

LITERATURE REVIEW: ECTOPIC URETER IN CHILDHOOD

Larasita Prameswari¹, H. Suharjendro^{2,3}

1. Medical Student of Mataram University
2. Department of Urological Surgery Faculty of Medicine Mataram University
3. Urologist of West Nusa Tenggara Provincial General Hospital

Abstract

Ectopic ureter is a rare and often overlooked disorder of the urinary tract that can cause urinary incontinence. Ectopic ureter is thought to be caused by the ureteral bud failing to separate from the mesonephric duct, resulting in more caudal insertion. This anomaly is related to genitourinary tract embryogenesis, which results in differences in anatomical and clinical manifestations between male and female. Delayed diagnosis and treatment resulted in years of suffering and disruption to social development and school years. The urinary incontinence due to this anomaly can also cause stress urinary incontinence and psychological disorders in children.

Keywords: ectopic ureter, congenital anomaly, the urinary incontinence

Introduction

The most frequently affected human organ system by congenital anomalies is the upper urinary tract. It because the urinary system moves up from the endoderm and mesoderm layers and merges to form the kidney.⁸ Congenital kidney and ureter anomalies include a broad spectrum of disorders, from simple variants with no clinical significance to complex anomalies that can result in life-threatening complications and end-stage renal disease. Anomalies of the urinary tract can be categorized as kidney form anomalies with their subclassifications and abnormalities in the development of the urine-collecting system.⁶

Ectopic ureter is a urogenital system congenital anomaly in which the ureter does not enter the bladder in its normal anatomic position. The term 'ectopic ureter' is used to describe a ureter that opens into the bladder neck more distal to one of the mesonephric ductal structures. It usually affects the upper segment of the duplex kidney, according to Weigert-Meyer's law. Ectopic ureteral orifices can occur anywhere in the genitourinary system, including the bladder neck, urethra, ejaculatory ducts, ductus deferens, seminal vesicles, vaginal or uterus.¹⁻¹⁰

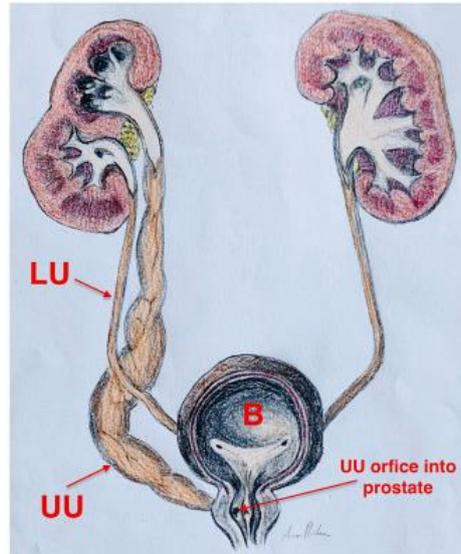


Figure 1. Anatomy of the right unilateral complete pelvic-ureteral system duplication with the ectopic opening into the prostatic urethra⁵

Epidemiology

The incidence of ectopic ureter is 1:2000 to 1:4000 of births or 0.025% in general population. This anomaly is more common in females than males with a ratio of 6:1 or 70-90% cases. Approximately 10% of cases of ectopic ureter involve both sides. More than 80% of ectopic ureter associated with duplication of the pelvic-ureteral system in females, while in males it generally occurs in a single ureteral system (15-20%).^{4,5,8,9}

In females, the ectopic ureter is located in the urethra from the neck of bladder to meatus (35%), vaginal vestibule (30%), vagina (25%), uterus and fallopian tubes (5%). In males, it is located in the posterior urethra above the verumontanum and never below the external sphincter (48%), seminal vesicles (40%), ejaculatory ducts (8%), ductus deferens (3%), or epididymis (0,5%).^{3,8,9}

Etiology

Defects in the genes RET, FGFR2, and GATA3 are believed to be responsible for abnormal ureter opening in the presence of other renal anomalies. To put it simply, the vesicoureteral junction forms as a result of cell rearrangement and apoptosis in the common nephric ducts, which connect to the urogenital tract. If apoptosis and cell migration are interrupted during ureter and bladder growth and maturation, the ureter is inserted ectopically outside the vesical trigone. This abnormal insertion phenomenon is strongly linked to the

formation of a ureterocele as a result of the abnormal development of ureterovesical junction muscle fibers.⁵

Anatomy of The Urinary Tract

The kidney is a bean-shaped organ that is located in the retroperitoneum. This organ is surrounded by perirenal fat and protected on the outside by Gerota's fascia. A kidney is typically 10-12 cm in length and 3-5 cm in width. This organ is located in the quadratus lumborum muscle, lateral to the psoas muscle, at the level of VT12-VL3. The psoas muscle's oblique position causes the upper pole to be oriented medially in relation to the lower pole. Because of its proximity to the liver, the right kidney is usually located 1-2 cm lower. The adrenal glands are located above and to the side of the kidneys.^{2,6}

