CASE REPORT

Dysmenorrhea in Renal Obstruction (Intrinsic Ureteral Endometriosis)

Robert Lee E. Pedragosa, MD and Kathleen G. Quezada, MD, FPUA

Section of Urology, Department of Surgery, AFP Medical Center

Extrauterine endometriosis occurs in less than 1% of cases and rarely involves the urinary system. Ureteral endometriosis is a rare disorder that can eventually lead to renal dysfunction/failure with an incidence of <1%. Ureteral obstruction resulting in hydronephrosis is a rare manifestation of ureteric endometriosis. It occurs as a consequence of intrinsic involvement of the ureter or from extrinsic compression by a pelvic endometriosis. Presented is a 42-year-old adult female with left sided intrinsic ureteral endometriosis presenting with left cyclical flank pain masked by dysmenorrhea.

Key words: Endometriosis, ureteral endometriosis, ureteral obstruction, obstructive uropathy

Introduction

Endometriosis is a clinical disorder in which functionally active endometrial cells are deposited in areas outside the uterus. Endometriosis occurs in 5 - 15% of women during the reproductive years and more common in nulliparous or infertile women. Extrauterine endometriosis affects the urinary system in <1% of cases. Distribution of urinary tract endometriosis for urinary bladder, ureter, kidney and urethra is at 84, 10, 4 and 2% respectively.[1,2] The ureters are rarely involved, however their close proximity with the female reproductive organs especially the distal ureter makes them susceptible to the development of extrinsic compression of the ureter. Ureteral involvement with minimal or extensive disease can lead to urinary tract obstruction and ureterohydronephrosis. In extrinsic form, it is localized to the adventitia or surrounding connective tissue of the ureter.[1] Nephrons are lost when ureteral endometriosis is present in 25 - 50%.[1,3] Intrinsic ureteral involvement usually affects the muscularis propria, lamina propia or ureteral lumen. Extrinsic involvement is 4 times more common than intrinsic disease.[4] The left ureter is more commonly involved than the right but bilateral ureteral endometriosis is seen in cases with extensive pelvic endometriosis.[1,5] Symptoms of patients with urinary tract endometriosis include chronic pelvic pain with urgency, frequency, dysuria, and dyspareunia with or without cyclical hematuria. Backpressure changes are seen in obstructed ureters and anuria with bilateral ureteral involvement. Diagnosis of genitourinary endometriosis relies heavily on clinical suspicion.[2] Intrinsic endometriosis is more symptomatic than extrinsic disease. Ureteral endometriosis is generally discovered at the time of laparotomy or laparoscopy for evaluation of

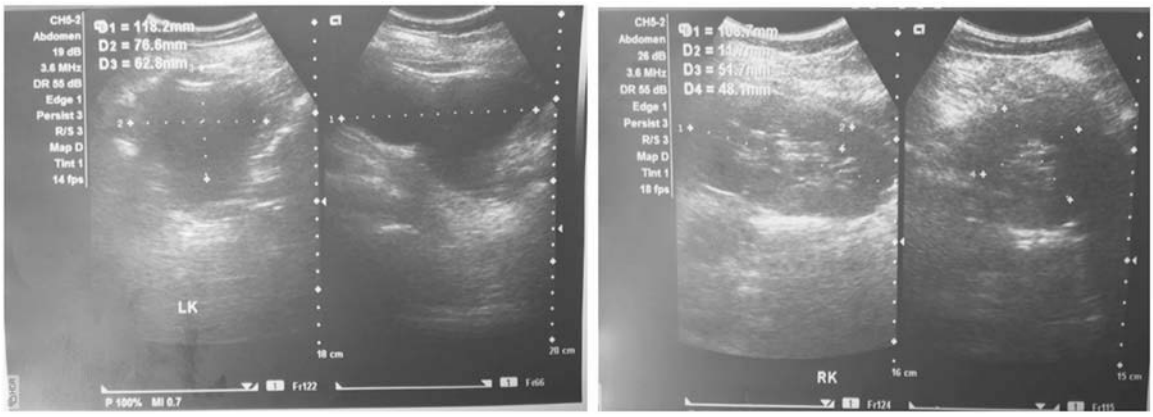
pelvic pain or other surgical indications. It usually presents with colicky cyclical flank pain (25%) and gross hematuria (15%), while up to 50% are asymptomatic.[5]

