives to surgery. The review aims to highlight critical gaps in current knowledge and suggest directions for future research to enhance patient outcomes in UTE.

2. Epidemiology

While endometriosis affects almost one-fifth of reproductive aged women, DE prevalence is 1% in reproductive aged women, and 15 to 20% of patients with endometriosis [9]. UTE, a rare entity affecting only 0.3 to 12% of pa-
patients with endometriosis [8], is more frequent among patients with DE with an incidence of 16.4% to 52.6% [10]. UTE mainly involves the bladder (70–85%), the ureters (9–23%), the kidneys (4%) and the urethra (2%) [11]. The peak age of incidence is 30–35 years.

As for all rare diseases, most of the studies consist of small retrospective cohorts and are performed in referral centers leading to a divergence between the published and the real occurrence. The lack of prospective trials and the short term follow up prevent us from establishing standardized diagnosis and therapeutic approaches.

BE is usually associated with other forms of pelvic endometriosis (superficial peritoneal, ovarian endometriomas, adhesions and extravasical DE). UE is rarely isolated; it is associated with ovarian endometriomas in half of the patients with a predilection to the left side [12].

Inversely, literature suggests that the presence of rectovaginal endometriosis multiplies the risk of developing UE by more than ten if the largest nodule is >3 cm [13].

3. Methods

A literature review was conducted using keywords specific to UTE and DE to identify peer-reviewed, original research articles published in English between 1996 and 2024.

4. Pathophysiology

When DE lesions invade the urinary tract (bladder, ureters or kidneys), it results in UTE. Similarly, to DE, the pathogenesis is still unclear. Non-UTE lesions can also remotely cause UTE like symptoms without an actual involvement, this can be caused by an inflammation or an infiltration of the hypogastric plexus resulting in an involvement of sympathetic and parasympathetic lesions [14].

The two mostly accepted theories are “Retrograde Menstruation Theory” and “Müllerian Remnants Theory”.

“Retrograde Menstruation Theory” suggests a retrograde flow of endometriotic tissue through the fallopian tubes. The asymmetrical distribution of endometriotic lesions is a major argument supporting this theory. The fact that most of DE lesions are located in the decidual parts of the pelvis, particularly the involvement of the bladder in UTE, is explained by the gravitational effect on regurgitated endometrial tissue and the presence of the recto sigmoid colon. This favors adhesion of sloughed endometrial debris on the left pelvic wall and peritoneum followed by inflammation and fibrotic nodules formation. Other anatomic observations supporting this theory are the absence of BE in patients with retroverted uterus, and the mode of progression of lesions from the bladder serosa inwards, sparing the mucosal layer most of the time [15].

“Müllerian Remnants Theory” or the “Müllerianosis” hypothesis relies on the histology of DE and UTE lesions to hypothesize that DE lesions are in fact adenomyotic lesions secondary to embryonic remnants of the Müllerian ducts and originating in the retroperitoneum. Thus, the presence of fibrotic tissue and smooth muscle cells surrounding the strains of gland and stroma in these lesions [16].

This theory may explain the presence of DE without concomitant peritoneal involvement which cannot be explained by the Retrograde Menstruation Theory.

Nisolle and Donnez [3] in 1997 suggested that DE, peritoneal and ovarian endometriosis are separate entities with different pathogenesis, with the DE presenting more invasive mechanisms.

Other theories include the “Hematogenic or Lymphatic Spread” of specific cell-free endometrial products capable of inducing the metaplasia of undifferentiated mesenchyme into endometrial epithelium and glands [17]. This can be responsible for distant implants and probably explaining intrinsic UE or isolated DE. The “Iatrogenic Theory” states that history of pelvic surgery predisposes the dissemination of endometrial cells in the abdominal cavity [17]. “The forgotten menstruation”, according to Brosens et al. [18], states that 5% of neonates have neonatal menstruation during the first week after birth which can play a role in the pathogenesis of endometriosis. “The metaplasia theory” was suggested because some women with Mayer–Rokitansky–Küster–Hauser syndrome developed endometriosis. “The genetic and epigenetic theory” since endometriosis is a hereditary disease with the prevalence increasing from 6 to 15% in first degree relative and depending on the severity of the disease [5].

