Diseases of kidney

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I. Glomerular diseases

1.Clinical Manifestations of Renal Diseases

- The clinical manifestations of renal disease can be grouped into well-defined syndromes.

a. Some are unique to glomerular diseases

b. and others are present in diseases that affect any one of the components.

I. Azotemia :

- Is a biochemical abnormality that refers to an elevation of blood urea nitrogen (BUN) and creatinine levels, and is related to a decreased glomerular filtration rate (GFR).

- Azotemia is

a. a consequence of many renal disorders, but it also arises from extrarenal disorders.

b. It is a typical feature of both acute and chronic kidney injury.

1. ***Prerenal azotemia***

- Is encountered when

a. There is hypoperfusion of the kidneys (e.g., hypotension or excessive fluid losses from any cause,

b. or if the effective intravascular volume is decreased due to shock, volume depletion,

Congestive heart failure

All impairs renal function in the absence of parenchymal damage

2. ***Postrenal azotemia***

- Is seen whenever urine flow is obstructed distal to the kidney.
- Relief of the obstruction is followed by correction of the azotemia

II. Uremia

- Means azotemia associated with constellation of clinical signs and symptoms and biochemical abnormalities,

- Uremia is characterized :

a. by failure of renal excretory function

b. a host of metabolic and endocrine alterations resulting from renal damage

- Uremic patients frequently manifest

a. Secondary involvement of the gastrointestinal system (e.g., uremic gastroenteritis),
b. Peripheral nerves (e.g., peripheral neuropathy),
c. and heart (e.g., uremic fibrinous pericarditis).

III. Nephritic syndrome

- Is a clinical entity caused by glomerular diseases and is dominated by

1. The acute onset of either grossly visible hematuria (red blood cells in urine) or microscopic hematuria

2. Red cell casts on urinalysis,

3. Diminished GFR,

4. Mild to moderate proteinuria, and hypertension.

Note: Nephritic syndrome is the classic presentation of acute poststreptococcal glomerulonephritis.

IV. Nephrotic Syndrome

- Is caused by a derangement in glomerular capillary walls resulting in increased permeability to plasma proteins.
- The manifestations of the syndrome include:

a. Massive proteinuria,

- With the daily loss of 3.5 gm or more of protein (less in children)

b. Hypoalbuminemia,

- with plasma albumin levels less than 3 gm/dL

3. Generalized edema
4. Hyperlipidemia and lipiduria

V. Asymptomatic hematuria or proteinuria, or a combination of these two

- is usually a manifestation of subtle or mild glomerular abnormalities.

VI. Acute kidney injury: Is characterized by :

a. Rapid decline in GFR (within hours to days),
b. Concurrent dysregulation of fluid and electrolyte balance,
c. Retention of metabolic waste products normally excreted by the kidney including urea and creatinine.

d- In its most severe forms, it is manifested by *oliguria* or *anuria* (reduced or no urine flow).

Note:

- It can result from glomerular, interstitial, vascular or acute tubular injury.

VII. Chronic kidney disease (previously called chronic renal failure)

- Is defined as the presence of a diminished GFR that is persistently less than 60 mL/minute/1.73 m^2 for at least 3 months, from any cause, and/or persistent albuminuria.

- It may present with :

a. In milder forms as clinically silent decline in renal excretory function,

b. In more severe cases, by prolonged symptoms and signs of uremia.

Note: It is the end result of all chronic renal parenchymal diseases.

VIII. ***In end-stage renal disease (ESRD)***

- The GFR is less than 5% of normal; this is the terminal stage of uremia.