The Case

This is a case of S.T 42-year-old female G1P1(1001) with regular menstrual cycle, asthmatic with no previous surgery, presented with a chief complaint of left flank pain. Pain started 2 years prior to consult. It was described as colicky with 2/10 severity non-radiating accompanied by hypogastric pain described as cyclical (monthly) in nature in which the patient attributed to her dysmenorrhea. No consult was done and patient self medicated with non-steroidal anti-inflammatory drugs with noted relief of symptoms. During the interim there was persistence of symptoms until 4 months prior to admission, left flank pain described as colicky now with 7-8/10 in severity accompanied by dysuria and hypogastric pain. Patient sought consult to an OB-GYN wherein the patient was treated as a case of Urinary Tract Infection given antibiotics and with slight improvement of symptoms. However, persistence of symptoms now with 10/10 in severity, prompted consult to a family medicine physician wherein KUB ultrasound was requested and revealed moderate dilatation of the left pelvocalyceal complex (Figure 1). No lithiasis or focal lesion was seen with unremarkable findings on the right kidney and urinary bladder. Patient was referred to a urologist and CT stonogram done which revealed no lithiases on both upper and lower tracts with severe hydronephrosis of the left pelvocalyceal system down to the distal ureter. An incidental finding of an adnexal mass, left noted with consideration of extrinsic compression of the left distal ureter (Figure 2). Upon referral to the service, patient had febrile episodes (TMax 38.5 C) and Urinary Tract Infection. Patient underwent Ultrasound guided Nephrostomy of the left kidney with ~ 1000ml of urine collected. Specimen was sent for gram stain and culture with sensitivity and treated accordingly. Daily monitoring of nephrostomy output was done by the patient with noted minimal to nil output. A referral to OB-Gyne service was done to evaluate the adnexal mass and their impression was that the mass was too small to be causing external compression to the ureter and no gynecologic and surgical intervention warranted. 1 month post nephrostomy, patient underwent Glomerular filtration rate (GFR) scan with Renal Scintigraphy using Tc99m DTPA. The study showed total GFR of 83ml/min with split GFR as follows: Right Kidney (73ml/min or 88% relative uptake) and Left Kidney (10ml/min or 12% relative uptake) (Figure 3). Primary consideration was a poorly functioning left kidney secondary to an obstructed left distal ureter. Cystoscopy with retrograde pyelography was done and showed dilated ureter with egress of dye into the left upper tract but with note of filling defects at the distal ureter (Figure 4). Ureteroscopy was done to visibly document the obstruction. A smooth, with regular borders intraluminal (ureter) mass approximately 3mm in widest diameter, and 6cm from the ureteral orifice (Figure 5) was seen. Biopsy with frozen section was done which revealed benign glandular cells. Laparoscopic nephrectomy was done with noted severely thinned out kidney approximately measuring 8cm in length, intraperitoneal and pelvic findings were unremarkable. Kidney and ureteral masses were sent for histologic assessment. The ureteral mass, a tiny tan tissue that measures 0.2cm x 0.2cm, showed presence of benign tubular glands with endometrial features, which is consistent with endometriosis (Figure 6). The kidney specimen measuring 7.5cm x 4.5cm x 3cm with surface areas showed uneven depressions of the cortex extending into the medulla with cortico-medullary junction effaced and calyces blunted showed chronic pyelonephritis. Patient was discharged stable and improved.

