Developmental & Structural Anomalies of the Genitourinary Tract

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Introduction

• Congenital Anomalies of the Kidney & Urinary Tract (CAKUT)
Objectives

• To review the embryogenesis of UGS and dysmorphogenesis of CAKUT

• To describe the common CAKUT in children

• To emphasize the role of imaging in the diagnosis of CAKUT
Introduction

• CAKUT refers to gross structural anomalies of the kidneys and or urinary tract present at birth.

• Malformation of the renal parenchyma resulting in failure of normal nephron development as seen in renal dysplasia, renal agenesis, renal tubular dysgenesis, and polycystic renal diseases.
Introduction

• Abnormalities of embryonic migration of the kidneys as seen in renal ectopy (eg, pelvic kidney) and fusion anomalies, such as horseshoe kidney.

• Abnormalities of the developing urinary collecting system as seen in duplicate collecting systems, posterior urethral valves, and ureteropelvic junction obstruction.
Introduction

• Prevalence is about 3-6 per 1000 births

• CAKUT is one of the commonest anomalies found in human.

• It constitute approximately 20 to 30 percent of all anomalies identified in the prenatal period

• The presence of CAKUT in a child raises the chances of finding congenital anomalies of other organ-systems
Why the interest in CAKUT?

• Worldwide, CAKUT plays a causative role in 30 to 50 percent of cases of end-stage renal disease (ESRD),

• The presence of CAKUT, especially ones affecting the bladder and lower tract adversely affects outcome of kidney graft after transplantation
Why the interest in CAKUT?

• They significantly predispose the children to UTI and urinary calculi

• They may be the underlying basis for urinary incontinence
Genes & Environment Interact to cause CAKUT?

• Tens of different genes with role in nephrogenesis have been identified. Notable ones include the PAX2, WT1, WAGR, RET, genes as well as genes involved in the renin angiotensin system.

• Genetic disorders are more commonly found in syndromic CAKUT than in non syndromic CAKUT.

• The mode of inheritance is usually multi-factorial but there are cases of mendelian inheritance e.g. Polycystic Kidney disease, nephronophthisis.
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<table>
<thead>
<tr>
<th>Gene (syndrome)</th>
<th>Genetic mechanism</th>
<th>Type of RTM</th>
<th>Manifestations other than RTMs</th>
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</thead>
<tbody>
<tr>
<td><em>PAX2</em> (renal coloboma syndrome)</td>
<td>Autosomal dominant</td>
<td>Renal hypoplasia (also renal dysplasia and VUR)</td>
<td>Visual acuity defects with optic disc coloboma (also sensorineural hearing loss, Arnold Chiari malformation, seizures and joint laxity)</td>
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<tr>
<td><em>HNF1B</em> (Renal cysts and diabetes syndrome)</td>
<td>Autosomal dominant</td>
<td>Renal dysplasia, usually with cysts (also glomerulocystic disease, renal hypoplasia and hydronephrosis)</td>
<td>Diabetes mellitus, hyperuricemia and gout, hypomagnesemia and uterus malformations (and possibly chromophobe renal tumor)</td>
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<td><strong>KAL1 (X-linked Kallmann syndrome)</strong></td>
<td>X-linked recessive</td>
<td>Renal agenesis (also renal dysplasia)</td>
<td>Anosmia and hypogonadotrophic gonadism (also high arched palate, pes cavus, and synkinesia)</td>
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<tr>
<td><strong>EYA1/SIX1 (branchio-oto-renal syndrome)</strong></td>
<td>Autosomal dominant</td>
<td>No typical manifestation but can include: renal agenesis, renal dysplasia, and calyceal cysts/diverticula</td>
<td>Pre-auricular pits, branchial fistulae, and deafness</td>
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<tr>
<td><strong>FRAS/FREM2 (Fraser syndrome)</strong></td>
<td>Autosomal recessive</td>
<td>Renal agenesis</td>
<td>Cryptophthalmos, syndactyly, abnormal genitalia, laryngeal malformations, and anal stenosis</td>
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Implicated environmental factors

• The environmental causes are equally difficult to implicate but recognized ones are

• Vitamin A deficiency in the mother: associated with reduced kidney size and nephron numbers

• Use of angiotensin converting enzyme inhibitors/angiotensin receptor blockers in early pregnancy

• Infants of diabetic mothers: renal agenesis
Development of the Genitourinary System (GUS)

• The urinary and genital systems are closely associated embryologically and anatomically.

