Anomalies and cystic diseases of the kidney

Fast introduction 🤔:

- 10% of individuals have urinary tract malformations (many of them asymptomatic)
- 15% of congenital urogenital anomalies —> secondary to chromosomal disorder
- Children --> 20% of chronic renal failure --> due to renal dysplasia or hypoplasia
- Adults —> 10% of chronic renal failure --> due to polycystic Kidney disease

Agenesis	Duplication of ureter	Ectopic (displaced) kidney	Horseshoe kidney	Hypoplasia
Meaning: Complete absence of renal tissue unilateral or bilateral Bilateral agenesis: incompatible with life • associated with large adrenal glands —> leads to Potter (oligohydramnios) sequence; possible causes include: maternal insulin dependent diabetes mellitus and male sex of fetus but usually no specific etiology Unilateral agenesis: not fatal	Usually asymptomatic may be associated with obstruction	kidney ال ما بتكون في مكانها Usually at pelvic brim may have kinking of ureters	1) Most common congenital kidney anomaly 2) 90% —> fused at lower pole 3) Associated with obstruction, anomalous superior vena cava 4) Complete fusion of the kidneys produces a formless mass in the pelvis (pancake kidney) ↳ Fused at upper and lower lobes 5) Has a clear association with turner syndrome	1) Rare 2) failure of kidney to develop to normal size without scarring 3) Usually unilateral with a reduced number of nephrons and pyramids (6 or less) 4) normal architecture 5) Associated with PAX2 mutations 6) Oligomeganephronia: type of hypoplasia with small kidney but hypertrophied nephrons due to compensatory hypertrophy caused by reduced number of nephrons

Done by: Kareem Obeidallat

Affect adults

Autosomal dominant polycystic kidney disease

1) mutations in genes coding for:
- polycystin 1 (PKD1, chromosome 16p, most common)
- polycystin 2 (PDK2, chromosome 4q)

**PDK1,2 encode proteins present in renal tubular epithelia cells

**PDK1:
-transmembrane protein
-located on primary cilia and cell membranes of renal tubular epithelial cells
-85% of ADPKD

mutation → Polycystin 1 / 2

**PDK2:
-Cation channel
-located on primary cilia and cell membranes and endoplasmatic reticulum of renal tubular epithelial cells
-15% of ADPKD

**Defect in PC1,2:

disrupt calcium homeostasis
↓
decreased intracellular calcium
↓
increased cAMP
↓
increased vasopressin action
(retention of fluid and cell proliferation)

- Can lead to impaired regulation of pathways.

2) Associated with TSC2 / PKD1 contiguous gene syndrome

3) Usually inherited
**new mutations without a family history occur in approximately 10%

4) Births 1,000 / 2 - 1 (كل ألف مولود ممكن تطلع عند ١ أو ٢)

5) M = F (مدى تأثيره على الذكور مساوٍ للإناث)

Pathophysiology

6) Mutated proteins are involved in:
- cell differentiation
- polarization
- proliferation and membrane transport

7) The exact mechanism of cyst formation is not yet understood

8) Cysts form in all regions of the nephron, enlarging and expanding throughout life

9) Normal renal function is maintained until mid adulthood in most patients

Clinical features

10) Third most common cause of end stage renal disease

11) Patients present with:
haematuria, abdominal pain, hypertension, urinary tract infection or urolithiasis (stones formation)

Affect children

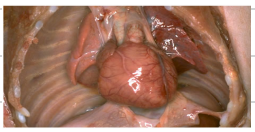
Autosomal recessive polycystic kidney disease

1) Mutations in PKHD1 gene
(Polycystic Kidney and Hepatic Disease 1
(produces fibrocystin / polyductin)
** at 6p12 expressed in kidney, pancreas and liver

2) Usually presenting with bilateral renal cystic disease

3) birth 1 per 20,000 live births

4) Patients present prior to or at birth with frequent complications due to:
- limited urine output including oligohydramnios
- Potter sequence
- joint deformities
- pulmonary hypoplasia →



