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PATHOPHYSIOLOGY AND MANAGEMENT OF URINARY TRACT ENDOMETRIOSIS

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Endometriosis: presence of endometrial glands and stroma outside of the uterine cavity

Predominantly affects the pelvic reproductive organs but also outside of the reproductive organs

Most common sites of extragenital endometriosis are intestine and urinary tract.
Theories:

1. Retrograde menstruation
   - 90% of women have retrograde menstruation, only 10% develop endometriosis
   - Further steps are necessary for endometrial cells to become endometriosis implants
   - Affects distal > proximal ureter
   - Affects left > right hemipelvis due to sigmoid colon
2. Altered immunity in the pathogenesis of endometrial implants

- Higher incidence of endometriosis in women with autoimmune disorders such as SLE, thyroid disease, RA, Sjogren’s syndrome, asthma, eczema
- Dysregulation of immune system might prevent normal clearance of ectopic endometrial cells, facilitating their implantation
3. Coelomic metaplasia

- Normal peritoneum transforms into endometriosis stimulated by hormonal or immunological factor
- Residual embryonic Mullerian rests stimulated by endogenous or exogenous estrogen exposure transforms into endometriosis
4. Benign metastasis
   - Endometrial cells from within the uterus flow through lymphatic or hematological circulation and spread to distant parts of the body

5. Iatrogenic
   - In port site and scar site
   - $\leq 50\%$ of bladder endometriosis found in women with prior cesarean

6. Genetic
   - 7% risk of endometriosis in first-degree relatives
Deeply infiltrating endometriosis (DIE) expresses invasive mechanisms including matrix metalloproteinases and activins more highly than in ovarian and superficial peritoneal endometriosis.
Most common signs:
- Chronic pelvic pain
- Infertility

1-6% of women previously diagnosed with endometriosis have urinary tract endometriosis.

Most common affected organs:
- Bladder > ureter > kidneys (40:5:1)
Ureteral Endometriosis

- Usually silent in ≥50% of patients
- Can be intrinsic or extrinsic
- Can cause silent kidney loss if resulting ureteral stricture is untreated and reaches critical severity level
- Symptoms: pelvic/back pain, cyclic, colicky flank/abdominal pain, dysuria, gross hematuria, uremia, pelvic mass, dysmenorrhea, dyspareunia
Extrinsic disease:
- Caused by endometriosis external to ureter that compresses the ureter from fibrosis of overlying peritoneum or uterosacral-cardinal complex
- Large endometrioma adherent to pelvic sidewall and compresses the ureter

Intrinsic disease:
- Accounts for 20% of ureteric endometriosis
- Involves ureteral wall, muscularis, or mucosa
- <15% of patients with cyclical hematuria
- Much more common with other deeply infiltrating disease, such as infiltration of uterosacral-cardinal complex and rectovaginal septum
Ureteral Endometriosis

Extrinsic ureter endometriosis

Intrinsic ureter endometriosis
Ureteral Endometriosis Diagnosis

- Imaging:
  - CT
  - MRI
  - Intravenous pyelogram (IVP)
  - Ultrasonography

- Ultrasonography:
  - Well-trained sonographer is able to examine bilateral ureters in 93% of scans
  - Measure degree of hydrourerter and location of constriction point
Ureteral Endometriosis Diagnosis

- **IVP:**
  - Also useful after treatment to evaluate ureteral continuity
  - If IV contrast is contraindicated, obtain retrograde pyelogram
  - Can predict intrinsic disease

- **MRI:**
  - Often overestimates frequency of intrinsic disease
  - Useful to evaluate degree of circumferential involvement of disease along the ureter
  - When endometriosis surrounded \(<180^\circ\) of ureter circumference, \(<10\%\) were diagnosed with intrinsic endometriosis
Ureteral Endometriosis Treatment

- Aim: to liberate the ureter from endometriosis, preserve renal function
- A kidney is considered salvageable if >10% of normal GFR remains.
- If preoperative renal function is <10%, nephrectomy is recommended.
- Laparoscopy with or without robotic assistance by a trained minimally invasive surgeon or urologist is recommended.
Ureteral Endometriosis Medical Management