• They both develop from a common mesodermal ridge (the Intermediate mesoderm).

• Initially ducts of both systems enter into a common cavity, the Cloaca.
Embryology of the kidneys and urinary Tract

• The foetal urinary system begins to develop in the first trimester.

• The kidneys and the urinary tract develop from the primitive kidneys and the primitive collecting system.
Embryology of the kidneys and urinary Tract

• The primitive kidneys are represented by the pronephros, mesonephros and metanephros (Definitive kidney). While the mesonephric duct and ureteric bud represent the urinary collecting system.

• The major part of the bladder is formed by the urogenital sinus
Pronephros

• The earliest and simplest.
• A vestigial system found in the cervical region.
• Appears at 3/52 of intrauterine life.
• Save for the caudal end of the pronephric duct it disappears at about 30/7 gestation
• It induces the appearance of the mesonephros.
Mesonephros

• The 2nd vestigial system, a more advanced system that extends from the upper thoracic to upper lumbar (L3) segments.

Its 1st excretory tubules appear early in the 4th week of intrauterine life as the pronephros regresses.

They lengthen rapidly, form an S-shaped loop, and acquire a glomerulus at their medial extremity with the tubules forming the Bowman’s capsule.
Normal Kidney Development
Some outcomes of (ab)normal embryology of the kidneys and urinary tract
Sequential & Reciprocal Induction between the ureteric bud and the metanephros

In humans each kidney has between 300,000-1,000,000 nephrons
RENAL AGENESIS

Denotes a total absence of one or both kidney-unilateral or bilateral.

• May occur because of an isolated failure of ureteric bud development or as a consequence or interference with the pronephric – mesonephric – metanephric systems.

• May be associated with partial or total absence of the genital duct systems and adrenals.
Bilateral Renal Agenesis

• BRA: 1 in 5000 foetuses
• Failure of urine production by the foetus – oligohydramnios, many affected infants demonstrate the typical POTTER FACIES which in association with BILATERAL RENAL AGENESIS = POTTER SYNDROME

CHARACTERISTIC FEATURES OF POTTER SYNDROME
• Low set and malformed ears
• Prominent epicanthic folds
• Beak-like nose with flattened tip
• Micrognathia
Bilateral Renal Agenesis

- Marked pulmonary hypoplasia
  Stillbirth and early neonatal death.
- Clubbed hands & feet
- Abnormality of joints
- Malformation of gentalia
- Many are still born & frequently low birth weight when born alive
- Survival beyond a few hours is uncommon & death is usually due to respiratory distress associated with pulmonary hypoplasia.
- N/B-: Potter facies also seen in: hypoplastic kidneys and Polycystic kidneys.
Unilateral Renal Agenesis

- More common
- Incidence of URA: 1 in 750-2900
- More frequently associated with congenital abnormalities affecting other systems e.g.
  Oesophageal atresia
  Anorectal atresia
  Congenital heart disease
- Often asymptomatic
- Incidental finding during investigation for other conditions.
Other Malformation of the Renal Parenchyma

- Renal hypoplasia/dysplasia
- Multicystic dysplastic kidney
- Polycystic kidney diseases
MINOR ABERRATIONS

- Ectopic Kidneys (A)  Horse-shoe kidney (B)
Horse-shoe Kidney

- If the 2 developing kidneys make contact in their ascent, fusion may occur resulting in Horse-shoe kidney.
- The fusion usually occurs in the lower poles.
- When the isthmus (the bridge) reaches the Inf. mesenteric artery the kidneys can rise no further.
- Kidneys are fixed in the midline and ureters are anteriorly placed leading to increase risk of trauma, UTI, Obstructive uropathy and renal stones.
Horse-shoe kidney contd.

- Commoner in Turner syndrome

- Wilms’ tumour is 2-8 x more frequent in children with Horse-shoe kidneys than in the general population.

- Increased risk of Renal cell carcinoma.