The cortex and medulla contain the renal parenchyma. The glomerulus and the proximal part of the collecting tubule are located in the cortex, which is the outermost part of the kidney. The renal pyramids and the distal portions of the collecting tubules are located in the medulla. The papillae are the renal pyramids' apex, and each papilla projects a minor calyx. Approximately 2-4 minor calyces join to form the major calyces, and 2-3 major calyces join to form the renal pelvis, a funnel-shaped structure at the kidney's hilum that opens into the ureter. The ureters are muscular tubes that are thin and long. The wall is 25-30 cm long and runs along the retroperitoneum. It is made up of 1) mucosal line by transitional cells, 2) circular smooth muscle, and 3) longitudinal smooth muscle. The ureter extends from the pelvis to the bladder and anatomically that are relatively narrower in diameter than in other areas. The ureteropelvic junction, the border between the renal pelvis and the ureter, the ureter crossing with the iliac arteries in the pelvic cavity, and the ureter entering the bladder are being narrowing areas (vesicoureteral junction). At this level, the ureters enter the bladder in a position that creates a valve mechanism to prevent reflux of urine.^{2,6}

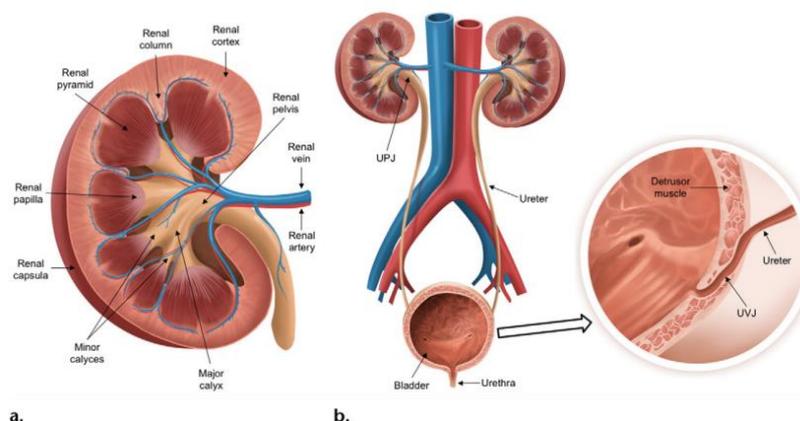


Figure 2. The anatomy of normal kidney and ureter.⁶

Embryology of Urinary Tract

The development of the urinary tract is a very complex process that requires several sequential steps to be maintained in order to achieve physiological development. This occurs between the fourth and tenth weeks of pregnancy. The kidneys and ureters develop from the intermediate mesoderm, an embryological structure located dorsally in the embryo.¹

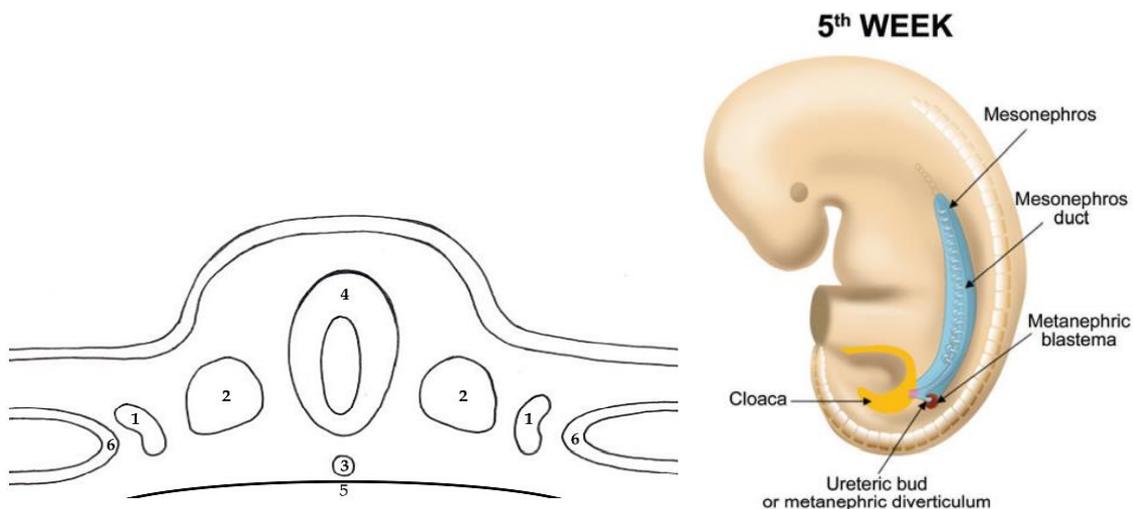


Figure 3. A) Dorsal embryo structure: (1) intermediate mesoderm, (2) paraxial mesoderm, (3) notochord, (4) neural tube, (5) yolk sac.¹ B) The kidney develops from the fusion of the ureteral bud and the intermediate mesoderm's metanephric blastema.⁶

