

## **Disorders of renal system:**

### **Glomerular diseases:**

Chronic glomerulonephritis of nephritic or nephritic syndrome type consider as the most common cause of chronic renal failure and to understand the pathogenesis of such diseases ,the histological composition of glomerular tuft should be explained.glomerulus consists of anastomosing network of capillaries invested by two layers of epithelium ,the visceral epithelium is the intrinsic part and in direct contact with capillary endothelium separated by glomerular basement membrane while parietal epithelium lines bowman's space (the cavity in which plasma filtrate first collect).so we have:

- 1-thin layer of fenestrated endothelial cells.
- 2-glomerular basement membrane(GBM),
- 3-visceral epithelial cells (podocytes)that are complex epithelial cells with foot processes adherent to the external part of the GBM.
- 4-the entire glomerular tuft is supported by mesangial cells laying between the capillaries.

### **Pathogenesis of glomerular diseases:**

Immune mechanisms underlie most cases of primary glomerulonephritis(GN) and even most of the secondary glomerular involvement,so,GN induced by antigen antibody reaction,and glomerular deposit of immunoglobulins in more than70% of GN.

Two forms of antibody associated injury seen;

- 1-deposition of soluble antigen-antibody complexes in the glomerulus.

In this form the inciting antigen is unrelated to glomerulus and it is either endogenous autoantigen as in SLE, or exogenous of bacterial(post streptococcal GN) or viral or parasitic,whatever the type of antigen ,antigen-antibody complexes has been formed , circulating throughout the circulation and trapped in the glomerulus where they produce injury mainly after binding with complement factor.The type of injury is usually associated with leukocytic infiltration of the glomerulus with proliferation of the endothelial,mesangial and parietal epithelial cells the deposition of immune complexes is either subendothelial(between endothelial cells and GBM),or subepithelial(between epithelial cells and GBM) or in the mesangium as illustrated by electron microscope.

- 2-injury resulting from antibody reaction in situ with glomerular antigen either the antigen is intrinsic to glomerulus or planted foreigner antigen.

So we find two types ,antiGBM nephritis ,in which the antibody is directed against GBM matrix and result in linear deposit along the entire length of GBM.

The other type include those foreigner antigens has been planted or trapped in the glomerulus ,antibody react with such antigen causing GN and immune complex deposition in the mesengium .

### **Nephrotic syndrome:**

Is a clinical complex made up of the following;

- 1-massive proteinuria with protein more than 3.5 gm/day
- 2-generalized edema
- 3-hypoalbuminemia ,plasma albumin less than 3gm/dl.
- 4-hyperlipedaemia and lipiduria.

At the onset there is mild or no azotemia,haematuria or hypertension. The initial event is a dearrangement in the capillary walls of the glomerulei resulting in increasing permeability to plasma proteins.The glomerular capillary wall with it's endothelium ,glomerular basement membrane(GBM)and visceral epithelial cells acts as a barrier through which the glomerular filtrate must pass.any increased in the permeability resulting from either structural or physicochemical alteration allows protein to escape from plasma to glomerular filtrate.

Massive proteinuria result in a significant decrease in plasma albumin ,generalized edema result from a drop in plasma osmotic pressure.there is a concomitant drop in plasma volume with diminished glomerular filtration will lead to compensatory secretion of aldosterone that cause sodium and water retention to replace the loss of plasma volume and will further aggravate edema.the cause of hyperlipidemia still obscure.

In children under 15 years the nephrotic syndrome is almost always caused by a lesion primary to the kidney ,where as among adults it may often be associated with a systemic disease;

Primary glomerular diseases causing nephrotic syndrome;

- 1-membranous glomerulonephritis
- 2-lipoid nephrosis(minimal change glomerular disease.)(65% of the cases in children)
- 3-focal segmental glomerulosclerosis.
- 4-membranoproliferative glomerulonephritis

Systemic diseases:

- 1-diabetes mellitus
- 2-amyloidosis
- 3-systemic lupus erythematosus(SLE)

### **The nephritic syndrome:**

Is a clinical complex characterized by ;1)haematuria, with red blood cells in urine and haemoglobin cast.2)some degree of oliguria and azotemia3)hypertension. The lesions that causing this syndrome characterized by proliferation of cells within the glomerulei and leukocytic infiltration.the inflammatory reaction injures the capillary wall

permitting escape of red cells into the urine and induce haemodynamic change that reduce the glomerular filtration this will lead to oliguria, fluid retention (edema) and azotemia. Hypertension is due to both fluid retention and renin release.

