Renal system pathology

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**Congenital anomalies:**

**Agenesis of the kidney:(No kidney)**

Bilateral agenesis is incompatible with life, seen in stillborn. Unilateral type is uncommon.

**Hypoplasia:(small kidney)**

Is failure of the kidney to develop to a normal size. This anomaly may occur bilaterally, resulting in renal failure in early childhood death.

* In **unilateral** cases of **both** **agenesis and hypoplasia**, the opposite kidney is usually enlarged as a result of **compensatory hypertrophy**

**Ectopic Kidneys: (abnormal location)**

These kidneys lie in different location, most commonly within the **pelvis.**

**Complications** :

* Pressure on the ureters may cause some obstruction to urinary outflow.
* Difficulty in labor in females.
* Misdiagnosis as pelvic tumors & abscesses.
* Have long renal artery that may have many complications like damage during surgery.

**Horseshoe kidneys:(fused kidneys)**

Fusion of lower poles of the kidneys that is continuous across the midline anterior to the great vessels. May cause many **complications:**

1. Partially obstructed the ureters, which result in hydronephrosis. 2. Recurrent UTI.

3. Stone formation.

**Cystic Diseases of the Kidney**

* They are heterogeneous group comprising hereditary, developmental and acquired disorders characterized by formation of cysts in the kidney.
* They are important for several reasons;
* They are reasonably common and often represent diagnostic problems for clinicians, radiologists and pathologists.
* Some forms are major causes of chronic renal failure.
* They can occasionally be confused with malignant tumors.   
  **Classification of cystic disease:**

1-congenital Polycystic kidney :

* Autosomal Dominant (AD-ults)
* Autosomal Recessive (Children)

2-Acquired

A-SIMPLE

B-(dialysis-associated) cystic disease.

C-Parasitic cysts (e.g. hydatid cyst).

**Adult poly cystic kidnedy:**

* Bilaterally enlarged kidneys with multiple expanding cysts that ultimately destroy the parenchyma and cause renal failure.
* The mode of inheritance is **autosomal dominance** .
* The cysts initially involve only portions of the nephrones, so renal function is retained until about the 4th or 5th decade of life.
* gene mutation located on chromosome **16p** (**PKD1**) and **4q (PKD2).**

Mutation of PKD1 accounts for about 85% of the cases and are associated with a more severe disease.  
**Morphologically:**

**Grossly** both kidneys are enlarged .The external surface appears to be composed of a mass of cysts , filled with clear serous fluid or hemorrhagic fluid.

**Microscopically** functioning nephrons exist between cysts, cysts arise from tubules and therefore have variable lining epithelium

**Clinical:** Many of these patients remain asymptomatic until renal insufficiency occurs.

Presentation (variable): 15-30 years old, flank pain, hypertension, hematuria, progressive renal failure ,

40% have cystic disease of the liver (most common), spleen, pancreas, brain

**Berry aneurysms** in circle of Willis and can cause death in about 4-10% of patients due to **subarachnoid hemorrhage**.

**No** increase in risk of development of renal cell carcinoma

Death due to uremia or hypertension or ruptured Berry aneurysm.

**Autosomal Recessive (Childhood) Polycystic Kidney Disease**

* Is rare anomaly. Perinatal, neonatal, infantile and juvenile types. The first 2 are the most common.
* Defective gene is , **PKHD1**, on chromosome **6**.  
  **morphology;**

The kidneys are enlarged (bilateral) and have a **smooth** external surface. On cut section, numerous small cysts in the cortex and medulla give the kidney a **sponge-like appearance**.

The cysts are **dilated channels** at **right angles** to the cortical surface (**perpendicular** to the corticomedullary junction)

**Clinical Features;** serious manifestations are usually present at birth, and the young infant might succumb rapidly to **renal failure**. Patients, who survive infancy, may develop **congenital hepatic fibrosis**.

**Acquired (Dialysis-Associated) Cystic Disease:**

* Occur in patients on chronic dialysis,
* numerous cortical and medullary cysts.
* The cysts measure 0.5-2cm, contain clear fluid, are lined by either hyperplastic or flattened tubular epithelium and often contain calcium oxalate crystals.

**Cause** of the cyst formation: They probably form as a result of **tubular obstruction** due to interstitial fibrosis or by oxalate crystals.

**Clinically:** Most are asymptomatic, but sometimes the bleeding inside the cysts cause hematuria.

**complication** is the development of **renal cell carcinoma** in the walls of these cysts in about 7% of patients during 10 years period.

**Simple cyst:**

* These occur as single or multiple, usually cortical.
* The size range from 1-10cm or more.
* They are translucent and filled with clear fluid.
* They are lined by a single layer of cuboidal or flattened epithelium.

They are common postmortem findings. On occasion, hemorrhage into them may cause sudden pain, and calcification may be visible radiologically.

The main importance of these cysts is in their **differentiation from kidney tumors.**

**Renal diseases can be divided according to the parts of kidneys into**

1. Glomerular diseases 2. Tubular diseases.

3. Interstitium diseases. 4. Blood vessels diseases.

**This division is useful because**

a. The early manifestations of each group of diseases tend to be distinctive.

b. These groups differ in their pathogenesis, for e.g., **glomerular diseases** are often **immunologically mediated**, whereas **tubular and interstitial** disorders are more likely to be caused by **toxic** or **infectious agents**. However, it should be noted that:

1. Damage to one component is almost always affects secondarily the others.

2. All forms of chronic renal disease tend ultimately to damage all four components of the kidney thus, eventuates in chronic renal failure (end-stage kidney disease).