During embryogenesis, the metanephros in the sacral region forms the kidney. The metanephros secretes a protein that stimulates the lateral growth of the ureteral bud in the mesonephric duct, which invades the metanephros and causes a reciprocal interaction known as renal induction. The metanephros will form the nephrons, while the ureteric buds will branch to form the collecting tubules. The kidneys are initially located close to each other in the sacral region, with the hila directed anterior to the pelvis. The kidneys are separated from each other and move gradually in a cranial direction towards the lumbar area until they reach their normal position adjacent to the adrenal glands between the 6th and 9th weeks of gestation. The first bifurcation gives rise to the kidney's cranial and caudal lobes, as well as the renal pelvis. This process will continue until the 32nd week of gestation, when the major and minor calyces, as well as approximately 1-3 million collecting tubules, will be formed.^{1,6}

During the ascending movement, the renal artery supply is constantly replaced and receives supply from higher branches. The caudal branch extends caudally from the common

iliac artery and then from the aorta. When the kidney reaches its final position, one of the branches becomes the main renal artery, while the other branches degenerate. More than one branch may persist and form the accessory renal artery in rare cases. The kidney rotates nearly 90° medially and is directed anteromedially when moving cranially. The ureters are extended and open into the superior bladder.⁶

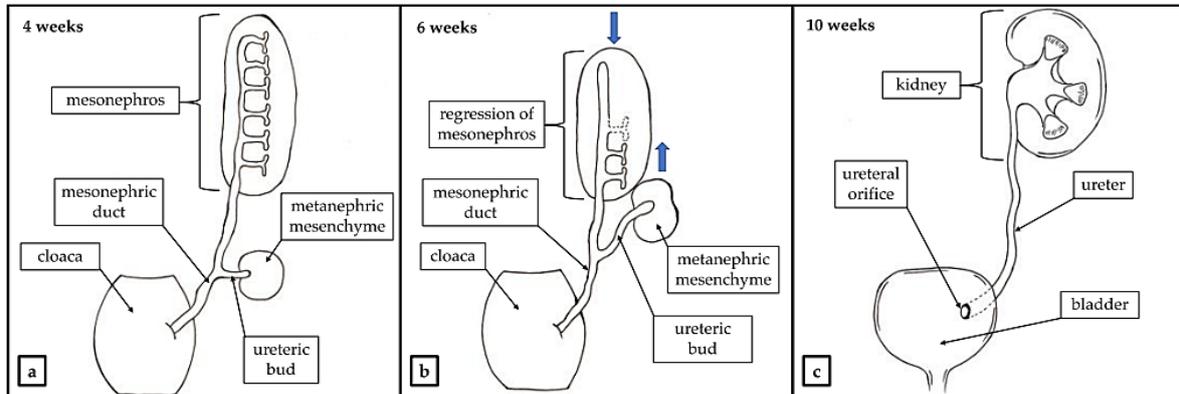


Figure 4. The renal system's physiological development. A) Development of the ureteral bud. B) The metanephric and ureteral buds migrate cranial to the kidney's final location. The mesonephros atrophies and dies. The mesonephric ducts migrate caudally and serve as reproductive organs. The blue arrows represent the structure's movement. C) Urinary system development.¹

Pathophysiology

Ureteral anomalies arise when the position of the ureteral bud: (1) does not appear in the normal place, (2) the ureteral bud is bifurcated, or (3) there are two ureteral buds that emerge from the mesonephric duct.^{2,7} During embryological development, the interaction of the ureteral bud and Wolffian duct structures determines the location of the ureteral opening, with early anatomic variations resulting in an ectopic position. During the fourth week of gestation, the ureteric bud grows cranially from the Wolffian duct toward the metanephros. Signaling pathways for the formation of kidney tissue are activated by connections between these structures. As a result, ectopic ureteral buds are frequently associated with abnormal nephrogenic blastema development, resulting in many patients with a single-system ectopic ureter having a dysfunctional or dysplastic ipsilateral kidney and other genitourinary abnormalities.⁵ Duplicated pelvic-ureteral systems are formed by two distinct ureteral buds originating from either the Wolffian ducts or incomplete union of the upper and the lower pole ureteral buds.¹⁰