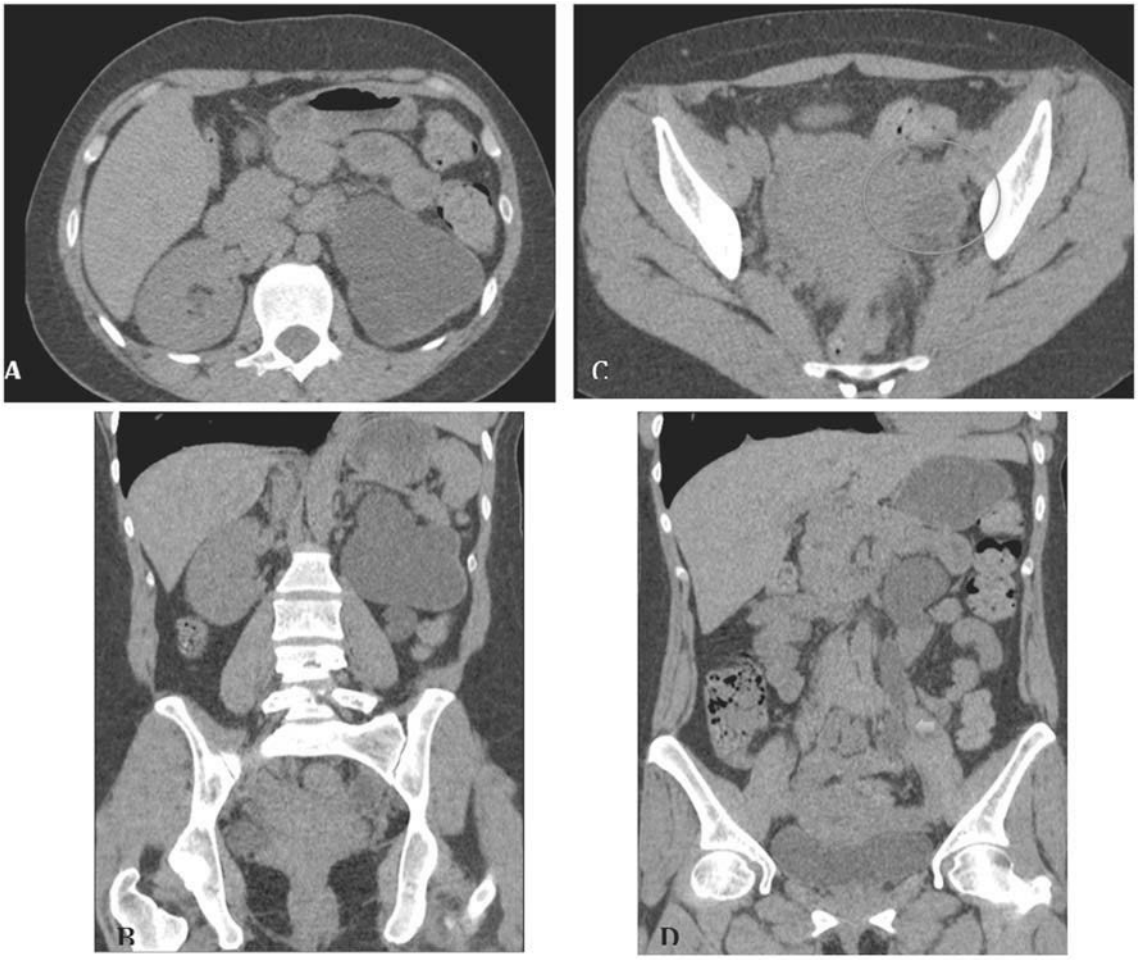
Discussion

Endometriosis in simplest definition is the presence of endometrial glands and stroma at extrauterine sites. Hypotheses on its pathogenesis are explained by the following theories: implantation theory - retrograde menstruation or trans-tubal regurgitation transports endometrial cells on pelvic structures or transplanted to surgical wounds/scars as a result of surgery (e.g.

