Glomerulonephritis Clinicopathological correlation

Dr. F M Mofakharul Islam
Associate professor of Medicine
Sir Salimullah Medical college

Glomerulonephritis

- Minimal change disease
- Membranous glomerulonephritis
- Focal segmental glomerulosclerosis
- IgA nephropathy
- Endocapillary proliferative glomerulonephritis
- Membranoproliferative glomerulonephritis
- Mesangioproliferative glomerulonephritis
- Anti glomerular basement disease

- There are 1.8 million glomerular capillary tufts in two kidneys.
- Fenestrated endothelial cells resting on a basement membrane line the capillaries.
- They reside within the Bowman’s capsule lined by epithelial cells.
- Delicate foot processes extending from epithelial podocytes covers the outer surface of the capillaries and form a selective filtration barrier.

- Glomerular capillaries filter 120 to 180 l/day of plasma containing various solutes for re-absorption and excretion.
- Most large proteins and cells are excluded from filter.

Causes

- Genetic mutation
- Autoimmunity
- Diabetes mellitus
- Hypertension & atherosclerosis
- Infection & toxin exposure
- Thrombosis & embolism
- Idoiopathic

Pathogenesis

- Some glomerular disease results from genetic mutations producing familial disease:
  - Alport's syndrome,
  - Congenital nephrotic syndrome,
  - FSGS in adult hood.

Pathogenesis

- Systemic hypertension and atherosclerosis produce pressure stress, ischemia and lipid oxidents that causes chronic glomerulosclerosis.
- Malignant hypertension can quickly produce fibrinoid necrosis of arterioles and glomeruli, thrombosis, micro-angiopathy and acute renal failure.

Pathogenesis

- Autoimmune glomerulonephritis may be
  - ♣ Primary: confined to the kidneys only
  - ♣ Secondary to systemic diseases like SLE, Infection, drugs, vasculitis etc.

In autoimmune GN

- 1. An auto antibody may react directly with the antigen. Anti GBM disease.
- 2. An antibody formed against an Exogenous antigen planted at the glomerulus at that time.
- 3. Antigen antibody reaction occurring systemically & trapping of that immune complex in the kidney.
- 4.Cellular immune response & vasculitis.

Pathogenesis

- Whatever the initial event
  there is activation of coagulation &
  complement cascade and production of pro-inflammatory cytokines, ultimately producing inflammation and glomerular damage.

Pathogenesis

- Finally haemodynamic alteration lead to hyperfiltration and intraglomerular hypertension with subsequent development of glomerular sclerosis which progress to fibrosis and scaring.
- Persistent GN leads to interstitial inflammation, tubular obstruction, fibrosis & renal failure.

Presentation

- However the cardinal features of glomerulonephritis are
  - Haematuria &
  - Sustained proteinuria

Presentation

- Nephrotic syndrome
- Nephritic syndrome
- Rapidly progressive glomerulonephritis
- Basement membrane syndrome
- Pulmonary renal syndrome
- Glomerular vascular syndrome
- Infectious disease asso. syndromes

Haematuria

- Is typically asymptomatic.
- Microscopic haematuria: 3 – 5 red cells in first voided morning urine is suspicious. When red cell cast or dysmorphic RBC are present in the sediment GN is likely.
- Macroscopic haematuria occurs in IgA nephropathy & sickle cell disease.

IgA nephropathy

- It is a immune complex mediated GN defined by diffuse mesangial IgA deposits often associated with mesangial hypercellularity.
- IgM, IgG, C3 or immunoglobulin light chain may also contribute with IgA.
- The pathogenic significance of IgA is not yet clear.

IgA nephropathy

- It is the most common form of GN world wide
- Male>Female
- Peak incidence is in 2nd & 3rd decade of life
- Two most common presentations:

  1. Recurrent episodes of macroscopic haematuria during or immediately after upper RTI, often with proteinuria.
  2. Persistent asymptomatic microscopic haematuria.

IgA nephropathy

- IgA nephropathy is a benign disease
- 30% go into complete remission.
- Others continue with haematuria but with preserved renal function.
- Minority will have slowly progressive disease causing renal failure over 20 – 30 years.