- They usually have multiple renal arteries.
Malrotated kidney

1. Failure to rotate-hilum remains anterior.

2. Rotation of the kidney proceeded too far – hilum faces posteriorly

3. Arrest of rotation-hilum faces laterally
   - Ass.-ectopic kidneys
   - risk of trauma
Ectopic kidneys

1. **Unilateral**
   - Commonly remain in the pelvis close to the common iliac artery.

2. **Discoid ("pancake") kidney**
3. **Crossed renal ectopia**
   - Both kidneys cross to one side
   - With or without fusion.

4. **Unilateral fused kidney**
   - Fusion occurs in the pelvis during development.
Supernumerary kidney

- Rare
- Results from the formation of two metanephric diverticula.
- It usually has its own ureter.
Abnormalities of migration of embryonic kidney

Pelvic kidney
- Horse shoe kidney
- Crossed fused ectopia
POLYCYSTIC KIDNEY DISEASE

- Usually bilateral
- Kidneys usually very large and consists largely of cysts of various sizes.
- There are 2 main forms of Polycystic Kidney Disease:
  - Autosomal Recessive Polycystic Kidney Disease (Infantile PKD, RPKD)
  - Autosomal Dominant Polycystic Kidney Disease
AUTOSOMAL RECESSIVE PKD

• Rare condition.
• Estimated incidence is 1 in 40,000
• Can present at any time from neonatal period to adolescence
• Recognised at birth b/c the kidneys are so large that they can obstruct labour
• A-R inheritance
• Clinical features vary with differing age but one constant feature is involvement of the liver.
• Early death is usually as a result of respiratory complications – RDS, pneumomediastinum, pulmonary hypoplasia.

• An early feature in young infants is severe hypertension, congestive cardiac failure.

• Other features in the N/B period include – Potter facies, FTT, Renal impairment.
• In older children features are:
  • - Progressive renal failure
  • - Failure to thrive
  • - Severe Hypertension
  • - Congestive cardiac failure
  • - Portal Hypertension (< 5 years)

• N/B Perinatal
• Neonatal Variants described
  • Infantile
  • Juvenile
JUVENILE TYPE

They have very marked cystic liver in addition to cystic changes in the kidney. They develop liver cirrhosis and die of liver failure.
AUSTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

Transmitted as A-D with almost 100% penetrance by the 8\textsuperscript{th}/9\textsuperscript{th} decade

Accounts for 8% of adults requiring ESRF management in Europe

Gene localized to chromosome 16

PDK1 and PDK2 genetic mutations described with PDK1 more associated with progression to ESRD.

Many patients will initially have symptomless abdominal masses
Usually present from about 40 years with
- Abdominal pain
- Haematuria
- Proteinuria
- Hypertension
- Chronic Renal Failure

There is liver involvement in about 30% of the patients.

Used to be called adult PKD but can present in childhood, even in the Neonatal period.
RENAL CYSTIC DYSPLASIA

May be bilateral or unilateral. Occur in 2 major situations

1) In association with congenital obstruction of the urinary tract

2) In association with certain hereditary syndromes e.g. Beckwith-Wiedemann syndrome, Zellweger’s Cerebrohepatorenal syndrome
1) Renal Cystic dysplasia is Bilateral in urethral atresia, Prune belly syndrome Posterior Urethral valves

Unilateral in ipsilateral obstruction e.g. Ectopic ureteroceles, Ureteric atresia
A histologic diagnosis –
Cortical and medullary cysts and structural disorganization of the kidneys.
+ presence of primitive ducts and cartilages.

Other cystic kidney disorders
Medullary Sponge Kidneys
Juvenile Nephronophthisis
MALFORMATIONS OF THE URINARY TRACT

PELVURETERIC JUNCTION
- Intrinsic-stenosis
- Extrinsic-aberrant artery

URETERO-VESICAL AXIS
  Ureterocoele, Ureteric

BLADDER
Urachal cyst
Persistent Urachus
ECTOPIA VESICA (Bladder Extrophy)
BLADDER EXSTROPHY

Occurs 1 in every 35,000 to 40,000 birth
Male : Female ratio is 2:1
Varies in severity
ECTOPIA VESICAE (The classical bladder exstrophy), there is
• Bladder protrusion from the defective abdominal wall with exposure of the mucosa
• The umbilicus is displaced downward
• The pubic rami are widely separated in the midline and waddling gait
• The penis is epispadiac and the scrotum broad