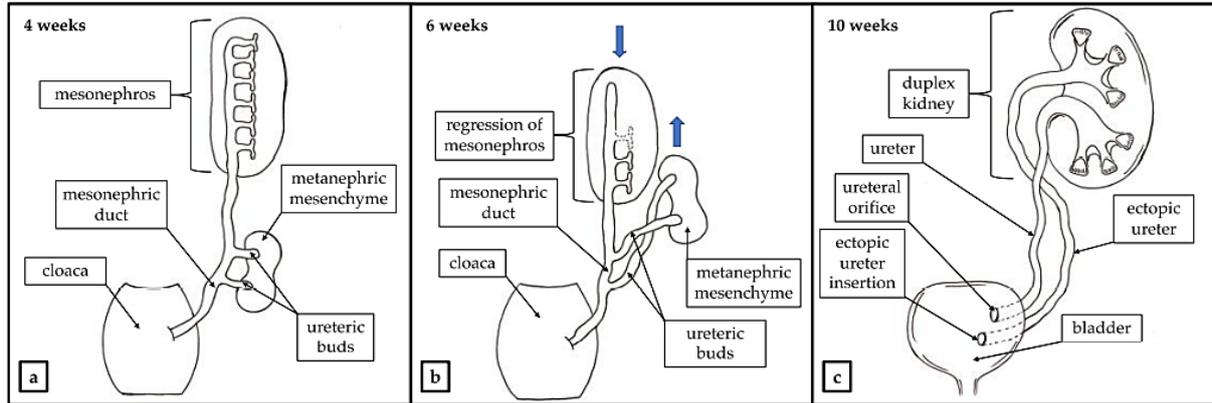


Figure 5. The formation of a duplex kidney. A) Development of two ureteral buds. B) According to Weigert-law, Mayer's the mesenchyme of the metanephric and ureteral buds migrates cranial to their final location. The mesonephros degenerates and atrophies. The mesonephric ducts migrate caudally and begin to reproduce. The blue arrows represent the structure's movement. C) A duplex kidney with an ectopic ureter developed.¹

Atypical opening of the ectopic ureter was determined embryologically according to the Mackie-Stephen hypothesis, which demonstrated that the initial position of the Wolffian duct results in a variation of the anatomical displacement of the ureter. The lateral ureteral bud moves caudally to the orifice, whereas the medial ureteral bud moves more cranially.⁵

The 'trigone precursor' hypothesis can also explain the ectopic ureteral origin. The trigone precursor is the medial portion of the Wolffian duct that connects to the remnant of the mesonephric duct near the ureteric bud's insertion. This hypothesis proposes that a more lateral ureter origin caused by elongated trigone precursors may delay ureter-urogenital sinus fusion, resulting in a more caudal ectopic. A short trigone precursor will result in a position medial to the ureteral bud's origin. Shortening of the trigone precursor is also linked to a lack of mesenchymal tissue, which leads to abnormal trigone formation and an increased risk of urinary reflux.⁵

A functional urinary tract has a contractile muscular membrane and an anti-reflux mechanism corresponding to the muscle fibers of the ureter and bladder forming an anti-reflux valve. The failure of functional muscle fiber development is caused by the abnormal location of the ureteral orifice outside the vesical trigone. This causes the ureteral opening to narrow or dilate, resulting in vesicoureteral obstruction or reflux.⁵

According to Weigert-Meyer's law, the pelvic-ureteral system is duplicated, with one ureter draining the upper pole into the infero-medial portion of the bladder and another draining the lower pole towards the supero-lateral portion of the bladder. Because it empties outside the trigone, a ureterocele can form in the ureter that drains the upper pole, and vesicoureteral reflux can occur in the ureter that drains the lower pole.^{2,5,7}

Single-system ectopic ureter is a rare condition often associated with dysplastic or poor function, referred to as a Multicystic Dysplastic Kidney (MCDK). The correlation between ectopic ureter and kidney dysplasia may be related to anomalies that occur after embryogenesis of the urinary tract. Single-system ectopic ureter is also associated with other congenital abnormalities, such as congenital heart disease, spinal cord malformations, and anorectal malformations.^{4,9}