5) Early mortality is most common
(usually due to pulmonary complications)

6) Perinatal mortality 30 - 50%
5 year survival is 80 - 95% if survive first month of life

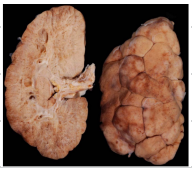
7) In surviving cases with pulmonary hypoplasia
(kidneys must be removed to allow for growth of lungs)

8) no cysts other than kidney and liver but liver is always affected

9) (every portal triad, every case) with:
- herring duct cysts (ductal plate malformation)
- congenital hepatic fibrosis

10) Patients later develop:
- hypertension
- renal insufficiency
- portal hypertension
- splenomegaly or cholangitis

11) May also include older patients presenting with:
- hepatosplenomegaly
- hypersplenism
- variceal bleeding and cholangitis



12) Gross Description

1) enlarged kidneys with smooth surface
2) Small cysts in cortex and medulla (collecting ducts)
3) Dilated channels are perpendicular to cortical surface

13) Microscopic (Histologic) Description

1) Radially arranged

2) Elongated cysts that form as dilations of all collecting tubules with fluid accumulation

3) Cysts lined by cuboidal or flattened cells from collecting tubules

4) Normal nephrons without cystic change
(interstitial fibrosis are present in between the cysts)

5) The liver shows portal fibrosis with complex bile ductular profiles

12) Associated with:

- Extrarenal cysts
- In CVS:

mitral valve prolapses (20%) and aortic aneurysms

- In CNS:

berry aneurysms (10% - 30%)

- In GI:

1) Cysts in pancreas, lung, spleen, pineal gland and seminal vesicles

2) Hepatic fibrosis and intestinal diverticula

- Von Meyenburg Complexes in liver
- Hepatic cysts (40% - 88%)

الدكتور حكى بالأرقام هاي فهاظا

13) Causes of death:

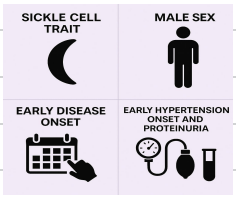
25% die from infection

40% from hypertension and heart disease

15% from berry aneurysms or stroke

(MC cause of death is ruptures berry aneurysms)

14) Prognostic factors



**Poor prognosis:

1- Male
2- Early disease onset
3- Sickle cell trait
4- Early hypertension
5- Proteinuria

Note

Healthy nephrons compensate for damaged nephrons in early stages of ADPKD

**Treatment:

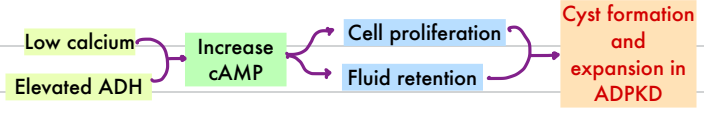
1- Laparoscopic nephrectomy
2- Transplant

Vasopressin (AVP or ADH)

1) powerful modulator of cytogenesis

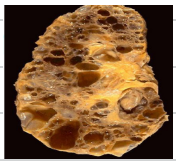
2) Act through binding V2 receptors and stimulation of cAMP production

3) Elevated in ADPKD



15) Gross description

- Markedly enlarged kidneys (up to 8 kg) composed of sub-capsular cysts up to 4 cm
- Cysts contain clear to brown fluid
- Cysts in cortex and medulla

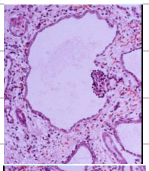


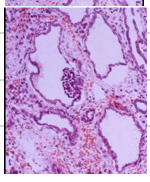
16) Microscopic (histologic) description

1) Cysts are lined by cuboidal or flattened epithelium, may have papillary projections or polyps

2) Functional nephrons exist between cysts with areas of global sclerosis, tubular atrophy, interstitial fibrosis and chronic inflammation