5. Clinical Presentation

In reproductive age patients, the presence of dysmenorrhea, dyspareunia and non-cyclic pelvic pain should evoke DE.

Endometriosis rarely involves both the bladder and the ureters. When the bladder is involved, the posterior wall is usually infiltrated [19] and the patient typically presents lower urinary tract symptoms (LUTS) such as frequency, dysuria, hematuria, urgency and bladder pain and it is frequently misdiagnosed for cystitis [19]. These symptoms are generally cyclic and worsen during menstruation but may as well be constant. As a matter of fact, hematuria is frequent because the lesions rarely infiltrate the mucosal layer. Bladder involvement rarely results in severe sequelae especially that this is a very symptomatic entity leading to investigation and early treatment. Ureteral dilation and renal failure could occur only if the ureteral tract is blocked by the endometriotic lesion [20].

UE, as well, is usually asymptomatic, thus delaying early diagnosis and efficient treatment. This may lead, in rare cases, to chronic unnoticed ureteral stricture resulting in renal failure or silent kidney loss. When symptomatic, UE causes non-specific symptoms such as dysmenorrhea, pelvic pain, flank pain, gross cyclical hematuria or pelvic mass [21].
Frequently, UTE is diagnosed incidentally during laparoscopy for extensive endometriosis.

6. Diagnosis

6.1 Clinical History & Examination

In patients presenting possible deep endometriotic lesions, physical examination should include pelvic, abdominal, vaginal and rectal examination. Vaginal examination is essential for evaluating patients with DE and especially for detecting BE [22]. A palpable nodule or a thickened area along the anterior vaginal wall may be felt and it is painful most of the time. The combined rectovaginal examination helps assessing the parametrial involvement and the palpation of deep infiltrating nodules in the pouch of Douglas or in the uterosacral ligaments associated. Since physical examination in UTE is usually normal, this diagnosis should be evoked if DE nodules are palpated on rectovaginal exam [23].

Differential diagnoses should be considered in patients with suspected UTE. When patients present lower urinary tract symptoms, the physician should consider BE but should also rule out infectious or interstitial cystitis, overactive bladder, bladder carcinoma, bladder pain syndrome and chronic urethral syndrome [24]. When UE is suspected, the physician should also consider other causes or intrinsic or extrinsic ureteral stenosis such as stones, primary or metastatic neoplastic lesions, retroperitoneal adenopathy, idiopathic retroperitoneal fibrosis and infection [21]. Imaging techniques should be used to rule out these entities.

6.2 Questionnaires

The modified American Urologic Association Symptom Index (AUASI) questionnaire is a 7-itemed questionnaire developed in 2007 to evaluate specific catamenerial symptoms, and was proven effective in identifying patient with BE [25].

The Bristol Female LUTS is another questionnaire validated in assessing the variety of LUTS symptoms associated with DE and UTE, as well as the follow up of patients after treatment. It is made of 3 domains: symptoms, sexual function and quality of life questions [26].

6.3 Imaging

6.3.1 Ultrasonography

Ultrasonography, a non-invasive, cost effective and reproducible diagnostic tool is recommended for systematic use in assessing women with DE [27]. In BE, it evaluates the location and size of lesions and measures the distance between the lesion and the ureteral orifices. When the bladder is full, endometriotic lesions appear as filling defects of the posterior wall with a variable protrusion into the lumen of the bladder. Bladder lesions are usually spherical, or comma shaped with regular contours. When contours are irregular, malignancy should be ruled out. Barra et al. [28], detected nodules with a mean diameter of 20 mm ± 9.1 mm. On colored Doppler, bladder endometriotic lesions present minimal to moderate internal blood flow. Abdominal ultrasonography does not visualize the entire ureteral course, making it impossible to directly detect ureteral endometriotic lesions, but it can evaluate the presence and the severity of hydronephrosis thus indirectly diagnosing UE and obstruction [29].

Both abdominal and transvaginal ultrasound (TVUS) may be used to detect vesical endometriotic lesions, with TVUS being the preferred method and should be used as first-line.