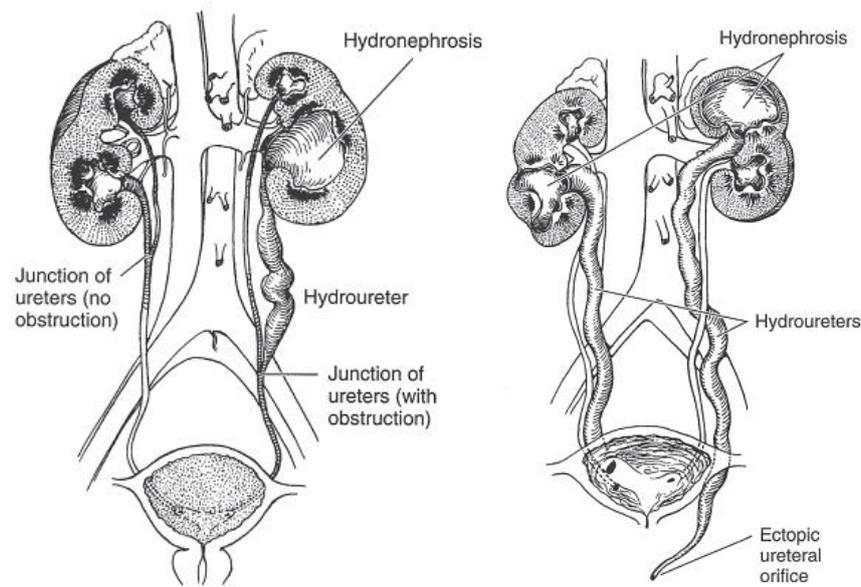


Figure 6. A) Incomplete duplication (type Y) with left renal lower pole hydronephrosis. B) Complete duplication with reflux to the right renal lower pole and chronic pyelonephritis scarring. The left renal upper ureteral pole is ectopic, and the renal parenchyma is frequently dysplastic.¹⁰

Clinical Manifestation

Clinical symptoms differ depending on the location of the anomaly (unilateral or bilateral ectopic, ureteral duplication, single ureter). The ectopic ureteral orifice in females is usually intravesical (opens into the bladder neck) or extravesical (located in the urethra or vaginal vestibule). Drainage of urine from the distal urethra to the sphincter (infrasphincter) or into the vagina usually causes classic symptoms of urinary incontinence, such as underwear that is always wet but can micturate normally.^{2,5,7,8,10} This is because urine flowed by the ectopic ureter bypasses the external ureteral sphincter and exits directly, while the contralateral ureter continues to fill the bladder and the micturition process continues as usual.^{2,7} In males, an ectopic ureter always inserts above the external sphincter, which is not associated with urinary incontinence. It is typically found posterior to the urethra. The ureter can sometimes open in the seminal vesicles, ductus deferens, prostate, epididymis, or even the rectum.¹

In males, this anomaly can be asymptomatic or mild. The ureteral opening to the ductus deferens frequently causes complaints of epididymitis, which is difficult to cure because the ductus deferens and epididymis are constantly flooded by urine.^{7,10} Patients can also experience vesiculitis, prostatitis, orchitis, bleeding and pain during ejaculation. This condition most often occurs over the age of 20.⁵ Other symptoms include hydronephrosis-related abdominal pain, urinary tract infection, and weight loss. Urinary retention or vesicoureteral reflux can both cause UTI. Toia et al. discovered that 45% of males with ectopic ureters experienced urinary tract pain, and 26% were treated for UTI. In the same study, 31% of females experienced recurrent UTI symptoms. Weight loss associated with increased ectopic distance from areas of normal anatomy is related to the severity of renal hypoplasia or dysplasia.^{5,7,8}

Clinical Workup

a. Anamnesis and Physical Examination

During the diagnostic process, a comprehensive history and physical examination are required. Understanding of this anomaly enables a precise and targeted diagnosis and is critical in selecting the appropriate treatment. Although the patient may present with UTI or urinary incontinence symptoms, the history and diagnosis must be expanded because they may be a manifestation of an ectopic ureteral opening.^{4,5} In some cases, clinical symptoms can lead to a diagnosis³:

- a. Neonates: pyuria and acute pyelonephritis.
- b. Girls: incontinence with normal voiding, vaginal discharge, ureteral orifice openings can be found in the area of the external meatus. The physical examination is carried out carefully under the influence of anaesthesia. differential diagnoses on this case are bladder dysfunction, overactive bladder, and ureterocele.⁹
- c. Boys: symptoms of epididymitis and seminal vesicles palpable on digital rectum.

b. Diagnostic Test

1. Ultrasound (USG)

In children, ultrasound examination is the initial diagnostic test, but sometimes ultrasound examination alone is not sufficiently helpful. In general, ultrasound examination and VCUG are used as first-line tests for diagnosis. Prenatal ultrasound is usually repeated after the child is born.⁷ Other imaging tests, such as a transrectal ultrasound, can assist to see ureter with the prostatic orifice. The physician should also be aware of rare variations of ectopic ureter, eg those that open into the prostate.⁵

2. Voiding Cystourethrogram (VCUG)

VCUG is used to rule out vesicoureteral reflux as a cause of swelling of the kidneys and ureters. VCUG is also used to differentiate if there is reflux in the ureter associated with ureteral ectopic. Usually with a combination of ultrasound and VCUG, the physician can distinguish if hydronephrosis occurs. Other diagnostic procedures such as renal-flow scan or kidney X-ray and IVP can clarify the anatomy.⁷