Renal Biopsy examination

1.Light microscope

Fixed in formaline and stained with:

- H&E
- PAS
- Silver jones
- Masson trichrome
- Amyloid

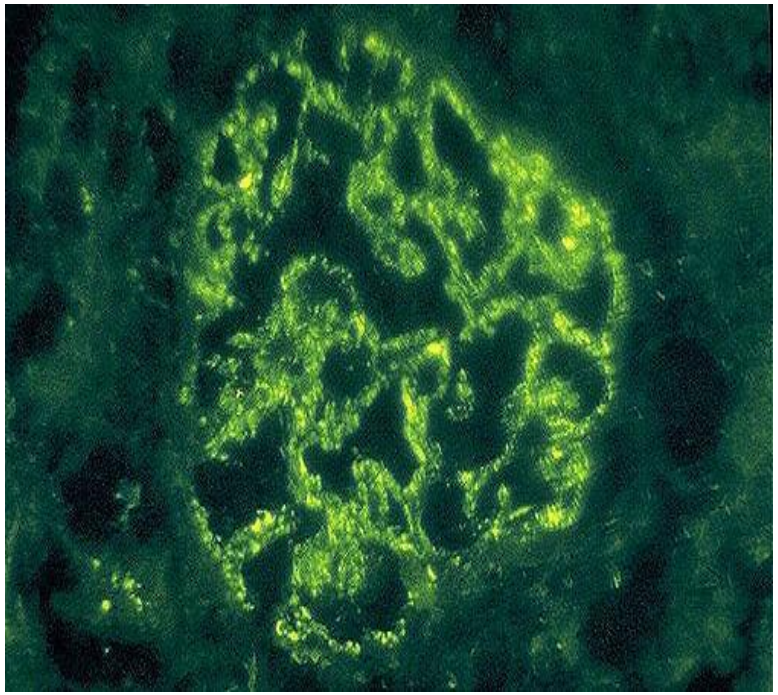
2. Electron microscope

- Fixed in gluteraldehyde
- Determine if the deposits are in the mesangium, subendothelial or subepithelial locations

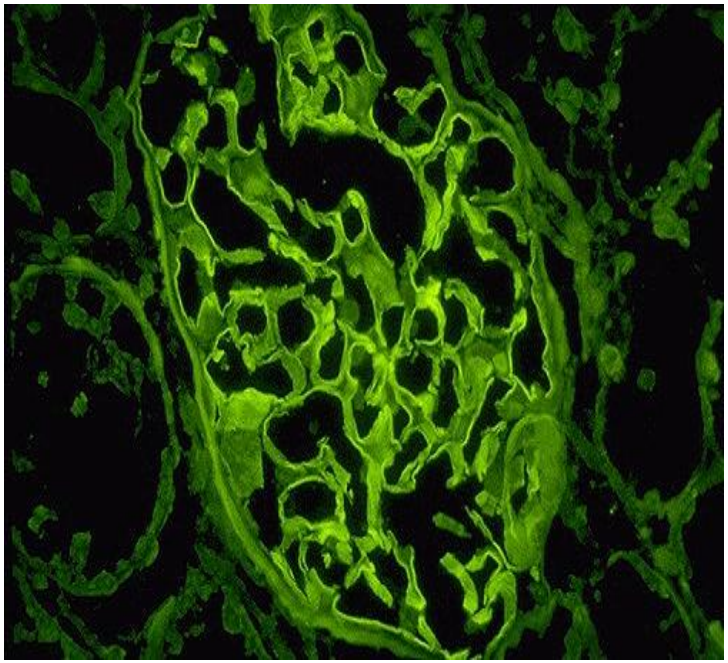
3. Immunoflurescence

- Normal saline
- Detect IgA, IgM,IgG
- Detect complement
- Detrimine if deposits are in granular or linear pattern

Granular deposits



Linear deposits



Glomerular diseases manifested as Nephritic Syndrome

A. Poststreptoccal GN

- These lesions are typically caused by deposition of immune complexes in kidneys
- It usually appears 1-4 weeks after streptococcal infection of the throat or skin infection
- Occurs most frequently in children 4-10 years of age

Etiology and pathogenesis:.