During ureteral dilation assessment, the location of the stenosis and its distance from the bladder should be evaluated as well as the ureteral diameter upstream and downstream the obstruction [21]. A ureteral diameter of ≥6 mm was associated with ureteral dilation [30].

With color Doppler, TVUS was found superior to cystoscopy in detecting BE nodules partially affecting the detrusor muscle [31] and at least as effective as the magnetic resonance imaging (MRI) in diagnosing and planning the treatment of BE. It is suggested that it may improve the assessment of endometriotic nodules, their sizes, volume and infiltration of the bladder wall [32]. Color Doppler can also help to evaluate Relative Jet Frequency which can be a good indicator of obstruction if reduced (<25%) [33].

Intraluminal ultrasonography is an invasive exam currently under evaluation, consisting of introducing a catheter-based ultrasound probe in the ureters, to assess the ureteral lumen, wall and peri-ureteral tissues [21].

6.3.2 Magnetic Resonance Imaging

MRI is the second-line imaging technique used for the evaluation of UTE. In BE assessment, it offers a higher resolution, better delineation of the bladder wall layers, better tissue characterization and better multiplanar analysis when compared to non-3D ultrasonography [34].

In MRI, BE lesions may manifest as localized or diffuse wall thickening associated with signal intensity abnormalities. Typical features are low signal on T2 weighted images with intermediated signal on T1 weighted images and spots of high signal on T1 and T2 weighted images representing hemorrhagic content. Systematic reviews showed no advantage for 3.0-T MRI or for Gadolinium-enhanced imaging. MRI reaches an 88% sensitivity and 99% specificity and 98% diagnostic accuracy for BE diagnosis [20].

It is the best imaging for UE assessment; lesions appear as solid nodules with spiculated margins surrounding the ureter and showing low intensity signal on T1 and T2 weighted images. Concurrent retractile adhesions appear as peri-ureteral hypo-intense linear foci with angular deviation. In cases of extrinsic endometriosis, the loss of fatty interface between the nodule and the ureter suggests ureteral infiltration. MRI showed to be more sensitive but less specific than laparoscopy in identifying intrinsic ureteral involvement [35].
A new pre-operative (MRI, TVUS) classification, #ENZIAN, can be used to describe DE lesions including UE [36].

Since MRI is more expensive but not superior to TVUS performed by experienced physicians, it should not be used as a first line diagnostic tool [34].

6.3.3 Other Imaging

Intravenous and retrograde pyelography were traditionally used to evaluate women with suspected UTE but have been replaced with MRI [37].

Renal scintigraphy should be performed in cases of severe hydronephrosis to assess the renal function and plan surgical treatment in association to nephrectomy or kidney preservation. A kidney is considered salvageable if preoperative glomerular filtration rate is more than 10%.

6.3.4 Cystoscopy

It is commonly performed in the outpatient setting to assess the urethra, bladder inner wall and ureteral orifices. Even in the presence of BE, cystoscopy findings are usually normal due to the sparing of the mucosal layer [24]. The lesions may appear as adenomatous nodular masses with varying shades of colors (red, blue, brown or black) [38]. Cystoscopy should be planned immediately before or during menstruation to best visualize the nodules when they are enlarged and congested. It helps planning the surgery by estimation of the distance between the nodules and the ureteral openings [7], especially when no feasible with TVUS, should also be used to rule out malignancy [24].

6.3.5 Urodynamics

Data in the literature evaluating the role of urodynamics in assessing patients with UTE and DE is very scarce. Patients present typically higher bladder sensation, painful bladder filling, voiding symptoms, urgency, frequency and bladder pain. Its use is not recommended in clinical practice and is currently limited to scientific research purposes [39].

7. Histology

As for all endometriotic lesions, definitive diagnosis is confirmed by histopathology. In contrast with surgery, histology can precisely assess the depth of invasion. The two main pathological subtypes are extrinsic and intrinsic endometriosis. Extrinsic endometriosis only invades the ureteral adventitia or surrounding connective tissue, while intrinsic endometriosis directly infiltrates the muscularis, submucosa and rarely the mucosal layer. The two subtypes can sometimes coexist [40].

When evaluating UE, two patterns were described: an endometriotic pattern corresponding to endometrial glands or stromal cells seen in the wall of the ureters or in the periureteral space and a fibrotic pattern made of fibrotic tissue only [41].

