Nephropathology

Renal disease Components:

- Glomerular disease
- Tubular and interstitial disease
- Diseases involving the blood vessels
- Cystic renal diseases
- Outflow obstruction (more in ♂ : prostate pathology) mimics renal conditions
- Tumours (majority are carcinomas < renal CC, papilary carcinoma) (benign, mets)

Clinical manifestation

Several major syndromes:

- Acute nephritis syndrome: gross hematuria with proteinuria and hypertension
- Nephrotic syndrome: Heavy proteinuria with hypoalbunemia, severe oedema and hyperlipedemia (↳ 3g/24hr)
- Asymptomatic hematuria or proteinuria: usually a combination – subtle manifestation of glomerular disease
- Acute renal failure: Due to glomerular disease, interstitial disease or acute tubular necrosis (ATN) (↳ acute pyelonephritis)
- Chronic renal failure: prolonged symptoms, end result of all chronic renal diseases

Secondary manifestations:

- Usually associated with renal failure
- Metabolic and endocrine alterations - cholesterol affected, Ca^{2+} - metabolism
- Gastrointestinal manifestations: uremic gastroenteritis
- Neuromuscular: peripheral neuropathy
- Cardiac: uremic fibrinous pericarditis

ATN: pt. can recover from it

Glomerular disease

- Major problem in renal disease
- Chronic glomerulonephritis (GN) is one of the major causes of chronic renal failure – adult and paediatric population
- Several entities encountered in the group of GN

- Normal Glomerular structure
- Complex network of capillaries
- Two layers of epithelial cells – visceral and parietal cells
- Parietal cells line the capsule of Bowman
- Visceral cells – incorporated into the capillary loops and forms part of the capillary wall
- Capillary wall is the filtering membrane and consists of:
  - Fenestrated layer of endothelial cells
  - Glomerular basement membrane (GBM)
  - Visceral epithelial cells (podocytes) with their foot processes
  - Mesangial cells – supporting cells present between capillary loops

Renal biopsy

Usual a needle biopsy submitted to the laboratory – in formalin

Standard examination of the biopsy:

- HE section
- Silver stain to examine the membranes
- Immunoperoxidase stains – IgG, IgM, IgA, C3 and C4 – evaluate the presence of immune complexes
- Immunofluorescence (alternative to Immunoperoxidase stains)
- Electron microscopy

Pathogenesis of Glomerular disease

- Specific aetiology agents may still be unclear
- Underlying mechanism is immune mediated
- Glomerular deposits of immune complexes are present in 70% of patients with GN
- Cell mediated immune reaction also play a role in GN
- Two forms of antibody associated injury occur:

- Deposition of circulating soluble complexes – SLE
- In situ reaction of antibodies in the glomerulus

response to Ag in loops of ↄ

(1) The Nephrotic syndrome

proteinuria 3g/24hrs

Clinical complex

- Relative frequency of the causes vary with age
- Children under 15 years of age – primary lesion of the kidney due to a
- Adults – more often systemic disease

Causes of Nephrotic syndrome:

1. Minimal change Disease / Lipoid nephrosis

   Most frequent cause of nephrotic syndrome in children

   Light microscopy (LM): Normal appearance

   Immunoperoxidase staining (IP's): None

   Dx: Electron microscopy (EM): Only effacement of foot processes

   Tubular epithelium – vacuolated appearance due to resorption of lipoproteins

2. Membranous Glomerulonephritis (MGN) BM gradually becoming thicker

   Slowly progressive disease more common in adults

   Characterized by sub epithelial deposits

   Early in the disease – glomeruli normal in appearance

   Later in the disease – diffuse thickening often the GBM

   MGN may occur in association with known disorders (secondary):

   - Infections – Hep B, syphilis, malaria
   - Malignant epithelial tumours – lung, colon and melanoma
   - SLE
   - Drugs – gold, penicillamine
   - Metabolic disorders – diabetes

   But: Idiopathic – 85% of cases

   Chronic immune complex nephritis

   Circulating complexes against known exogenous antigens (Hep B) and endogenous antigens (DNA in SLE)

   Idiopathic forms – induced by antibodies reacting to in situ glomerular antigens

Morphology

LM: Diffuse thickening of the GBM

IP's: Granular deposits of immunoglobulins and complement along the GBM

EM: Sub epithelial deposits nestled against the GBM (btwn spikes)

Small spike like protrusions of GBM

Progression – closure of the spikes over the deposits incorporating them into the membrane