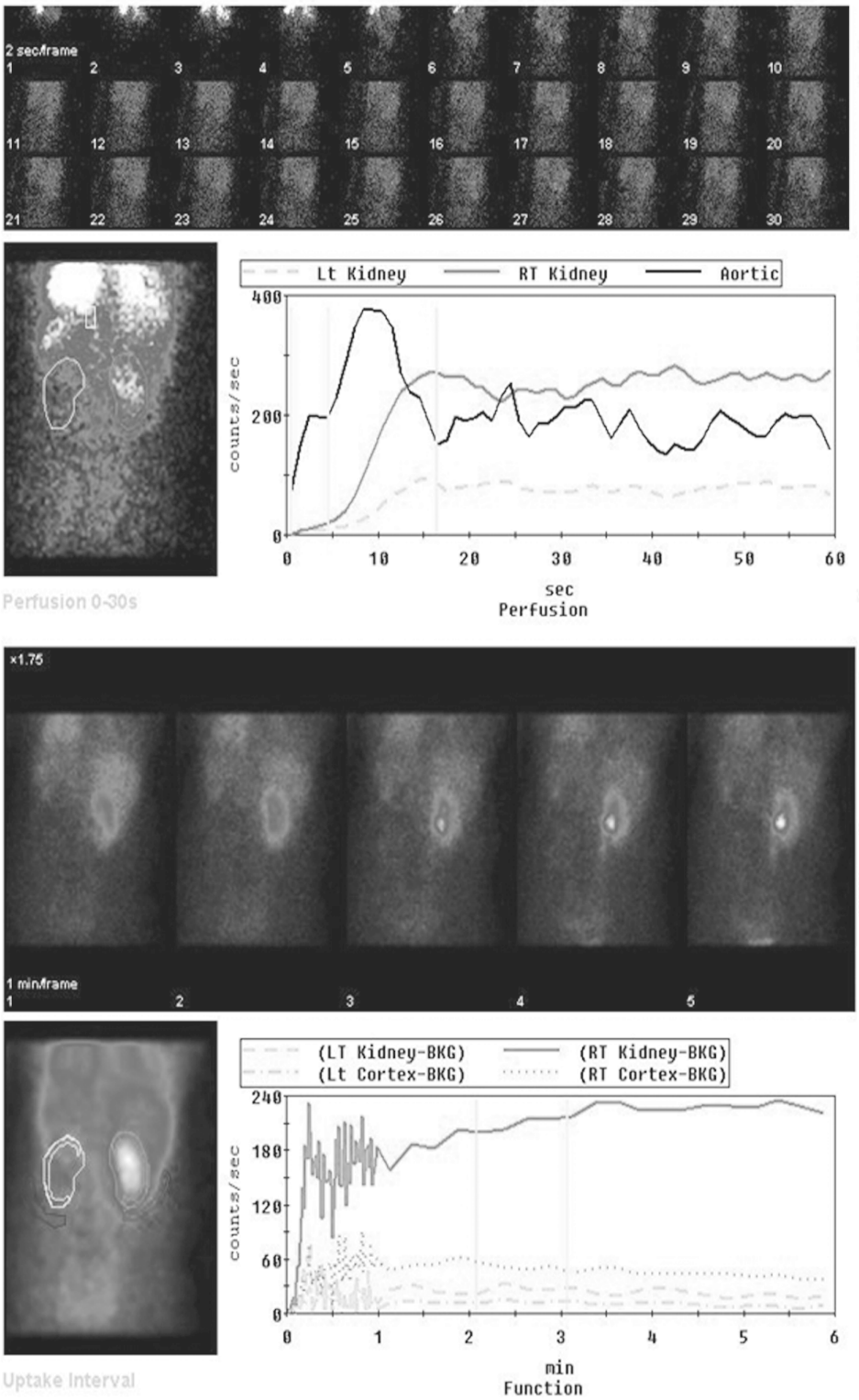


A. B.

Figuere 1. Left kidney showing moderate dilatation of the pelvocalyceal system (A) while the right kidney showing normal echopattern and configuration (B)



Figuere 2. Computed tomography in cross (A) and coronal section (B) showing severe hydronephrosis with thinned out cortex of the left kidney. Suspicious adnexal mass located anterior to the distal ureter compressing it (C) and Coronal view showing severely dilated ureter indicated in arrows (D)