If untreated, urinary incontinence and increased incidence of bladder cancer usually adenocarcinoma

Mx – cover with plastic wrap to keep moist
  - prompt transfer to appropriate centre
  - staged reconstructive surgery
OBSTRUCTIVE UROPATHY

Obstruction to urine flow in the urinary tract leading to stasis, dilatation and infection. If not diagnosed early renal failure results. Normally urine flow occurs in a stream and without effort. With obstruction there may be dribbling, straining and dysuria, + reflux of urine.
May have distended bladder + urinary ascites

Kidneys may become hydronephrotic in long-standing cases, renal impairment, failure to thrive, anorexia and vomiting

N/B lower urinary tract obstruction is the most common cause of neonatal ascites – Rupture of dilated renal pelvis and extravasation of urine
PELVICURETERIC JUNCTION (PUJ OBSTRUCTION) OR (UPJ OBSTRUCTION)

This is the most common obstructive lesion in childhood and is usually caused by intrinsic stenosis.

At times an accessory artery to the lower pole of the kidney also causes extrinsic obstruction.
PELVIRETIC JUNCTION (PUJ OBSTRUCTION) OR (UPJ OBSTRUCTION)

Most commonly presents

1. On maternal ultrasonography revealing foetal hydronephrosis
2. As a palpable renal mass in a N/B or infant
3. As abdominal, flank or back pain
4. As a febrile UTI or
5. As haematuria after minimal trauma

~ 60% of cases occur on the left side
M:F ratio = 2:1
10% are bilateral
Rx-Pyeloplasty
PRUNE-BELLY SYNDROME (TRIAD SYNDROME OR EAGLE-BARRETT SYNDROME)

Characterised by – Deficient abdominal muscle
- Undescended testes
- Hydronephrosis

(Probably resulting from severe urethral obstruction in foetal life)
Prune belly syndrome
Occurs in 1 in 40,000 births
95% of affected individuals are male
May have other abnormalities
- Very large bladder and ineffective bladder emptying
- Musculoskeletal
- Cardiac
- Malrotation of the bowel and
- of urethra, uterus and vagina in females.
Ultimate prognosis depends on degree of Pulmonary hypoplasia and renal dysplasia.
~ 30% develop E S R D → Transplantation
POSTERIOR URETHRAL VALVES

Most common cause of severe subvesical obstruction in the male infant.
Valves appear as mucosal folds in the posterior urethra.
Early obstruction during renal development may result in Renal dysplasia
CLASSICAL FEATURES

Dribbling
Poor urinary stream in neonates and infants
Bladder distention
± Symptoms of uraemia and infection
Diagnosis can be made prenatally by USS which reveals an enlarged bladder and hydronephrosis.
Later in infancy-
Vomiting
  Failure to thrive – $2^0$ to CRF
  Dehydration – $2^0$ to Diabetes Insipidus
  Consequent on the obstructive uropathy

Older children
Enuresis may be the presenting complaint
Micturating cystourethrogram is diagnostic and shows dilated, elongated posterior urethra and trabeculated bladder
Imaging & Investigations

• USS
• MCUG
• Cystoscopy
• Dimercaptosuccinic acid scan
• Urodynamics
• Others: serial electrolyte, urea and creatinine, acid-base status
Kidney & Bladder USS

Hydronephrosis

Thickened bladder wall & key hole appearance
MCUG

Sacculations  Bilateral severe VUR

High Grade VUR

Trabeculated Bladder

Dilated posterior Ure

Valves
Voiding cystourethrogram in an infant with posterior urethral valves. Note the dilatation of the prostatic urethra and the transverse linear filling defect corresponding to the valves.
Dimercaptosuccinic Acid Scan

- Cortical defects
- Delayed clearance of tracer from both kidneys
+ IVU – Not routinely done
  May show extensive hydronephrosis and hydroureters

**Immediate Rx**
- Fluid and electrolyte correction
- Metabolic acidosis
- Na\(^+\) depletion
- Dehydration
Establish bladder drainage by urethral or suprapubic catheterisation
Urinary diversion – bilateral loop ureterostomy in very ill pts.

Sepsis screen and Give Antibiotics if sepsis suspected

Definitive Rx
Surgical Excision of valves
Obliteration of valves with diathermy, laser surgery
Antenatal intervention – prenatal bladder decompression by percutaneous vesico-amniotic shunt
- Open foetal surgery etc.