- Not recommended due to disease progression and increased incidence of recurrence
- Can be considered for mild disease
- Contraindicated when ureteral obstruction or hydronephrosis is present
- Goal: to induce regression of endometrial tissue, prevent endometriosis proliferation and ureteral obstruction
Ureteral Endometriosis
Medical Management

- GnRH analogues (Leuprolide acetate)
- Danazol
- Combined contraceptives
- Progestin
- Aromatase inhibitors (Letrozole)
Ureteral Endometriosis Surgical Management

- Standard approach
- Bosev et al. study
  - 96 patients underwent laparoscopic ureterolysis, endometriosis excision/ablation
  - 2 patients were determined to have intrinsic disease, underwent ureteral resection and ureteroneocystotomty
  - 6 patients had Double-J stent to prevent ureteral obstruction/leakage caused by extensive ureterolysis
- Follow-up:
  - 1 patient with ureteroneocystotomty had partial ureteral stricture at 3 months postop, was dilated with Double-J stent
  - No urinary tract recurrence during 2-50 month follow-up period
Mu et al. study

- 23 patients with ureteral endometriosis
- 5 patients with mild disease were treated with ureterolysis
- 18 patients with greater degree of disease were treated with segmental ureteral resection and/or ureteroneocystotomy
- >90% patients had pain relief after laparoscopic surgery
- All had fewer signs of hydronephrosis on postop ultrasonography at a median of 3 years.
Camanni et al. study

- 80 patients treated with laparoscopic ureterolysis
- 95% had complete removal of ureteral endometriosis with high satisfaction rate at 6, 12, 24 months follow-up
- 9% had recurrence
- Postop complications most common when ureteral endometriosis involved >4 cm of ureteral length
Our approach:
- Laparoscopic ureterolysis when ureteral endometriosis is observed
- CO2 laser and hydrodissection as laser beam is unable to penetrate fluid
- Peritoneal incision is made in unaffected area (usually at pelvic brim) using laser to create 0.5 cm opening
- Then LR or NS solution is injected into this space by inserting the suction irrigator tip into peritoneal opening
- Advantage: to minimize risk of laser beam penetrating underlying tissue, minimize the depth of invasive surgery and prevent thermal lateral spread
- A circular line with 1-2 cm margin is made to excise the lesion
- CO2 laser is used to peel away peritoneum while grasping it under tension
- Suction irrigator is used as a backstop to the laser
- Excise peritoneal fibrotic lesions completely when possible
- Alternative: electrocautery, harmonic scalpel, Plasmajet, monopolar needle or scissors
Laparoscopic ureterolysis is adequate in 90% of cases.

If proximal dilatation persists, ureteral resection is indicated.

Anastomosis of ureter to bladder must be free of tension.

Short distance to bladder -> ureteroneocystostomy ± psoas hitch

Larger distance -> Boari flap, ileal interposition, autotransplantation

Endometriosis of middle or upper third of ureter -> ureteroureteral anastomosis
Donnez *et al.* study

- 18 patients had laparoscopic ureterolysis with similar technique to ours
- 2 patients needed ureter resection with intrinsic disease
- 6 patients had Double-J stent to facilitate ureterolysis
- 6 patients had remaining fibrotic ring around the ureter after ureterolysis, raising suspicion for intrinsic disease.
  - 4 required incision of adventitial sheath to release the stricture
  - 2 required ureteral resection
Uccella *et al.* study

- 109 patients treated laparoscopically similar to our and Donnez *et al.*’s technique
- DIE was treated with bilateral ureterolysis
- 3.7% required ureterolysis to excise endometriotic nodules from ureter
- Retroperitoneum was opened, then bipolar grasping forceps and scissors were used to dissect and excise all fibrotic and endometriotic nodules to free the ureter
- IV Methylene blue was injected to prove integrity of urinary tract
- If the ureter was skeletonized, a ureteral catheter was placed and left for 2-3 months to avoid late fistula
Ureteral Endometriosis Follow-up

- Monitor for recurrence with annual physical exam, symptoms review, ultrasound, renal function tests
- IVP, CT, or MRI with suspected recurrence
- Postop suppressive therapy with progestin (IUD/pill), COC, GnRH agonist, or aromatase inhibitor
Bladder Endometriosis