- In this type of nephritis, glomerular injury is caused by deposition of Antigen-antibody immune complexes

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- The antigens that trigger the formation of circulating immune complexes are exogenous and it is the bacterial products (streptoccocal antigens
- Only certain strains of group A β-hemolytic streptococci are nephritogenic,
- More than 90% of cases being traced to types 12, 4, and 1,

- The streptococcal pyogenic exotoxin B as the principal antigenic deter-minant in most case
- At the outset, the inciting antigens are exogenously planted from the circulation in subendothelial locations in glomerular capillary walls, leading toformation of immune complexes, where they elicit an inflammatory response.

- Subsequently, through mechanisms that are not well understood, the antigen-antibody complexes dissociate, migrate across the GBM, and re-form on the subepithelial side of the GBM.,

Evidence of immune mediated disease

1. There is a latent period between infection and nephritis which is compatible with time required for production of antibodies and formation of immune complexes
2. Elevated titers of antibodies against streeptocccal antigens

3. Serum complement levels are low, compatible with activation of the complement system and consumption of complement components.

Morphology

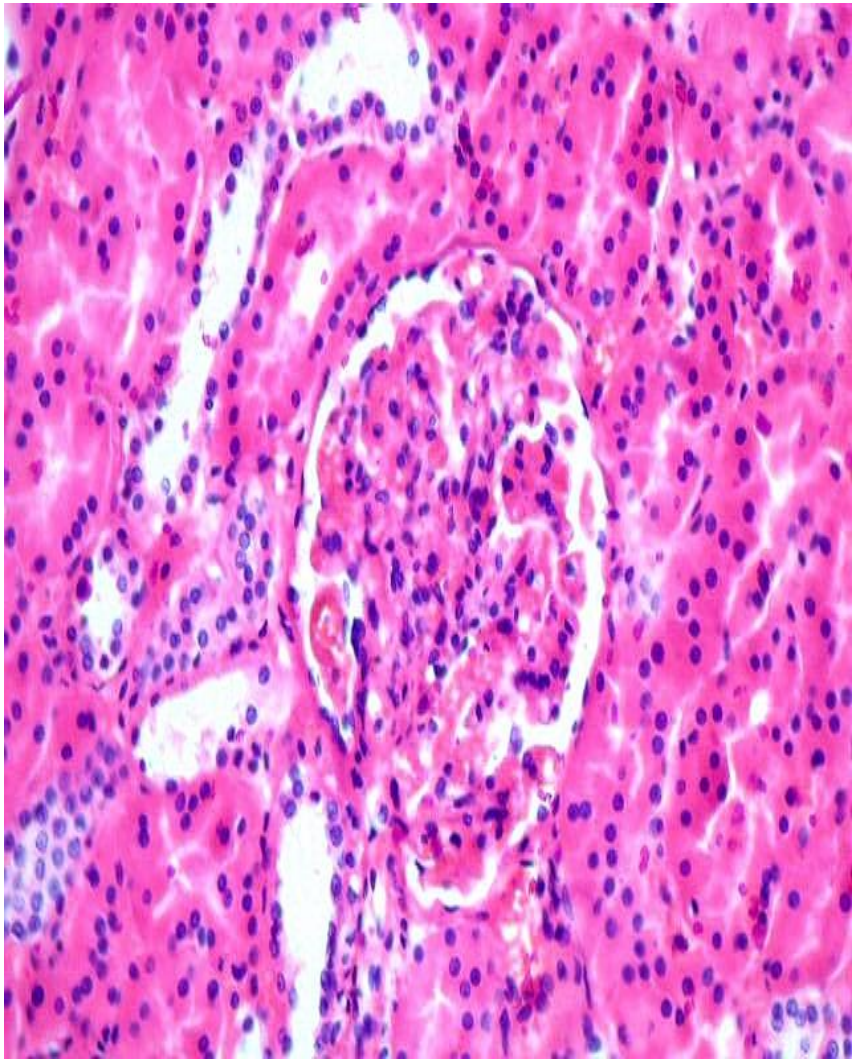
Light microscope: global diffuse

- Enlarged hypercellular glomeruli caused by

a. Infiltration by neutrophils and monocytes

b. Proliferation of endothelial and mesangial cells

Note: The proliferation and leukocyte infiltration is global (involve more than 70%bof glomerulai)and diffuse(involves the whole glomerulus)