To be followed up.
Prognosis depends upon the severity of renal damage and dysplasia at the time of diagnosis.
Prognosis

Favorable prognostic factors include:

• Having a normal prenatal ultrasonogram between 18 and 24 wk of gestation,
• A serum creatinine level less than 0.8 to 1.0 mg/dL after bladder decompression,
• Visualization of the corticomedullary junction on renal sonography.
• There are several situations in which a “popoff valve”; may occur during urinary tract development, which preserves the integrity of one or both kidneys.
Unfavorable prognostic factors include:

- The presence of oligohydramnios in utero,
- Identification of hydrenephrosis before 24 wk of gestation,
- A serum creatinine level greater than 1.0 mg/dL after bladder decompression,
- Identifying cortical cysts in both kidneys
- Persistence of diurnal incontinence beyond 5yr of age.
Situations with Pop-off valves

• For example, 15% of boys with posterior urethral valves have unilateral reflux into a nonfunctioning dysplastic kidney, termed the VURD syndrome (valves, unilateral reflux, dysplasia).

In these boys, the high bladder pressure is dissipated into the nonfunctioning kidney, allowing normal development of the contralateral kidney.
• In newborn boys with urinary ascites, the urine generally leaks out from the obstructed collecting system through the renal fornices, allowing normal renal development.
Causes of Antenatal Hydronephrosis

- Anomalous PUJ/UPJ obstruction*
- Multicystic Kidney*
- Retrocaval ureter
- Primary obstructive mega ureter*
- Nonrefluxing nonobstructed megaureter*
- Vesicoureteral reflux*+
- Midureteral stricture*
- Ectopic ureter*
• Posterior urethral valves+
• Prune belly syndrome+
• Urethral atresia+
• Hydrocolpos+
• Pelvic tumour*
• Cloacal abnormality+
• May be unilateral or bilateral
+ Bladder may be distended
Primary vesicoureteric reflux is thought to be caused by a maturational abnormality of the vesicoureteric junction, so that urine passes in a retrograde manner up the ureter.

Although the exact prevalence in the general childhood population is unknown, about 1/3rd of children with UTI have consistently been found to have reflux.

Urinary tract infection occurs in approximately 5–10% of children, and so 1–3% of children are identified with vesicoureteric reflux.
VUR

• It is believed that vesicoureteric reflux is a predisposing factor for urinary tract infection, which in turn may involve the kidney substance and cause permanent renal injury.

• Thus, the central management strategy for children with vesicoureteric reflux has been the avoidance of urinary tract infection induced damage.
This has been attempted by surgical correction of reflux and long term antibiotic prophylaxis, either singly or in combination.

In addition to the common Politano-Leadbetter and Cohen surgical techniques, new, less invasive techniques which involve endoscopic periureteral injection of polytetrafluoroethylene, glutaraldehyde cross linked bovine collagen, dextranomer/hyaluronic acid copolymer, or polydimethylsiloxane have been carried out.
Renal Dysplasia/Multicystic Dysplastic Kidney

• Commonest CAKUT
• Dysplasia = abnormal differentiation
• characterized by the presence of primitive ducts and cartilages on histology.
• The corticomedullary differentiation and reiform shape of the normal kidney are lost
• Unilateral, Bilateral, Focal or Segmental.
• In unilateral or bilateral RD the ureter is usually atretic and non functional
• Multicystic Dysplastic Kidney: Dysplastic kidneys PLUS multiple non-communicating cysts. It is usually unilateral.
• 20-30% have dysplasia or vesico-ureteric reflux in the other kidney

The natural history of MCDK: complete or partial involution in the first few years; compensatory hypertrophy of the contralateral kidney
Preserved corticomedullary differentiation  No corticomedullary differentiation
USS: Multicystic dysplastic Kidney

DMSA Scan

Hydronephrosis
Malformation of the Bladder

**Trigonitis:** a transitional type to squamous type epithelium which can overproliferate and lead to urinary blockages

**Abnormal attachment of the ureters:** the ureters can sometimes be attached to either to the urethra or parts of the reproductive tracts.

**Urachal fistulas, sinuses, and cysts:** occur when a remnant of the allantois persists
• Thank You