3. Focal Segmental Glomerulosclerosis (FSGS)

Sclerosis affecting some but not all the glomeruli and involving only segments of the glomerulus

Can occur in the following settings:

Primary disease

Secondary event in other GN due 2 glomerular scarring

Association with other known conditions – HIV and heroin addiction

Important cause of Nephrotic syndrome in children – need to distinguish from minimal change disease FSGS: <50% of Glomeruli involved. } (*)

Higher incidence of hematuria and hypertension

50% develop end stage renal failure (ESRD)

Adults fair much worse than children

Morphology

LM: onl some glomeruli – segmental involvement of the glomeruli tuft

Increased mesangial matrix, collapsed basement membranes and deposition of hyaline material

IP's: mesangial deposits of IgM

EM: effacement of the foot processes and detachment of the podocytes

Lesion progress: total sclerosis of the glomeruli, with tubular atrophy and interstial fibrosis

The Nephritic Syndrome

less proteinuria + hematuria

Clinical syndrome

Usually acute onset with hematuria and hypertension

Glomerular lesions associated with nephritic syndrome – proliferative with an associated influx of leucocytes + neutrophils

↳ ↑ in mesangial cells (compressing capillary vessels)

Primary or secondary to systemic disorders like SLE

1. Acute Proliferative GN (PGN)

More frequent type of GN

Caused by immune complexes

- circulating in blood → kidney

May be due to exogenous or endogenous antigens

Prototype exogenous – post streptococcal/ post infectious (immune complexes) (nephritic synd 7-3wks after sore throat)

Prototype endogenous - SLE

Infections other than Streptococci may also cause proliferative GN

Pneumococcal and Streptococcal infections

A number of common viral infections may also cause PGN:

- Mumps
- Measles
- Chickenpox
- Hepatitis B

Classic post streptococcal GN develops in a child between 1 – 4 weeks after a Streptococcus group A infection only

Nephrogenic subtypes will cause the GN

Usually a pharyngitis or skin infection

Post infective

the humps & bumps of post infective gN. (large deposits - exogenous immune complex into subepith. pait cm membr.)

Pathogenesis

Typical type III reaction with the formation of immune complexes

Deposition of the complexes in the glomerulus

Circulating or in situ complexes

Granular deposition of IgG and complement on the basement membrane

Chronic GN

Unfortunate outcome of a lot of the GN's (present late) - scarring (>80% glomerulus)

Important cause of end stage renal disease

30 – 50% of patients needing haemodialysis or renal transplantation have chronic GN

By the time it is diagnosed the lesion is so far progressed that the original lesion can not be identified

FSGS, MGN and MPGN often progress to chronic GN
└membranoproliferative GN.

↓cortex
↓medulla

Tubulointerstitial Nephritis

Group of inflammatory disease involving the interstitium and tubules

Glomeruli may be spared or affected late in the course

Most common – pyelonephritis

Non infectious causes include:

- Drugs toxic effect < tubules interstitium
- Metabolic disorders – hypokalemia
- Physical injury – radiation
- Immune reaction against tumulointerstitial component

Acute tubular necrosis (ATN)

⊛ Most common cause of acute renal failure

Acute destruction of tubular epithelial cells

95% Reversible condition that occur in a variety of clinical settings regenerative possibility of tubules.

due to:

- Ischemia – shock, sepsis
- Toxic – heavy metals, drugs

Cystic Diseases

Heterogeneous group

– Hereditary
– Developmental

} can lead 2 chronic renal fail.

—Acquired assoc: underlying glomerulo / tubulo interstitial dis

Fairly common

Some forms important cause of chronic renal failure

Picture: renal cortical cysts Picture 2: Polycystic kidney disease

Polycystic Renal Disease

Two major forms :

Adult type – outosomal dominant

Gene situated on chromosome 16 (AKPD 1) or 4 (AKPD 2)

Infantile type – outosomal recessive type

Adult type: AD

Does not have symptoms until adulthood

Flank pain, intermittent hematuria

Hypertension

Urinary infection

Associated lesions:

Saccular aneurysms in circle of Willis ∴ take headaches seriously!

Asymptomatic liver cysts 

Infantile type: AR

Perinatal, neonatal, infantile and juvenile type

Earlier forms more common with most severe manifestations - live an hour / two then die

Associated liver cysts (SMALL) and proliferation of bile ducts

If they survive – liver cirrhosis (fibrosis) (pre-cirrhotic hepatic fibrosis)