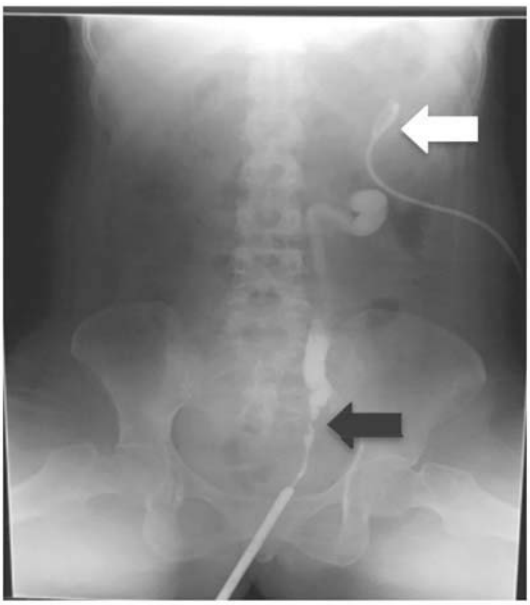


Gates GFR
Age:42.7 Years
Height:(cm): 152.4
Weight:(kg): 47.7
Radiopharmaceutical: TcDTPA
Injected dose:(mCi): 4.16
BSA (m^2): 1.42

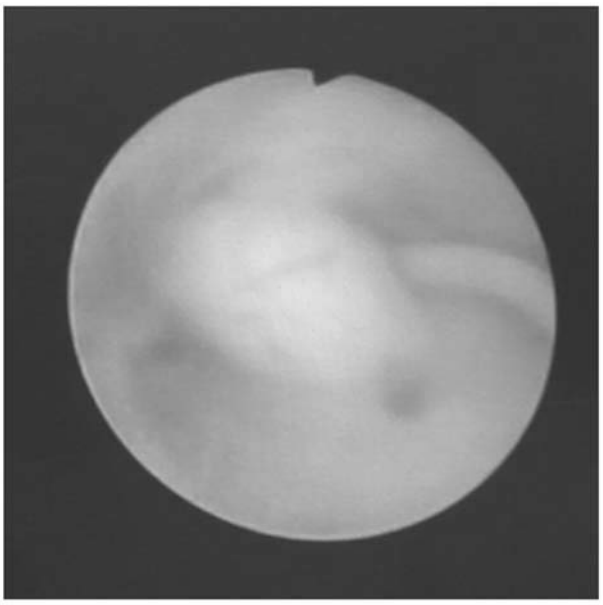
Kidney	Left	Right
Kidney Area (cm^2):	46.65	51.34
Kidney depth (cm):	4.83	4.86
Perfusion% (Int):	24.06	75.94
Perfusion% (Slo):	27.11	72.89
Uptake% (Int):	11.64	88.36
GFR:	5.08	38.55
Time to peak:	2.3	5.3
Peak to 1/2 peak:	2.5	NA
20min/peak ratio:	NA	NA
20min/3min ratio:	NA	NA

Cortex		
Time to peak:	2.3	1.8
Peak to 1/2 peak:	2.25	5.15
20min/peak ratio:	NA	NA
20min/3min ratio:	NA	NA

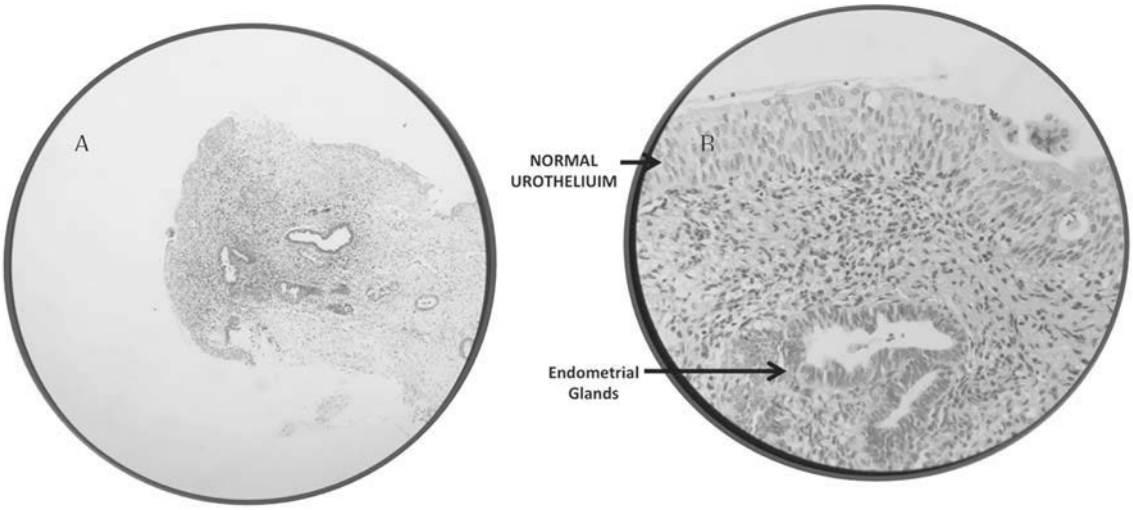
Figuere 3. Renal scintigraphy using Tc99m DTPA shows relative uptake of 11.54% on the left kidney (as shown in cyan broken lines) and 88.36% on the right kidney.