- Usually symptomatic
- DD: UTI, interstitial cystitis, bladder stone, neoplasm
- If endometriotic lesion implants on top of ureteral orifice, it can lead to hydroureter and kidney failure.
- Symptoms: hematuria, suprapubic pain, dysuria, urinary frequency, elevated intravesical pressure
Thorough history, urine culture

Ultrasonography and MRI have high specificity unless lesions <3 cm

- MRI unlike ultrasonography is unable to measure distance between endometriotic nodules and ureteral meatus, which is important to counsel patients on the risk of ureteral reimplantation
- 3D ultrasonography and Doppler may improve sensitivity

Cystoscopy can identify DIE and help determine need for ureteroneocystotomy if lesions are <2 cm from ureteral opening

IVP can show filling defect
Ultrasonography image of DIE at the bladder base
Cystoscopic view of DIE of the bladder
Temporary solution, unless asymptomatic
Must be maintained through menopause
Preferred if endometriosis lies within or very close to trigone, as excision can cause postop neurogenic bladder and retrograde bladder reflux due to disruption of innervation and blood supply
ER and PR are expressed in glands, stroma and smooth muscle of the bladder endometriosis.
Synthetic estrogens and progestins induce hypoestrogenic state causing atrophy and decreased inflammation leading to decreased prostaglandins and cytokines release, which are the cause of pain fibers overstimulation.
Symptoms recurrence when discontinued
Bladder Endometriosis Medical Therapy

1. **GnRH agonists**
   - Can cause superficial bladder lesions to regress substantially
   - More effective than COC
   - Recommended for bladder endometriosis near the trigone
   - Treatment duration of 6 months. If symptoms remain severe, then oophorectomy or excision can be offered.

2. Combined oral contraceptives

3. Oral progestins (Dienogest)
Bladder Endometriosis Surgical Treatment

- Treatment of choice
- For superficial bladder lesions
  - Simple excision or fulguration
  - Excision preferred to remove entire lesion and pathological confirmation
- For detrusor muscle involvement (bladder endometrioma) and DIE
  - Excision
Laparoscopic segmental bladder endometriosis resection usually heals well due to abundant vascularization.

Best results for symptom relief, diseases progression, and recurrence risk

Concomitant laparoscopic excision and cystoscopic evaluation to ensure correct margins

One- and two-layer closures have excellent results.

Barbed suture instead of monofilament suture for bladder closure showed improved efficiency and more-secure wound closure.

Double-J stents placement when lesion is near the trigone, within 2 cm of ureteral meatus

Ureteroneocystostomy if lesion is close to interureteric ridge

Routine postop cystogram at 7-14 day prior to urinary catheter removal

Urology consult or laparotomy may be necessary
Deeply Infiltrating Endometriosis

- Definition: invasion of endometriosis >5 mm below peritoneum
- Most commonly found in posterior pelvis
- Often associated with lower urinary tract symptoms
- Lesions remote from bladder or ureter can have downstream effects on urinary function, perhaps due to infiltration or inflammation of nervous structures as in hypogastric plexus, parasympathetic and sympathetic nerves involvement
Serati et al. compared 12 patients with DIE to 13 patients with ovarian endometriosis without DIE

- All detrusor-related parameters were statistically different between the groups
- 41.7% patients with DIE had painful bladder filling and significantly higher maximal detrusor pressure during filling cystometry (18 vs 4 cmH₂O) and during pressure flow study (46 vs 29 cmH₂O)
- 91.6% patients with DIE had detrusor overactivity compared with 7.7% with ovarian endometriosis
- Conclusion: DIE can influence urinary function despite a lack of overt urinary symptoms
Panel et al. performed preop screening for urinary symptoms via questionnaire and urodynamic testing

- Patients with confirmed anterior endometriosis (lesions invading vesicouterine space) were more commonly found to have increased rate of bladder hypersensitivity and painful bladder filling (bladder pain, urgency, and/or increased urinary frequency)
- Urinary symptoms in patients with anterior DIE were similar as those observed in patients with bladder pain syndrome and interstitial cystitis
- Majority of patients had voiding dysfunctions (voiding symptoms, impaired flowmetry, and increased maximum urethral pressure)
- Symptoms were not associated with a specific location of bladder endometriosis
- Voiding dysfunction might be a result of entrapment or infiltration of autonomic nerves in the deep posterior pelvic space
Transvaginal ultrasonography is the first-line method with high specificity for diagnosing DIE involving uterosacral ligaments, rectovaginal septum, vagina, and bladder with respective sensitivities of 93%, 98%, 96%, and 100%.

