Inherited Kidney Diseases and Developmental Abnormalities of the Urogenital Tract

Block 11

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Congenital Abnormalities of Urogenital Tract

• **Congenital abnormalities of the UGT are common**
  – Occurs in up to 10% of the population
  – Contributes to $\frac{1}{3}$ of all congenital abnormalities

• **Discovered when complications develop**
  – UTI
  – Abdominal mass palpated
  – Investigation for poor weight gain
  – Routine urine test (co- incidental finding)

• **Often detected with routine antenatal u/s**
Embriology

The kidney originates from two main structures

- **Ureteric bud** –
  Abnormal development affects the –
  - Renal collection system
  - Calyces
  - Pelvis & ureter

- **Metanephros (Metanephric blastema)**
  Abnormal development affects the –
  - Nephrons
Genitourinary Tract Embriology

- Pronephros
- Mesonephros
- Metanephros
- Intermediate mesoderm
- Cloaca
- Ureteric bud
- Metanephric blastema
Development of UGT at 6-8 weeks
Renal Parenchymal Abnormalities

- **Renal agenesis / renal hypoplasia**
  - Result of abnormal induction of nephrogenesis
  - Apoptosis is a programmed form of cell death
  - Due to imbalance of apoptotic and growth factors
  - ↑ apoptosis or
  - Relative deficiency of cellular growth factors
Renal Agenesis and Hypoplasia

• Renal agenesis = absent kidney

• Hypoplasia = kidney $\leq \frac{1}{3}$ of normal size
  – May occur uni- or bilaterally
  – 90% is sporadic
  – 10% is familial
Unilateral Renal Hypoplasia

• Patients usually remain asymptomatic

• Contralateral kidney
  – Compensatory hypertrophy
  – Compensatory function

• Renal function is normal

• Occasionally hypertension develops
Renal outcome of children with one functioning kidney from birth

Study of 99 patients and a review of the literature

Does progressive CKD develop in patients with a single functioning kidney from birth within a period of 10 years?

Vu K-Hahn Van Dyck M et al
Pediatr Nephrol 2008;167: 885-89
Literature

- 9 ± comparable studies on fate of solitary kidneys in childhood over past 22 yrs
- All indicate: variable % will develop HT, ↓ GFR and proteinuria
- Study that best illustrates the risk of solitary kidney: (Baudoin et al)
  - heterogeneous cohort of 111 patients
  - nephrectomy < 16 years
  - demonstrate that the incidence of
  - ↓ GFR, HT, and proteinuria increases with time to become striking with FU of over 25 years
Conclusion

Individuals with single functioning kidney for whatever reason deserve long-term FU during and after childhood.
Bilateral Renal Hypoplasia

- Degree of renal functional impairment varies
- Clinical problems:
  - polyuria
  - polydypsia
  - dehydration
- Tubulopathy: “salt-losing nephropathy”
  - → poor growth
- Develop progressive renal functional impairment
Bilateral Renal Agenesis

- Occurs in 1/4000 pregnancies
- Mother has oligohydramnios
- Baby has Potter Sequence
- Baby dies shortly after birth due to respiratory distress / hypoplastic lungs
Cystic Renal Diseases

• Multicystic kidney

• Polycystic Kidney Disease
  – Autosomal Recessive PCKD
  – Autosomal Dominant PCKD
  – Medullary Cystic Kidneys
Multicystic Kidney

- Usually unilateral

- Morphology
  - Large irregular mass
  - Consists of undifferentiated *dysplastic* elements and cysts of different sizes

- Non-functional kidney

- Associated with pelvis/ureter abnormalities on contralateral side

- Because MCDK is usually unilateral, it is
  - Asymptomatic or
  - Discovered when abdominal mass is detected
Multicystic Dysplastic Kidney
Polycystic Kidneys (PCKD)

• Inherited kidney diseases

• Two different forms of inheritance
  – Autosomal Dominant (ADPCKD)
  – Autosomal Recessive (ARPCKD)

• Bilateral enlarged kidneys
ADPCKD ("Adult PCKD")