Figuere 4. Retrograde pyelography showing ureteral filling defect and dilated ureter (black arrow) Nephrostomy seen in place (white arrow).



Figuere 5. Round, with regular borders intraluminal (ureteral) mass ~3mm in widest diameter. Guidewire as shown above.



Figuere 6. (A) Ureteral mass in cross section in low magnification (B) Presence of normal urothelium (shown in short arrow) located at the base and presence of endometrial glands and stroma (shown in long arrow) located obstructing the ureteral lumen.

laparotomy, episiotomy), next is the coelomic metaplasia theory, in this theory, the undifferentiated cells in the peritoneal cavity are capable of differentiating into endometrial tissues, repeated inflammation to the mesothelial cells induces metaplasia to the endometrial epithelium. And lastly, as in the present case, thru lymphatics and blood vessel dissemination, cases of extraperitoneal diseases such as endometriosis of the pancreas, breast, extremities, vertebra, central nervous system as well as the urinary system is the most probable route affecting these organs. An individual's susceptibility to endometriosis may have genetic pathology. First-degree relatives

have 7% likelihood of developing the disorder compared with 1% in unrelated persons. Twins were also observed to have the same predilection.[5]

There is evidence for altered humoral and cell mediated immunity in the pathogenesis of endometriosis such as deficient cellular immunity, improper natural killer cell activity and increased concentration of leukocytes and macrophages in the peritoneal cavity and ectopic endometrium. The inability to recognize the presence of endometrial tissue in abnormal locations, decreased cytotoxicity to autologous ectopic endometrium and secretion of cytokines and growth factors by leukocytes and macrophages are a result of variations in immune system. One hypothesis is that secretion of various cytokines by inflammatory cells into the peritoneal cavity leads to proliferation of implants and recruitment of capillaries. Oxidative stress may be another component of the inflammatory reaction. Thus, the immune system plays a role in determining who will develop endometriosis, as well as the extent and clinical manifestation of the disease.[5]

Women with autoimmune diseases, hypothyroidism, fibromyalgia, chronic fatigue syndrome, allergies and asthma, have higher rates of the disease compared with the general female population which proves/support the theory of altered immune system in women with endometriosis. The risk of endometriosis developing into a cancerous lesion is very low (1 - 2.5%).[5]

The clinical manifestation could be attributed to the behavior of endometrial glands/tissues. The endometrial tissue acts just like the normal ones in the uterus, responding to cyclical hormone levels, growing and bleeding at certain times of the cycle. These ectopic tissues bleed during menstruation, causing the surrounding tissues to become inflamed. This inflammation causes fibrosis leading to adhesions, and as in our case this causes the obstruction of ureteral lumen and eventually renal dysfunction.[5]

Ureteral obstruction is insidious in onset and slowly progressive that leads to renal failure. In women with non-calculous obstruction, with symptoms related to menstruation, a high index of suspicion of ureteral endometriosis is considered.[1] The prevalence of urinary tract endometriosis is approximately 1% or 3.5 million worldwide. Ureteral endometriosis is 10% or 350,000 women in cases of genitourinary tract endometriosis. Patients who developed renal dysfunction is 30% of those patients with ureteral endometriosis or 100,000 women worldwide and among these women with renal dysfunction an unknown number of patients presents with loss of kidney function. As such, just like the case presented here, it is exceedingly rare.[3]