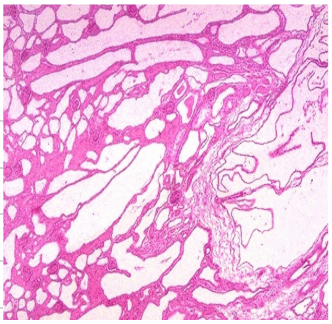
3) Infants may show primarily cystic dilatation of Bowman's space have renal adenomas 20%

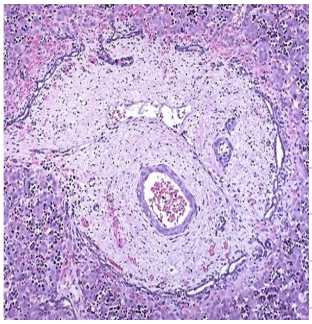




Note

Progression of ADPKD can be difficult to track because kidney function alone is not an effective indicator of disease advancement





Done by: Kareem Obeidallah

Acquired Cystic Kidney Disease

General features

1) Three or more cysts per kidney

2) Occurs:
10-20% –> first 3 years of dialysis
50% –> first 5 years of dialysis
90% –> after 10 years of dialysis

3) occurs in patients with long term uremia prior to dialysis

4) Increased (7 – 50x) risk of renal cell carcinoma ((7% at 10 years), but death is rare)

Cause:
longstanding hemo- or peritoneal dialysis for end stage renal disease (unrelated to underlying renal pathology)

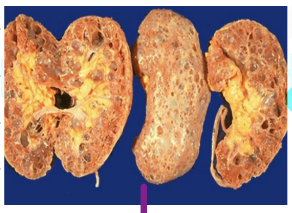
Affect Males > females
(during first ten years of dialysis)

** Not restricted to adults
(occurs in children and young adults on dialysis)

Gross Description

Moderately enlarged kidneys (usually < 800 g) with cortical and medullary cysts (containing clear fluid)

replacement of kidney with cysts < 40%



kidneys are about normal in size
have few scattered small cysts
(none of which is over 2 cm in size)
This is cystic change associated with chronic renal dialysis

Microscopic (Histologic) Description

1) Cysts lined by:
flattened or cuboidal epithelium that may show focal pseudo papillae with:
1) nuclear enlargement 2) loss of polarity

2) Cysts may contain oxalate crystals

3) Surrounding parenchyma shows:
- global glomerulosclerosis
- interstitial fibrosis
- tubular atrophy

Medullary Sponge Kidney

(Sporadic cystic disease)

congenital disease but most often occurs sporadically without a defined inheritance pattern

General features

0.1 to 0.5 cm cysts involving the inner medullary and papillary regions in this kidney

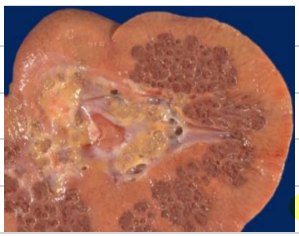
1) Bilateral cystic dilations of medullary collecting ducts
** normal cortex
** incidental and found only on radiologic imaging studies
** incidence of 0.5 to 1% in adults

2) 1 per 5000 births

3) no gender preference (not familial)

4) Associated with:
- hemihypertrophy of body (25% of cases)
- Marfan's syndrome
- Caroli's syndrome
- Ehlers-Danlos syndrome

Gross Description



1) Normal sized kidneys

2) multiple, small cysts in medullary pyramids

3) papillae, giving medulla a sponge-like appearance

4) Most often bilateral

Stones هي أحد الأسباب لأنه بتفرز من acidity إلي

Management
- Cranberry juice to maintain urinary acidity
- Nephrectomy is NOT recommended

5) Usually presents in adulthood

6) Usually asymptomatic with normal renal function

There will be:
- Calcifications on X-rays
- stones
- haematuria
- infection at age 30+ years

7) Does not progress to end stage renal disease

8) Diagnosed with intravenous pyelography

9) MSK may become symptomatic in young adults
- with onset of recurrent hematuria
- and/or urinary tract infection as a consequence of formation of calculi (which develop in 60% of cases)