The International Deep Endometriosis Analysis (IDEA) recommends ultrasonography of kidney in all DIE cases to rule out hydroureter.
Deeply Infiltrating Endometriosis
Medical Treatment

- Often unsuccessful
- Symptoms recurrence is common once medications are discontinued.
- In the case of isolated bladder lesions, treatment with COC can substantially improve symptoms if surgery is not performed.
- Continue observation with clinical exam and ultrasonography to monitor disease progression and determine if definitive surgical treatment is indicated in the future.
Surgical removal includes extensive dissection and manipulation of the deep pelvic spaces.

Can be associated with postop urinary dysfunction.

DIE often infiltrates the pelvic plexus, which controls the pelvic floor muscles and voiding function, which can exacerbate or result in de novo urinary dysfunction (urinary retention, dysuria, incontinence, and voiding pain).

Surgical resection of DIE with posterior involvement may worsen existing symptoms and trigger new urinary dysfunction with 6.8-17.5% incidence of de novo symptoms.
Deeply Infiltrating Endometriosis Nerve-sparing Surgery

- Kockel et al.’s technique:
  - Pelvic ligaments that contain component of peripheral nervous system are spared.
  - Use of liposuction to expose autonomic pelvic nerves

- Possover et al.’s technique:
  - LANN technique: addition of electrostimulation of the nerves to identify and avoid parasympathetic pelvic nerves during resection
  - Results: decreased postop morbidity, <1% rate of postop bladder dysfunction
Ceccaroni et al. compared laparoscopic nerve-sparing approach vs. classic laparoscopy (n=126)

- Similar operative complications
- Significant difference in the rates of severe bladder, rectal, and sexual dysfunction
  - 86.2% patients with classic laparoscopy had severe neurological pelvic dysfunctions vs 1.6% in the nerve-sparing group
Benefits of laparoscopy:
- Shorter hospital stay for laparoscopy (3 vs 5 days)
- Less narcotic requirement postop for laparoscopy
- Less blood loss for laparoscopy (100 vs 150 ml)
- Better magnification and view of intraperitoneal contents enabling thorough evaluation and treatment, delicate and microscopic nerve-sparing procedures

Disadvantage of laparoscopy:
- Longer (279 vs 200 min)

No differences in long-term outcomes (e.g. reoperation)
Conversion rate to laparotomy 3-7%
Robotic Assisted Laparoscopy

Benefits:
- 3D visualization
- Expedite learning curve of standard laparoscopy
- Improved dissection with possible reduction of nerve lesions
- Facilitation of suturing techniques
Sampson et al:
- Endometriosis is associated with endometrioid and clear cell ovarian carcinoma

Melin et al. and Brinton et al.:
- Patients with long-standing ovarian endometriosis and endometriosis diagnosed at a younger age had a higher relative risk for ovarian cancer

Melin et al.:
- Increased risk of non-Hodgkin’s lymphoma, brain tumors, and endocrine cancers
- Unilateral oophorectomy or radical surgical excision of visible endometriosis decreases risk of developing ovarian cancer
Risk factors for progression to malignancy:
- Long-standing endometriosis
- Diagnosis at early age
- Infertility
- Characteristically changing endometriomas

All women with endometriosis should be counselled regarding this increased risk of malignancy and potential benefits of excisional surgery.
Urinary tract endometriosis is rare. Its depth and severity can frequently be predicted preoperatively. Medical management is usually a temporary measure, and best used post-operatively after excision. When advanced-stage disease is suspected, imaging with ultrasonography, MRI, and/or IVP is necessary. Thorough physical exam for evaluation of rectovaginal endometriosis, which can predict an increased rate of ureteric involvement and DIE is important. Preoperative mapping of lesions can determine the need for coordination between gynecologists, urologists, and colorectal surgeons with training in minimally invasive surgery. The majority of ureteral lesions are superficial and can be treated by ureterolysis. Nerve-sparing surgery shows considerable promise in decreasing the rate of postop bladder dysfunction in deeply infiltrating disease.
Thank You!

Questions?