The endometriotic pattern is more prevalent and associated with the presence of ureteral obstruction and hydronephrosis. The fibrotic pattern is associated with the rectovaginal nodules which might be related to the inflammatory process caused by a DE close to the ureters [3,41].

8. Treatment

DE involves mainly the posterior compartment of the pelvis and is frequently associated to UTE and causes LUTS. Treatment modalities for DE/UTE include medical and surgical treatments. Medical treatment can be chosen for asymptomatic women without hydronephrosis. Persisting symptoms along with ureteral obstruction and hydronephrosis require surgery. Compared to minimally invasive surgery (MIS), laparotomy is associated with poorer visualization of small infiltrating lesions resulting in larger incisions, increased blood loss, increased post-operative pain and recovery time. Laparoscopic management of severe extra genital endometriosis was published in the 1980s. Surgical treatment of UTE is still not very common due to its underdiagnoses and failure to identify endometriotic lesions by unexperienced surgeons. Furthermore, most of the general, urology and gynecology surgeons are not trained to treat DE.

8.1 Medical/Hormonal Treatment

Combined hormonal contraceptives and progestogens are the first line therapies for patients with DE and UTE and have proven efficacious in the treatment of different DE including UTE [42].

Recent data suggest that symptoms and lesions may not respond completely to medical therapies because of the desmoplastic reaction within the tissues resulting from repetitive bleeding and resorption of menstrual debris [43].

Gonadotropin-releasing hormone agonists (GnRH-as): leuprolide acetate and danazol are second line therapy because of the hypoestrogenism related adverse effects ranging from hot flashes, sleep disturbances, irregular vaginal bleeding, weight gain and vaginal dryness. Furthermore, once the treatment is discontinued, symptoms tend to recur [44].

Aromatase Inhibitors can be prescribed to patients refractory to conventional therapies in the setting of clinical research [45].

Women treated medically must undergo regular clinical examination, ultrasonography and laboratory testing to monitor renal function, disease progression, and necessity for surgery [24].

Medical treatment is contraindicated in patients with ureteral obstruction because of the risk of disease progression and increased severity of ureteral stricture and hydronephrosis, thus surgery is the standard approach for mild to severe UE. However, post-operative medical treatment may be useful in preventing recurrence of endometriosis.
8.2 Surgical Treatment

The aim of surgical treatment is to entirely resect the UTE lesions, relieve related symptoms, ureteral obstruction, preserve renal function and avoid recurrence. The surgical approach should be tailored to the extent of the disease, the renal function and the surgeon’s skills, thus the major importance of preoperative accurate mapping of all lesions and their distance to the ureteral meatuses [46].

MIS remains the recommended approach because laparoscopy has demonstrated its superiority to laparotomy for treating UE [21].

During surgery for UTE, identification of the ureters is essential to avoid iatrogenic injury and to evaluate for possible ureteral involvement [29]. Surgical options for BE include trans urethral resection (TUR) and partial cystectomy [24]. For UE, surgical options include conservative ureterolysis and radical approaches such as ureterectomy with an end-to-end anastomosis, ureteroneocystostomy or nephroureterectomy.

Conservative treatments like ureterolysis should be limited to patients with minimal ureteral involvement. When ureteral endometriosis does not cause stenosis and hydronephrosis, ureterolysis with or without ureteral shaving may be considered. The indication for ureteroneocystostomy should be the presence of moderate/severe hydronephrosis due to ureteral obstruction.

The risk of conservative treatment is mainly stenosis with a risk up to 12 to 20% of patients who underwent ureteroureterostomy and ureterolysis, respectively [12].

8.2.1 TUR Surgery

TUR is a proposed technique to treat BE without enough evidence supporting its efficacy or safety. Since BE develop from the bladder serosa inwards, complete excision of endometriotic lesions is impossible by trans urethral resection without exposing the patient to increased risk of bladder perforation or short-term recurrence in case of incomplete resection [47].

8.2.2 Segmental Bladder Resection

Partial cystectomy is a bladder conserving option proven effective with excellent long-term results in controlling symptoms and lowering the risk of recurrence. It consists of partial bladder resection for detrusor endometriosis performed via laparotomy or MIS with or without robotic assistance. Suturing the bladder defect can be performed in 1 or 2 layers, continuous or interrupted sutures [19].