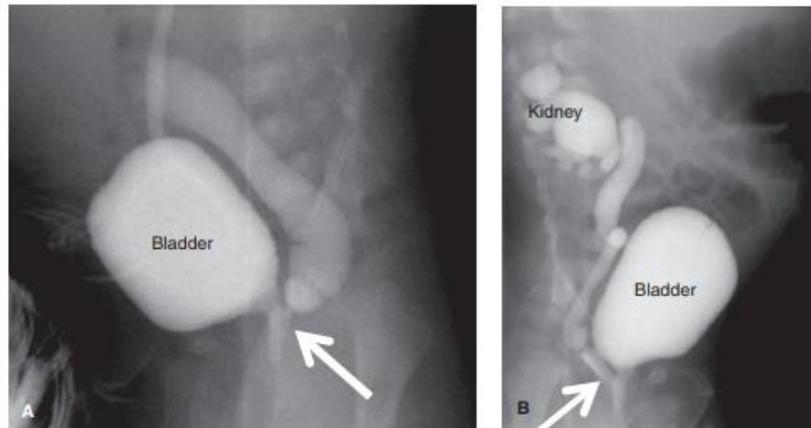


Figure 7. A) VCUG in a boy is seen to drain into the posterior urethra with reflux into a greatly dilated ureter and into the prostatic urethra (arrow). B) CUG in a girl with reflux into a very dilated ureter and continuing to the dilated lower pole of the right renal. An ectopic ureter is seen in the proximal urethra (arrow).¹⁰

3. Cystoscopy

Cystoscopy examination may be able to find an ectopic ureteral opening in the urethra or a hemi-trigonum (no one of the ureteral openings in the bladder) is found. This examination is usually performed under general anesthesia, a small cystoscope is placed into the urethra, but ectopic ureter not always can be identified. If an ectopic ureteral opening is found in the urethra, an ureteral catheter can be tried and followed by retrograde ureterography.^{2,7}



Figure 8. Ectopic ureteral orifice.¹¹

4. Intravenous Pyelogram (IVP)

Intravenous pyelogram is commonly used to find abnormal duplex kidneys and ectopic ureter. On this examination, hydronephrosis of the kidney pushes the caudal segment pushed downward and laterally that it looks like a dropping lily.² Because there is no polar upper lid, dysplastic parenchyma, or very thin pyelonephritis, approximately 16% of ectopic ureters cannot be detected by intravenous pyelogram. This may necessarily require the use of additional imaging modalities such as a CT scan, MRI, or Dimercaptosuccinic acid (DMSA) scan.⁵

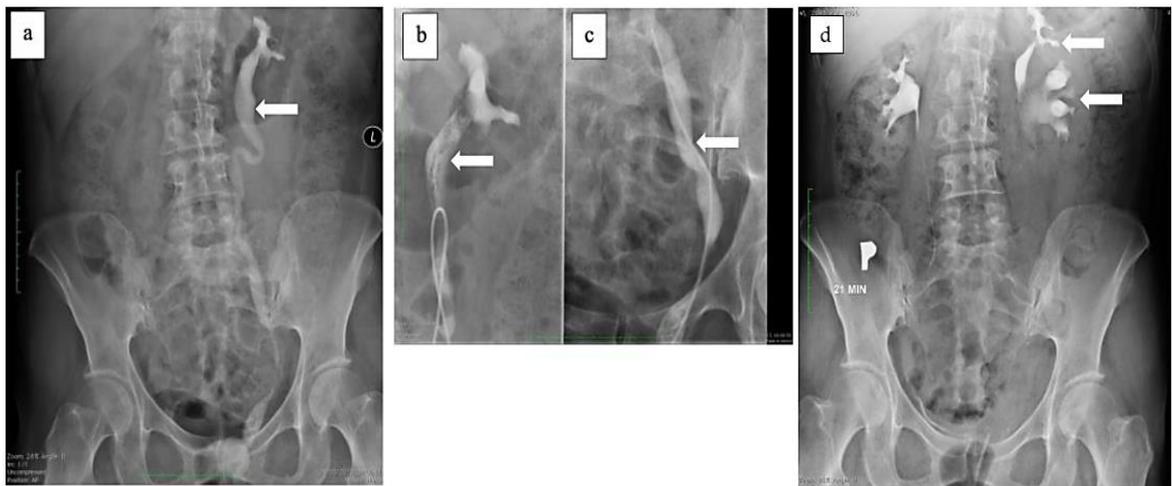


Figure 9. A) Ectopic ureter with contrast (a white arrow). B) Ectopic ureter proximal (white arrow). C) Ectopic ureter at the distal end (white arrow). D) The left side has a duplex kidney (white arrow) and the right side has a normal pelvic-calyx system.¹