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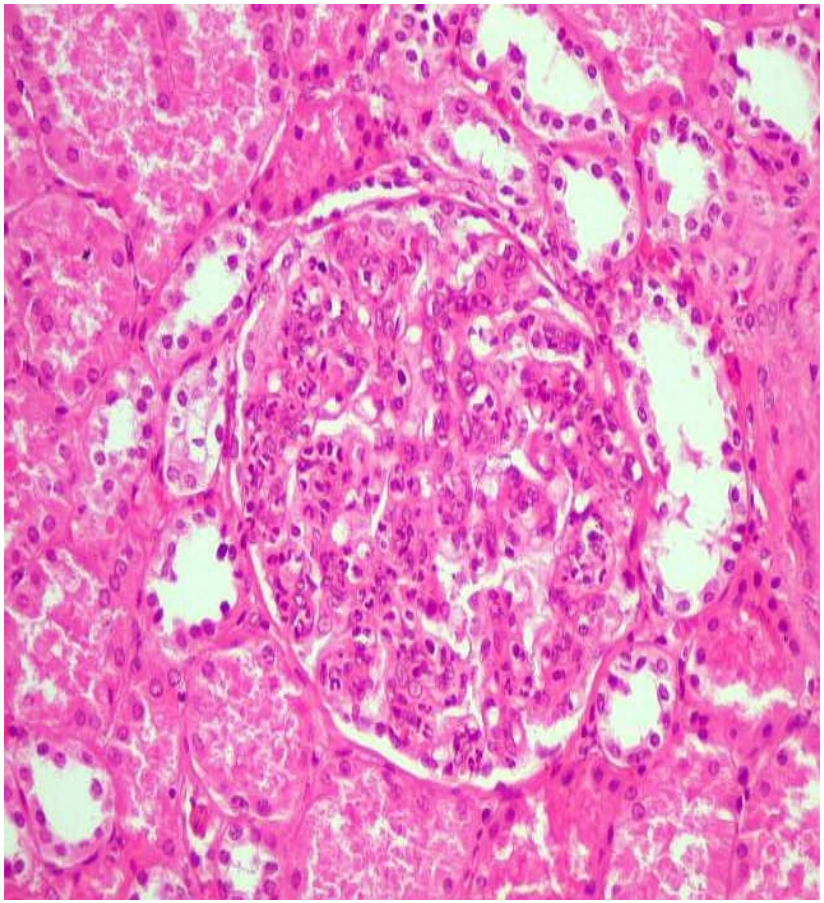
