**Renal pathology**

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**Glomerular Diseases**

**Acute Glomerulonephropathy:**

This group is characterized by inflammatory alterations in the glomeruli and clinically by **acute nephritic syndrome**

**Acute proliferative (poststreptococcal, postinfectiuos) glomerulonephritis:**

* Common disorder (**follow Group A beta hemolytic Streptococci pharyngitis or skin infection)**
* Pathogenesis: Caused **by Immune complexes** (endogenous or exogenous complex)
* **Exogenous complex** is typically follow infections (**poststreptococcal)**
* **Endogenous complex** associated with **SLE.**

Important note:

Many infections can cause glomerulonephritis e.g. **Streptococci, Pneumococci, Staphylococci, & viruses like mumps, measles, HBV, HCV.**

**Clinically:**

* Typically occurs 1-4 weeks after a streptococcal infection of the pharynx or skin.
* It affects most frequently children aging 6-10 years, but adults of any age can be involved.
* Only certain strains of group A, Beta-hemolytic streptococci are nephrogenic.
* It is not known if these represent planted Ag, part of circulating immune complexes, or both.
* Abrupt onset of fever, malaise, oliguria and gross hematuria (smoky urine).
* The patient exhibits red cell cast in the urine, mild proteinuria, periorbital edema and mild to moderate hypertension.
* Diagnostic tests are low C3, increased ASOT.

**Morphology of poststreptococcal glomerulonephritis:**

***Under light microscope;***

1. **Diffuse** and **global** increase in the cellularity of all glomeruli.
2. Increased cellularity is due to proliferation of endothelial, Mesengeal cells, & by neutrophils & monocytes infiltration.
3. **Crescent** formation within Bowman's capsule, only **in severe cases**.

**EM: Subepithelial** deposition **of Immune complex** along the glomerular basement membrane appears as a”hump”.

**IF**, there are **granular** deposits of IgG, IgM and C3 along the basement membrane.

***Prognosis:***

* In children is better than adult. More than 95% of affected children eventually recover completely with conservative therapy.
* less than 1% do not improve, and develop a rapidly progressive form of glomerulonephropathy.
* Some of the remaining patients undergo slow progression to chronic glomerulonephropathy.
* In Adult , the disease is less benign, as only 60% of patients do recover promptly15 – 50% of patient develop End Stage Renal Disease (ESRD) within 1 – 2 decades.

**2/Rapidly Progressive (Crescentic) Glomerulonephropathy**

It is a syndrome associated with severe glomerular injury and is characterized clinically by rapid and progressive loss of renal function, and if untreated, death from renal failure within weeks or months.

Regardless of the cause, the classic histologic picture is the presence of **crescents in most of the glomeruli**

**Morphology,**

The kidneys are enlarged and pale, often with petechial hemorrhages on the cortical surfaces (flea bitten kidney).

**The histologic picture** is dominated by the formation of **crescents.**

**Electron microscopy** shows distinct **rupture in the basement membrane**.

**immunofluorescence microscopy**: according to the cause

* postinfectious cases exhibit granular immune deposits;
* Goodpasture syndrome cases show linear deposits and
* pauci-immune cases have little or no deposits.

**Nephrotic Syndrome**

**I.Minimal Change disease(Lipoid Nephrosis):**

Most common cause of nephrotic syndrome in children (mainly 2- 3 years).

**Pathogenesis of Minimal Change disease:**

* Disorders of T- Cells (unknown mechanism).
* Nephrin gene mutation (recently discovered) & mainly seen in congenital type of nephrotic syndrome (Finnish Syndrome).

**Morphology of Minimal Change disease:**

**light microscope** (LM): 1.the Glomeruli appear nearly normal.

2. Cells of proximal convoluted tubules are heavily laden with lipids (due to reabsorption of lipoproteins through diseased Glomeruli).

**Electron microscope(EM)**, there is uniform & diffuse effacement of the foot processes of the Podocytes (visceral cell).

**Clinical features**: insidious onset Nephrotic syndrome in otherwise healthy child.

**Prognosis:**

Is good (90% respond to steroid) & less than 5% of cases develop chronic renal failure.

Although adults are slower to respond, the long-term prognosis is also excellent.

**II- Membranous Glomerulonephropathy**

It is the most common cause of nephrotic syndrome in adults. Age: 30- 50 years

**Etiology and pathogenesis,**

 It is a form of chronic **immune-complex**-mediated disease.

1. **idiopathic** in about 85% of cases, and is called **primary MGN**.
2. secondary forms are identified in association with;
* Drugs (penicillamine, captopril, NSAIDS).
* Underlying malignant tumors, particularly bronchogenic carcinoma, carcinoma of colon and melanoma.
* SLE.
* Infections (Chronic hepatitis B and C, syphilis, malaria).
* Autoimmune diseases such as thyroiditis.