10) Renal failure is unlikely to occur, but may result from severe pyelonephritis

Microscopic (Histologic) Description

1) Medullary cysts lined by cuboidal epithelium or urothelium

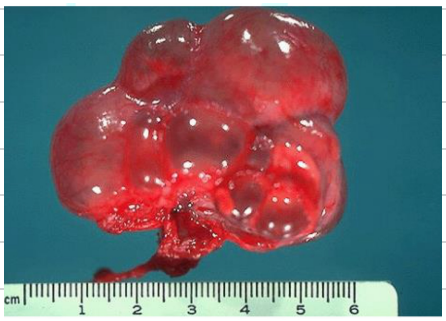
2) May have concretions adherent to cyst wall

3) Often severe inflammation

4) Scarring in interstitium

5) Tubular atrophy near papillary tips.

multicystic dysplastic kidney



must be distinguished from ARPKD, why??

1- occurs only sporadically

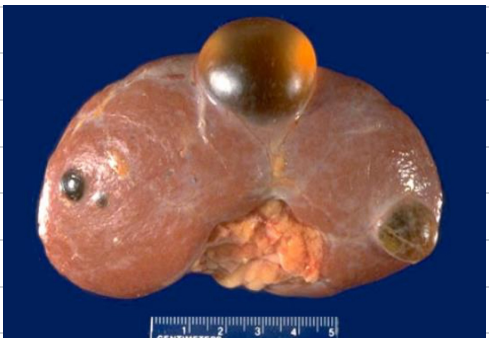
2- not with a defined inheritance pattern
(it is more common than ARPKD)

3- Cysts are larger
(more variably sized than those of ARPKD)

** Often is unilateral
- If bilateral, it is often asymmetric
- If bilateral, oligohydramnios and its complications can ensue,

(just as with ARPKD)

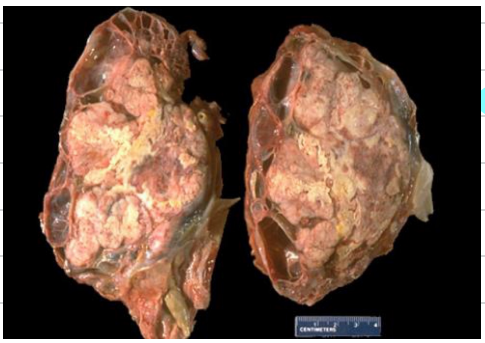
Simple renal cysts



1) Thin walls and are fluid filled

2) They can be multiple, but:
- they are never as numerous as with polycystic change
- They do not predispose to chronic renal failure or to neoplasia.

3) become more common as persons become older



- Cystic change resulting from long-term renal dialysis may rarely give rise to renal cell carcinoma

- A large irregular tan variegated mass is seen

Done by: Kareem Obeidallah

UGS-Pathology Lecture 5

1. One of the following causes end stage renal disease :

a. Autosomal dominant polycystic kidney disease

b. horseshoe kidney

c. floating kidney

d. ectopic kidney

Clinical features

10) Third most common cause of end stage renal disease

11) Patients present with:
haematuria, abdominal pain, hypertension, urinary tract infection or urolithiasis (stones formation)

Ans: a

2. which of the following is false :

a. Autosomal dominant PKD is most commonly caused by polycystin 2 mutaion

b. Acquired cystic kidney disease may progress to renal cell carcinoma and is not exclusive to adults

c. Autosomal recessive PKD is caused by fibrocystin mutation

Ans: a

Affect children

Autosomal recessive polycystic kidney disease

1) Mutations in PKHD1 gene
(Polycystic Kidney and Hepatic Disease 1
(produces fibrocystin / polyductin)
** at 6p12 expressed in kidney, pancreas and liver

4) Increased (7 – 50x) risk of renal cell carcinoma
((7% at 10 years), but death is rare)

** Not restricted to adults
(occurs in children and young adults on dialysis)