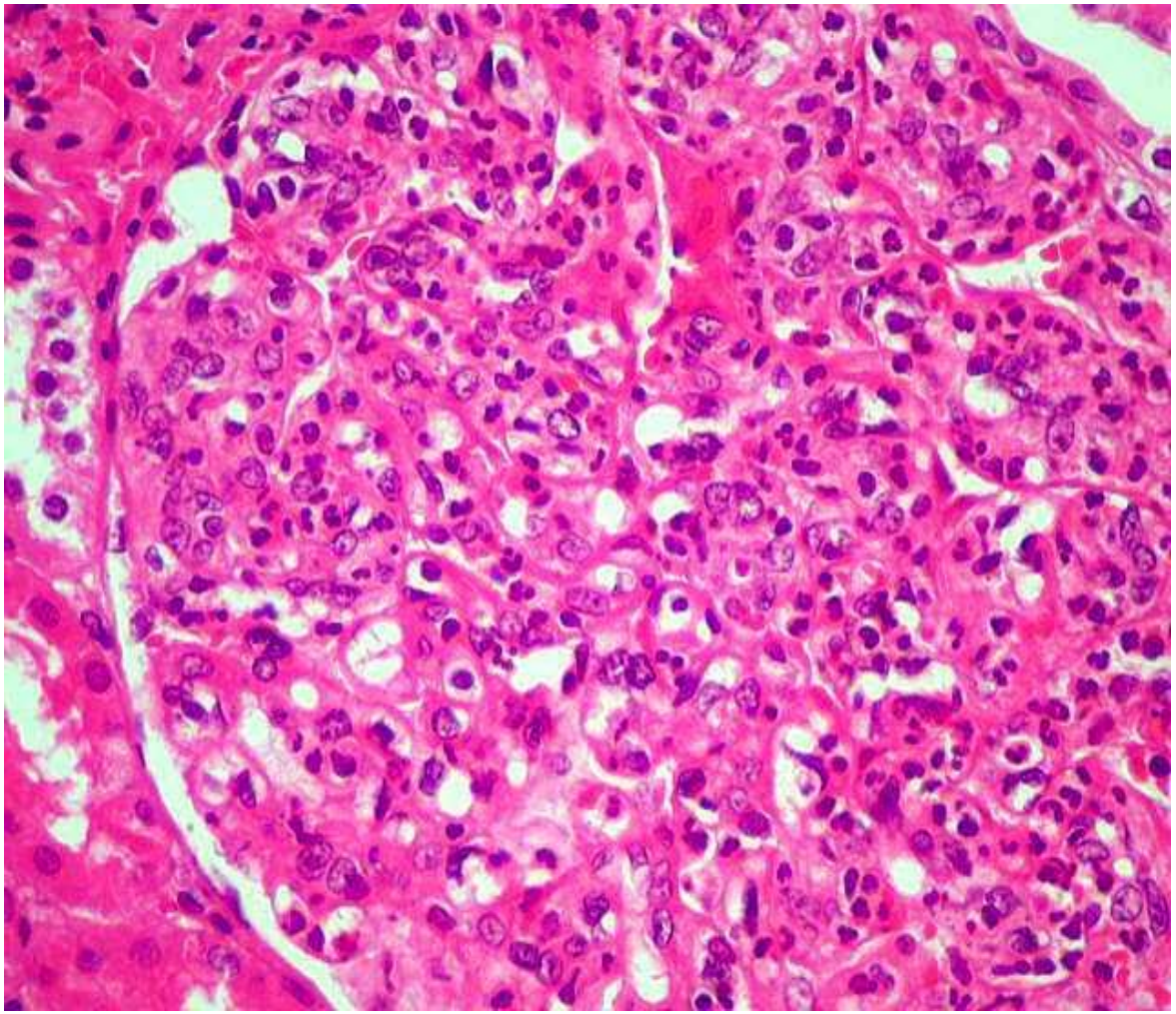
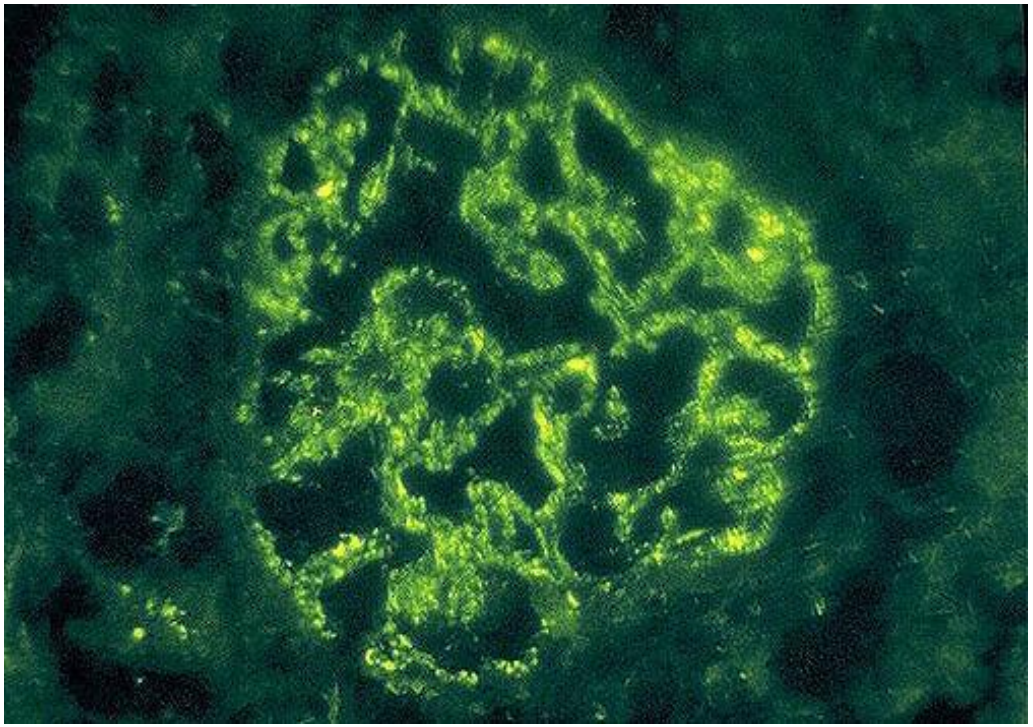