**Morphology,**

By **LM:** the glomeruli exhibit diffuse thickening of the glomerular capillary wall.

By **EM:** there are irregular dense deposits between the basement membrane and the epithelial cells (**Subepithelial deposits),** appearing **as irregular spikes**,

**IF:** demonstrates the **granular deposits** to contain IgG and C3 along glomerular BM.

**Prognosis:**

The disorder begins with the insidious onset of nephrotic syndrome ( **non selective proteinuria**).

The course of the disease is **variable** but generally indolent.

60% show persist proteinuria, 40% show progressive renal failure.

**III- Focal Segmental Glomerulosclerosis:**

Is characterized by **sclerosis** affecting some but not all glomeruli(focal); & involving only segments of each glomerulus(segmental).

**Causes:**

1. Idiopathic (primary disease).
2. Secondary to glomerular disease (e.g. IgA nephropathy).
3. In association with other conditions (HIV infection, heroin addiction, sickle cell disease and massive obesity).
**Morphology:**

**LM:** sclerosis may involve few glomeruli and segment of the glomerulus.

**EM:** both sclerotic and non-sclerotic glomeruli show **diffuse loss of foot** processes of visceral epithelial cells and in addition, there may be **focal detachment** of the **epithelial cells.**

**IF:** **IgM and C3** in the **sclerotic areas** and/or in the **mesangium.**

**Prognosis:**

There is little tendency of spontaneous remission and responses to corticosteroid therapy are variable. In general, children have a better prognosis than adults do.

**IV. Membrano proliferative Glomerulosclerosis(MPGN):**

Causes:
 1. Primary (idiopathic).
 2. secondary, associated with;

* chronic immune complex disorders (SLE, hepatitis B and C infection, HIV infection).
* Malignant tumors (leukemia, lymphoma).
* Hereditary deficiency of complement regulatory proteins.

**Morphology:**

**LM:**the glomeruli are large due to hypercellularity secondary to proliferation of measngial cells, capillary endothelial cells and leukocytic infiltration. The glomeruli have a **lobular appearance**

The GBM is clearly **thickened**. The glomerular capillary wall often shows a **double contour or "tram-track" appearance.**

**Morphology:**

**Type I** (great majority of cases):

* there is **subendothelial electron-dense deposits**.
* **IF:** **C3** is deposited in a granular pattern, and **IgG** and (**C1q and C4**)

**Type II** (dense-deposit disease DDD),

* the GBM is transformed into an irregular, **ribbon-like**, extremely **electron-dense structure**,
* **C3** is present in **granular or linear pattern**. **IgG and C1q and C4 are usually absent.**

**clinical features:** nephrotic/nephritic syndrome occurring in older children or young adults.

**Prognosis:** Medical treatment has NOT been proved to be effective.

50% develop chronic renal failure within 10 years.

 **IGA nephropathy** **(Berger Disease)::**

* It is the frequent cause of recurrent gross or microscopic hematuria .
* Mild proteinuria is usually present,
* Nephritic syndrome may occasionally develop.
* Rarely, patients may present with RPGN.

**Pathogenesis:**

There is either a genetic or acquired abnormality of immune regulation leading to increased mucosal IgA synthesis in response to respiratory or gastrointestinal exposure to environmental agents (viruses, bacteria, food proteins).IgA then trapped in the mesangium.

**Morphology**

**By light microscope,** there is variable mesangial proliferation +/- sclerosis.

**immunofluorescent microscopy** : mesangial deposition of **IgA + C3.**

**Electron microscopy** confirms the presence of electron dense deposits in the mesangium**.**

**Prognosis:**

The disease affects people of any age, but older children and young adults are most commonly involved.

Many patients present with gross hematuria after an infection of respiratory tract, or GIT

Many patients maintain normal renal function for decades. Slow progression to chronic renal failure occurs in 15-40% of cases over a period of 20 years.

**Chronic Glomerulonephropathy**

* It is an important cause of end stage renal (ESRD).
* It is an important outcome of many Acute glomerulonephritis
* Gross: Contracted kidneys (symmetrically), with red- brown granular surface.

**Mic:**

* Scarring of glomeruli & Bowman space.
* Interstitial fibrosis and lymphocytic infiltration.
* Tubular atrophy.
* Thick wall arteries.

**Clinical features:**

* Proteinuria, Azotemia on routine medical investigations.
* Unexplained edema.

**Prognosis:** Poor without treatment.

In most patients, chronic glomerulonephropathy develops insidiously and slowly progresses to renal insufficiency.