5. CT-scan

Hanson et al. demonstrated that a contrast-enhanced CT scan can be used to diagnose ectopic ureter. This method is considered more sensitive and can provide a clear anatomical picture, including the location of the ureteral ectopic opening.⁴ This examination is performed to look for a small upper pole moiety that is not detected by IVP or ultrasound.³

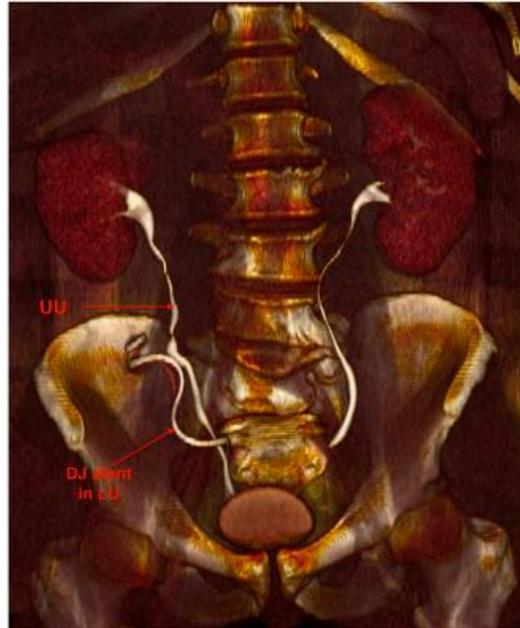


Figure 10. CT scan reveals that the ureters in the right kidney are duplicated. The upper pole is drained by the first ureter, which has a distal opening in the prostatic urethra, while the lower pole is drained by the second ureter, which has a characteristic opening into the vesical trigone.⁵

6. *Magnetic Resonance Imaging (MRI)*

MRI can be used in patients with reduced kidney function, clear anatomy, and no radiation exposure. This tool can detect the presence of ureteral ectopic. Not all hospitals have MRI facilities and this examination require more money than other examinations.⁴

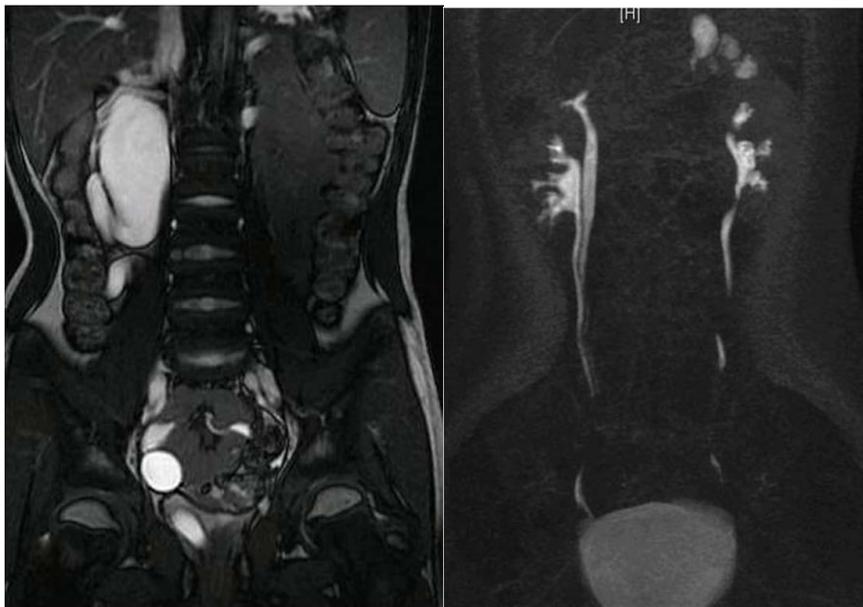


Figure 11. MR Urography: A) Ectopic insertion and dilatation of the upper pole ureteral. B) Bilateral ureter and right kidney duplication with nonfunctioning upper pole dilatation.¹¹

Management

The main goals in surgical management are to maintain renal function, prevent recurrent infection, and improve incontinence. The current management strategy aims to provide treatment based on the patient's renal function.^{5,11}

1. Nephrectomy (Upper Pole Heminephrectomy)

Ectopic ureter with a single pelvic-ureteral system often has poor kidney function. This surgical technique is more often chosen, either by open or laparoscopic approach urine into the ectopic ureter.^{2,4,7} This can eliminate urinary incontinence and lower the risk of infection. This surgical technique easy to perform and has the lowest risk of complications. Traditionally, this operation was performed by making an incision under the ribs, but now it can be performed laparoscopically. The disadvantage of this procedure is that the functioning kidney tissue at the ectopic end of the ureter is also wasted.⁷