**Glomerular disease**

**Clinical manifestations of renal diseases in general:**

1. Acute Nephritic Syndrome: characterized by

* Gross hematuria (macroscopic).
* Mild to moderate proteinuria.
* Edema.
* Hypertension
* Typical example is Poststreptococcal glomerulonephritis.

2. Nephrotic Syndrome:

* Heavy Proteinuria (> 3.5 gram of protein / 24hours).
* Hypoalbuminemia.
* Severe edema.
* Hyperlipidemia & lipiduria.

3. Asymptomatic hematuria & / or Proteinuria: Mild Glomerular abnormality.

4. Rapidly Progressive Glomerulonephritis:

* Loss of renal functions in a few days or weeks.
* Manifested by active urine sediment (hematuria, Dysmorphic RBCS, RBCS Casts).

5. Acute Renal failure:

* Oliguria (< 500 cc) or Anuria (no urine flow).
* Recent onset of Azotemia. (in Latin Azot=Nitrogen)

6. Chronic Renal failure:

* Prolonged symptoms & signs of Uremia.
* Can be the end result of all chronic renal diseases.

7. Urinary tract infection: Characterized by Bacteruria & Pyuria.

8. Nephrolithiasis: Characterized by Renal colic.

Important notes:

1. Azotemia: biochemical abnormality e.g. increases urea & creatinin in blood & largely related to decreased GFR.

Could be Prerenal Azotemia (Hypoperfusion of kidneys), renal ( due to kidney diseases), Postrenal Azotemia (obstruction below the kidney).

1. Uremia: characterized by
   * Clinical Signs, Symptoms & Biochemical abnormalities.
   * Renal damage (impair excretory, endocrine, & metabolic functions of kidneys).

**Glomerular diseases:**

**Glomeruli consist of:**

1. Capillaries (fenestrated endothelial cells, basement membrane).

2. Two layers of epithelial cells (visceral & parietal layers) & the Bowman space between them.

**Glomerular Capillary wall: consist of**

1. Endothelial cells. 2. Basement membrane.

3. Visceral layer (Podocytes with foot processes). 4. Mesengeal cells (support the whole glomerular wall).

The glomerular basement membrane shows **selective permeability**, which is **size** dependent and **charge**-dependent. **The major characteristics of normal glomerular filtration are:**

1. A high permeability to water and small solutes

2. Almost complete impermeability to molecules of the size and molecular charge of albumin.

The **podocyte**(**foot process)** is important to the glomerular barrier function by providing a distal resistance to the flow of water and a barrier to the filtration of proteins.

**Histological alteration in glomerular diseases in response to injury (in general)**

There are 5 basic tissue reactions to injury:

**1. Increased glomerular cellularity**

a. Proliferation of mesangial or endothelial cells.

b. Leukocyte infiltration, including neutrophils, monocytes, and, in some diseases, lymphocytes.

c. Formation of crescents (proliferation of parietal epithelial cells).

**2. Basement membrane thickening,** By EM, it can be resolved as one of 2 alteration;

a. Deposition of amorphous electron dense material, of immune complexes, on the endothelial or epithelial side of basement membrane, or within the GBM itself.

b. Thickening of the BM proper, as occurs in diabetic glomerulosclerosis.

3**-Hyalinization and sclerosis**, made up of plasma proteins and collagen material deposited exracellularly.

**These histologic changes can be further subdivided into;**

**Focal:** some of the glomeruli (less 80%) involved

**Diffuse**:most of the glomeruli are involved

**Segmental:** portion(segment) of the glomerulus is involved.

**Global**: entire glomerulus involved

**Pathogenesis of Glomerular diseases:**

**immune mechanisms** underlie most forms of primary glomerulopathies, and many of the secondary forms.

Immune-mediated mechanisms;  
 **1. Ab-mediated,**  
 a. In situ immune complex(Ag-Ab) deposition,

In this form of injury, immune complexes are formed **locally** by antibodies that react with **intrinsic tissue antigen** or with **extrinsic antigens "planted**" in the glomerulus from the circulation

* **Fixed intrinsic antigens** e.g. (BM) like Goodpasteur syndrome (Ab against glomerular and pulmonary BM) the deposition appears **linear** by Immunofluorescence microscopy .
* **Planted antigens** :Antibodies can react in situ with antigens that are

**Not normally** present in the glomerulus but are "**planted"** there like:

* exogenous as infectious agent or drug and
* endogenous as DNA, immunoglobulins)
* The pattern of immune deposition by immunofluorescence microscopy is **granular**

b. Circulating immune complex deposition

* Endogenous Ag (DNA, tumor)
* Exogenous Ag (infectious products)

**2. Cell-mediated T cell-mediated injury may account for some cases of glomerulonephritis (GN)**

3. Activation of **alternative complement** pathway.  
**Localization of immune complexes in the** Glomerulus

1. Subepithelial humps, 2. Epimembranous deposits, 3. Subendothelial deposits,

4. Mesangial deposits, 5. Basement membrane.

***Glomerular diseases***: either

1. **Primary Glomerulonephritis: (Major part)**

* **Diffuse Glomerulonephritis.**
* **Cresentic Glomerulonephritis.**
* **Membraneous Glomerulonephritis.**
* **Lipoid Nephrosis.**

1. **Secondary Glomerulonephritis for SLE, DM infectious diseases, malignant tumors or vascular diseases**
2. **Hereditary Glomerulonephritis.**