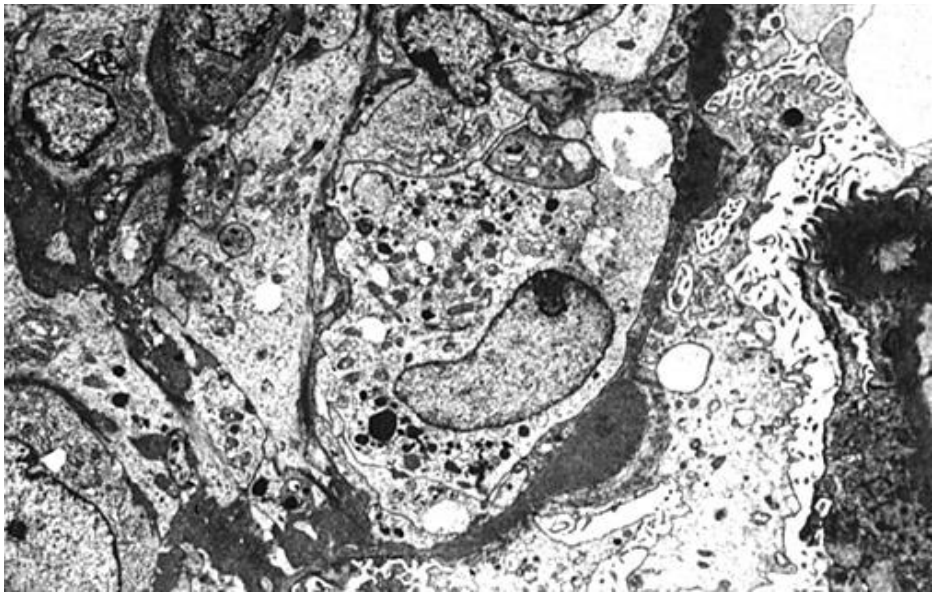



NEUTRÓFILOS NOS TUFOS CAPILARES



Immunofluerescent microscope

-Granular deposits of IgG and C3 in the mesangium and along GBM



- **<u>Electron microscope:</u>**

1. Discreet electron-dense deposits on the epithelial side of GBM
2. Subendothelial deposits are also seen early in the disease course

Clinically

- In the typical case , a young child develops malaise and, fever, nausa, oliguria , hematuria in the form of smoky or cola colored urine two weeks after recovery from throat infection

- The patients have

1. Dysmorphic RBC cast in the urine
2. Mild proteinuria
3. Mild to moderte hypertension

Outcome

- More than 95% of affected children recover after with conservative therapy aiming at maintaining water and sodium balance
- 1% of children do not improve and become oligouric and develop rapidly progressive GN
- Some of the remaining patients may progress to chronic GN