2. Ureteropyelostomy

This surgical approach can be minimally invasive or open surgery. This operation is performed on a kidney still functioning properly.³ According to the American Urological Association, this procedure has an increased risk of complications compared to other ureteral ectopic repair surgeries.⁷

3. Ureteral Reimplantation

This surgery is performed on properly kidney function or in conditions of duplication of the pelvic-ureteral system with the upper pole still functioning properly.^{3,4} The ureters are split at the bottom and then sewn to the bladder in such a way as to make urine flow well and not flow to the back. Surgery is performed by making an incision above the pubic symphysis bone. This procedure has a higher risk of complications than the others and is also technically difficult to perform on babies. Like an ureteropyelostomy, this operation saves all the tissue and removes more abnormal ureteral ectopic than other two procedures and can stop ureteral reflux. Infants and young children are usually treated 1-5 days after surgery.⁷

Complication

In adulthood, if not treated early, urinary incontinence may be accompanied by stress urinary incontinence, overactive bladder, urinary fistula, or urethral sphincter insufficiency. Renal abscess, renal failure, and urolithiasis are late complications. Two risk factors for chronic kidney disease are recurrent UTI and obstructive uropathy. Because of the abnormal ectopic

passage of the ureter and the non-anatomical position of the orifice, this anomaly can predispose to stone formation, resulting in urinary retention and the development of megaureter and crystallization of the nucleus. Severe hydronephrosis can result from an ectopic ureter with a single or duplex pelvic-ureteral system.⁵

Prognosis

The management of an ectopic ureter is determined by symptoms, renal function, patient age, and quality of life. Renal dysplasia and less than 10% function can be restored.⁹

Conclusion

The incidence of ectopic ureter is rare among congenital disorders of the urinary tract. To evaluate and establish the diagnosis of ureteral ectopic pathology, a comprehensive history and physical examination, as diagnostic tests are required. The entire series of diagnoses besides being a reference in determining management, is also useful in looking for the possibility of other congenital abnormalities that appear together. The management of these cases varies and is adjusted to the patient's renal function.

Reference

1. Kulniec, I., et al. 2021. Urinary Incontinence in Adulthood in a Course of Ectopic Ureter—Description of Two Clinical Cases with Review of Literature. *Int. J. Environ. Res. Public Health* 18 (7084): 1-8. DOI: 10.3390/ijerph181370
2. Purnomo, B.R. 2011. Dasar-dasar Urologi Edisi Ke-3. Bab 14: Anomali Traktus Urinarius. Jakarta: Sagung Seto.
3. Sigunmonrong, Y. dkk. 2016. Panduan Penatalaksanaan (*Guidelines*) Urologi Anak (*Pediatric Urology*) di Indonesia. Jakarta: Ikatan Ahli Urologi Indonesia.
4. Oktavius, D. dan Duarsa, G.K.W. 2020. Sistem Tunggal Ureter Ektopik dengan Ginjal Multikistik Displastik di RSUP Sanglah, Bali, Indonesia: laporan kasus. *Intisari Sains Medis* 11(1): 228-232. DOI: 10.15562/ism.v11i1.551
5. Balawender, K. et al. 2022. Ectopic ureter: A concise narrative review with anatomical and clinical commentaries. *Translational Research in Anatomy*. DOI: 10.1016/j.tria.2022.100220
6. Houat, A.P. et al. 2021. Congenital Anomalies of the Upper Urinary Tract: A Comprehensive Review. *RadioGraphics* 41(2) :462–486. DOI:10.1148/rg.2021200078

7. Jonatan, B. dan Kholis, K. Laporan Kasus: Ektopik Ureter. Makassar: Fakultas Kedokteran Universitas Hassanudin
8. Saygin H, et al. 2021. One Method that can be Applied in the Ectopic Ureter is Uretero-Ureterostomy: Case Report. *Journal of Surgical Techniques and Procedures* 5(1): 1044.
9. Grover, J.K. et al. 2021. Successful management of single system ectopic ureter with preserved renal function in a female child: a case report. *International Surgery Journal* 8(3):1033-1035. DOI: 10.18203/2349-2902.isj20210944
10. McAninch, J.W. and Lue, T.F. 2020. Smith & Tanagho's General Urology 19th edition. Chapter 37: Disorders of The Ureter and Ureteropelvic Junction. McGraw-Hill Education
11. Senel, U. et al. 2015. Ectopic Ureter Accompanied by Duplicated Ureter: Three Cases. *Journal of Clinical and Diagnostic Research* 9(9): 10-12. DOI: 10.7860/JCDR/2015/13933.6446