- Incidence 1/1000 of the general population
- Bilateral large kidneys, with normal shape
- Large cysts of varying sizes
  - May have cysts in liver, lungs and pancreas
- Usually symptomatic by 3\textsuperscript{rd} to 4\textsuperscript{th} decade
- Presents with HT, UTI and CRF
- Cerebral aneurisms -\↑ risk of intracranial haemorrhage
ADPCKD
("Adult PCKD")
Large kidneys
Discreet cysts
Varying sizes
Areas of normal parenchyma
ARPCKD ("Infantile PCKD")

- Bilateral large kidneys, normal shape
- **Small cysts**
- Invariably associated with **hepatic fibrosis**
- Two peak periods of presentation
  - **Neonate** –
    - Potter sequence due to oligohydramnios
    - RDS due to hypoplastic lungs, respiratory failure
  - **Older child** –
    - Poor growth
    - Severe hypertension
    - CRF and hepatic fibrosis
ARPCKD
Diffuse small cysts & bilateral renal enlargement
ARPCKD
Developmental Abnormalities of the Ureteric Bud & Urinary Drainage System

Pelvo-Ureteric Junctional Obstruction (PUJ)

– Dilated pelvis

– Usually unilateral

– Contralateral kidney may have abnormality -
  
  • Vesico-ureteric reflux (VUR)

  • Cystic dysplastic kidney
Vesico-Ureteric Reflux (VUR)

- More common in Caucasians compared to Blacks
- Genetics play a role
- Occurs in 30-50 % sibs of index case
- Usually presents with recurrent UTI
Pathogenesis of VUR

- Abnormal development of the ureteric bud
- VUR more common in young babies
- May outgrow VUR by age 2 years
- In adults the ureters
  - pursue a 1-1.5 cm sub-mucosal oblique course through the bladder wall – longer tunnel
- In infants the ureters
  - have a shorter tunnel and open perpendicular into the bladder wall
Etiology and Pathogenesis of VUR

• Pathologically refluxing ureters
  – Located more lateral and cephalad in the bladder
  – Short submucosal tunnel
  – Perpendicular course through bladder wall
  – Gaping opening in the bladder
5:1 tunnel length to wall ratio

Paquin (1959)
Aetiology of VUR

Balance of functional and anatomical factors
International Classification
Vesico-Ureteric Reflux Grades
Voiding cystogram
Grade I VUR in the right ureter
VCUG
Right Grade IV
VUR
VCUG

- Grade V VUR
- Severe hydronephrosis
- Blunting of calyces
- Thinning of renal cortex
- Tortuous and wide ureters
Developmental Abnormalities of the Urethra

**Congenital Obstructive Posterior Urethral Membrane (COPUM)**

- Usually in boys (95%); rarely in girls
- Developmental abn. of the posterior urethra $\rightarrow$ outlet obstruction of the bladder
- Associated with
  - oligohydramnios
  - varying degrees of renal dysplasia
- If oligohydramnios develops before 16$^{th}$ week of gestation $\rightarrow$ very poor prognosis
Clinical Presentation

• Potter sequence

• Respiratory distress at birth

• Bilateral palpable kidneys

• Bladder palpable above pubis

• Dribbling of urine or total obstruction

• May present with urinary ascites
Prune Belly Syndrome

- Consists of triad:
  - Non obstructive megacystis
  - mega-ureter and hydronephrosis
  - Absence of abdominal wall muscles
  - Undescended testes (cryptorchidism)
Potter Facies
Voiding cysto-urethrogram

Dilated posterior urethra
Indentation by prominent bladder neck
Small trabeculated bladder
Voiding cysto-urethrogram

Dilated posterior urethra
Indentation : Narrowing
Trabeculated bladder
Recommendations

• All patients with congenital abnormalities of kidneys or single functioning kidneys deserve regular FU
• At 2 years kidney function is mature – good time to evaluate kidney function
• At all visits do
  – Growth assessment
  – Blood pressure
  – Urine dipstix
  – Spot u: protein:creat ratio or micro albuminuria (marker of glomerular hypertrophy and hyperfiltration)
  – GFR should be estimated once a year
• If signs of progression are documented, ACEI may be indicated
References

Illustrations, diagrams and photos

• Thomas DFM, Rickwood AMK, Duffy PG. Essentials of Paediatric Urology. London: Martin Dunitz Ltd; 2002