Ureter catheterization is not systematic and depends on the distance between the caudal margin of the lesion and the inter-ureteric ridge; if the distance is less than 2 cm, catheterization is advisable. But in case of recurrent endometriosis, lesions tend to be closer to the ureteral meatuses, thus catheterization is mandatory.

This surgery is considered as simple and safe with fast healing of bladder sutures and low risk of vesical fistula if prolonged drainage is performed [46].

Some surgeons combine the TUR surgery with the segmental bladder resection to overcome the limitations of both techniques by allowing complete resection of the nodule (contrary to the TUR) without any accidental excision of healthy tissue [48].

8.2.3 Ureterolysis

Safe and efficient, it aims to mobilize and free the ureter from the surrounding endometriosis and fibrosis. It is indicated in patients presenting minimal extrinsic non-obstructive UE, but it is also performed in cases of mild to severe obstruction in order to clearly visualize the stenotic area [13].

Intra-urethral injection of near infra-red Indocyanine Green improves the visualization of ureters, therefore preventing iatrogenic injuries [49]. Moreover, it helps assess ureteral perfusion after conservative surgery.

8.2.4 Endoscopic Excision

Retrograde ureteroscopy is a minimally invasive procedure allowing effective excision in cases of polypoid endometriotic lesions obstructing the ureteral lumen. It is not efficient for patients presenting deep ureteral wall fibrosis and periureteral connective tissue fibrosis [50].

8.2.5 Ureteral Stentings

Literature shows that the risk of ureteral injury during laparoscopic surgery is 1.5% for patients having UE versus 21% for patients presenting hydronephrosis [51]. Ureteral stenting serves mainly to release the obstruction, improve renal function, facilitate ureteral identification, guide ureterolysis and prevent ureteral injury as well as preventing postoperative ureteral obstruction due to the local inflammation and edema.

8.2.6 Partial Ureteral Wall Resection

Described by Nezhat et al. [52] and Ghezzi et al. [53] in 1996 and 2007, respectively with no major complications reported. But this technique should undergo further evaluation [52].

8.2.7 Ureteral Resection with End to End Anastomosis

This technique allows complete excision of the involved segment of the ureter and its surrounding fibrosis. Anastomotic breakdown or anastomotic stricture are the most described complications. By preserving the distal part of the ureter and the vesico-ureteral junction, patients are at a higher risk of recurrent endometriosis [54]. This technique is indicated in patients presenting severe segmental ureteral obstruction limited to the middle or upper parts of the ureter.
8.2.8 Uretero-Neocystotomy

This technique is indicated for cases of extensive ureteral involvement, lesions close to the bladder insertion and lesions extending over a long pelvic ureteral segment making ureterolysis and end to end anastomosis impossible. It consists of excision and reimplantation of the ureter into the bladder, bypassing the endometriotic zone and its surrounding fibrosis. Depending on the length of the resected area, a psoas bladder hitch or a Boari flap may be required to insure tension free anastomosis [14].

Literature shows a significant improvement of the symptoms with this procedure, a low rate of recurrence at 24 months (1.2%) and a low rate of major complications (4.4%) [21].

8.2.9 Nephrectomy

Chronic gradual ureteral stenosis can ultimately lead to loss of renal function and eventually silent kidney loss (End Stage Renal Disease). This can be evaluated by kidney scintigraphy in patients presenting UE related hydronephrosis [13]. Nephrectomy is indicated in patients with renal functions less than 15%, suffering from flank pain, kidney stones, renovascular hypertension and recurrent urinary tract infection or pyelonephritis [55].

9. Conclusions

UTE is rare but frequently documented in the context of DE. Careful preoperative planning should be scheduled to diagnose an advanced-stage disease defining the depth, severity and site of these lesions.

Medical management could be proposed in a subset of patients, however, the minimally invasive surgical treatment remains associated with a long-term optimal outcome.

Author Contributions

HEH: Data collection, manuscript writing. RS: Data collection, manuscript editing. EF: Interpretation of Data, manuscript editing. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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