Acute nephritic syndrome may also be caused by systemic disease such as SLE in addition to primary glomerular disease.

Types of acute nephritic syndrome;

- 1) acute poststreptococcal glomerulonephritis.
- 2) crescentic glomerulonephritis
- 3) IgA nephropathy.

### **Tubulointerstitial nephritis (TIN)**

Include diseases that primarily affect renal tubules and interstitium, the glomeruli may be spared or affected, in most cases of TIN caused by bacterial infection the renal pelvis is prominently involved, hence the more descriptive term is pyelonephritis, while the interstitial nephritis is reserved for non-infectious cases. TIN can be divided into acute and chronic pyelonephritis:

#### **Acute pyelonephritis:**

Is a common suppurative inflammation of the kidney and renal pelvis, is caused by bacterial infection. It is an important manifestation of urinary tract infection (UTI) which includes either lower (cystitis, urethritis and prostatitis) or upper (pyelonephritis) urinary tract. The most common causative organisms are gram-negative bacteria (E. coli, Klebsiella and Pseudomonas). There are two routes through which infection reaches the kidney, ascending infection from the lower urinary tract and haematogenous via blood stream. The latter is less common.

The histologic picture of acute pyelonephritis is the suppurative necrosis or abscess formation of the renal substance, with a large number of neutrophilic infiltration.

#### **Chronic pyelonephritis:**

It is of two types according to the etiology:

- 1) chronic obstructive PN: as in urethral or ureteric obstruction by stone or congenital anomaly.
- 2) reflux pyelonephritis: due to recurrent reflux of urine from vesicoureteric junction or intrarenal reflux.

The main microscopic features in chronic PN are, interstitial fibrosis, chronic inflammatory cellular infiltration, tubular dilatation or contraction with intraluminal cast similar to thyroid colloid, and vascular sclerosis with glomerular sclerosis in advanced stages of the disease.

**Acute renal failure (ARF):**

Is the acute suppression of the renal function and urine flow reaching to less than 400 ml/day (oliguria).

The most common cause of ARF is the acute tubular necrosis (ATN). Other causes include; severe glomerular disease such as crescentic GN, diffuse renal vessels disease, acute pyelonephritis, drug induced nephritis and diffuse cortical necrosis.

Most cases of acute renal failure are reversible if well treated, ATN for example associated with tubular epithelial cell injury due to toxins, shock states in hypovolaemia and septicemia this injury appears as tubular epithelial necrosis, presence of proteinaceous tubular casts, edema of the interstitium with inflammatory cellular infiltrate formed by neutrophils, lymphocytes and plasma cells. If the patient survives for a week, regeneration of tubular epithelial cells occurs unless destruction of basement membrane has been developed.

**Drug induced nephropathy:**

Two forms of tubulointerstitial nephritis seen in drug renal injury:  
-acute drug induced interstitial nephritis:

Occurs after many synthetic antibiotics like rifampicin, methicillin, thiazide diuretics and non steroidal anti-inflammatory agents, the disease usually started after 15 days from exposure to drug with fever, eosinophilia, skin rash, with haematuria, pus cells in urine and mild proteinuria.

The renal pathology is that of ARF with edema of interstitium, lymphocyte and macrophage infiltration with few neutrophils and eosinophils, glomeruli are usually not affected.

-analgesic nephropathy:

Consumption of large amount of analgesic drugs may be associated with chronic interstitial nephritis, especially non steroidal anti-inflammatory drugs.