The diagnosis of ureteral endometriosis requires a high index of suspicion and is aided by clinicians' awareness of the condition. The diagnosis is suggested by the finding of hydronephrosis in a patient with suspected or known endometriosis, particularly if symptoms consistent with ureteral involvement are present. Direct visualization and biopsy of the implants can provide definite diagnosis but histologic confirmation remains to be the gold standard.[5]

Upper tract imaging is the initial step in assessing patients with obstruction in the clinical setting. Tests such as ultrasonography, which is a non-invasive test, suggest obstruction in cases with ureterohydronephrosis, Intravenous urography is a better test in highly suspicious cases. Intrinsic disease appears in IVU as ureteral filling defects, whereas extrinsic disease causes smooth strictures. The exact location and extent of the disease are defined through retrograde ureteropyelography, CT or MRI, which are valuable for planning treatment.[5] MRI is sensitive and specific, although ureteral lesions are underestimated. MRI is accurate in differentiating between intrinsic and extrinsic forms of ureteral involvement. Ureteral endometriosis is identified as a hypointense nodule on T2-weighted images and hyperintense foci on T1-weighted images. MRI also detects periureteral involvement (Extrinsic) rather than ureteral wall lesions (intrinsic).[1] Ureteroscopy, cystoscopy and laparoscopy allow direct visualization of the urinary tract lesions. In the present case, Ureteroscopy was proven helpful in the diagnosis.

Goals of treatment are to preserve renal function, to manage and control endometriosis, and to provide relief of symptoms. Ureteral endometriosis with hydronephrosis is managed surgically. Medical treatment/therapy does not

treat the fibrotic component of endometriotic lesions, which is largely responsible for ureteral obstruction; however, patients with mild or intermittent hydronephrosis are treated initially with a combination of medical therapy and drainage (ureteral stent). In such cases, close monitoring of renal function is required.[5] In the present case, however, the delayed diagnosis of Ureteral Endometriosis years after the onset of symptoms, led to progressive damage to the left kidney until it has become poorly functioning (as evidence by the GFR).

Surgical management of ureteral endometriosis includes ureterolysis in cases of extrinsic disease. Laparoscopic ureterolysis is undertaken with transperitoneal approach and allows superior assessment of endometrial implants on the peritoneum. In the case of intrinsic disease, distal ureterectomy with reimplantation is preferred due to difficulty of removing the lesions especially when it infiltrates the ureteral wall.[5] For the present case, with poorly functioning kidney, Laparoscopic Nephrectomy with biopsy of the implants was done.

Understanding the pathogenesis and clinical presentation is the key in preventing progression of the disease. Preoperative assessment with a thorough history, physical exam and imaging can help in the diagnosis. Patients who presented with the same symptoms and diagnosed early with no signs of renal dysfunction may have been managed conservatively. Anti-gonadotropin such as Danazol may be given to patients with endometriosis and placement of ureteral stent could be done for drainage. Currently there are no specific tests that could help determine the presence of endometriosis in the ureters that will improve early detection and treatment. Best diagnostic modality is direct visualization and biopsy of implants (Laparoscopy in cases of extrinsic disease and Ureteroscopy in intrinsic disease).

Currently, there are still no specific blood tests that could determine the presence of ureteral endometriosis. Tumor marker such as CA 125 has a low sensitivity but may be elevated in extensive endometriosis, which is present in cases of ureteral endometriosis. It is also a valuable adjuvant in the follow up of recurrence in patients with advanced endometriosis and initially elevated CA-125 levels.[6] Studies in developing diagnostic tests are promising but require extensive knowledge of endometrial pathogenesis and prognosis.

Conclusion

Early detection of endometriosis on patients presenting with flank pain and dysmenorrhea is a challenge. Initial imaging such as KUB ultrasound provides information on suspicious renal obstruction and subsequent imaging such as a CT scan can be requested. Renal failure could be prevented with these initial imaging tests with appropriate medical and surgical management. This patient was well advised about her condition. Regular check up with her Nephrologist and Gynecologist in assessing renal function, control of symptoms medically and urinary tract infections are advised to provide good quality of life especially in post nephrectomy patients.

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