Proteinuria

- Proteinuria is sustained & >1gm/day.
- Non-selective
- May be asymptomatic
- Proteinuria >3gm/24 H is called nephrotic range proteinuria.

Nephrotic syndrome

- Oedema
- Heavy proteinuria
- Hypo-albuminaemia
- Hypercholesterolemia
- With or without hypertension & minimal Haematuria.

Causes of nephrotic syndrome

- Minimal change disease:
- Focal segmental glomerulosclerosis:
- Membranous glomerulonephritis
- Glomerular deposition disease

Minimal change disease (MCD)

- No glomerular lesion seen by light microscopy and negative for deposits by immunofluorescent microscopy.
- Electron microscopy shows effacement of podocyte foot process and weakening of slit pore membrane.
- Usually it is primary renal disease but may occur secondary to

  Hodgkin's disease, NSAID

Minimal change disease (MCD)

- 70 - 90% of childhood &10 - 15% of adult NS
- 30% of the children have spontaneous remission, nearly all respond to steroid.
- Only the non responders need biopsy
- Relapse is common in children
- Relapse is less common in adult but more resistant to treatment.

Focal segmental glomerulosclerosis (FSGS)

- Characterized by segmental glomerular scars that involves some but not all glomeruli.
- Primary
- Secondary to

Virus : HIV, HBV
Drugs: NSAID, Heroin
Hypertension, Lymphoma
Reflux nephropathy Sickle cell dis.
Radiation Familial.

Focal segmental glomerulosclerosis (FSGS)

- FSGS causes one third of cases of adult Nephrotic syndrome.
- Presents with haematuria, hypertension, any level of proteinuria and renal failure.

Membranous Glomerulonephritis (MGN)

- Uniform thickening of basement membrane.
- Immunofluorescence demonstrate diffuse granular deposits of IgG & C3.
- Electron microscopy reveals electron dense subepithelial deposits.
- Causes about 30% cases of adult NS, peak incidence between 30 -50 years with M:F 2:1.

Membranous Glomerulonephritis (MGN)

- Secondary to
  - Infection: *HBV, HCB, malaria, leprosy*
  - Cancer: *Breast, Colon, Lungs*
  - Drugs: *NSAID, Gold, Mercury*
  - Autoimmune disease: *SLE, RA, PBC*
  - Others: *diabetes, sickle cell disease, GBS*

Membranous Glomerulonephritis (MGN)

- 80% of patients present with nephrotic syndrome & nonselective proteinuria.
- Spontaneous remission occurs in 20 -33% cases.
- One third have relapsing NS but with normal renal function.
- One third develop renal failure & die from its complications.

Nephritic syndrome

- Hypertension
- Oedema
- Haematuria
- Pyuria &
- Mild to moderate proteinuria (1- 2gm/24h)
- Raised s. creatinine level.

Acute endocapillary proliferative GN

- Poststeptococcal glomerulonephritis is the prototype of acute endocapillary GN.
- Renal biopsy demonstrate
  Hyper cellularity of mesangial and endothelial cells, Glomerular infiltration of polymorph
  Granular subendothelial deposit of IgG, C3
  Subepithelial deposits as hump.

Poststreptococcal glomerulonephritis

- Epidemic in under develop countries.
- Affect children more between ages of 2 -14
- Male>Female
- Occurs 1 -3 weeks after streptococcal pharyngitis by M type 1,2,3,4,12,25 & 49.
- 2 -6 weeks after skin infection with M type 2, 49, 47, 55, 60 & 57.

Poststreptococcal glomerulonephritis

- Classically present with nephritic picture.
- Systemic symptoms like headache, malaise, anorexia and flank pain is found in 50%
- Nephrotic range proteinuria may be found in 20% cases.
- C3 level is low with normal C4.

Poststreptococcal glomerulonephritis

- Raised ASO titer, Anti-DNAse or Anti-hyaluridase antibody can help confirm diagnosis, rarely requiring a biopsy.
- Sub clinical disease is 4 – 5 times more common characterized by asymptomatic microscopic haematuria with low C3 level.

Poststreptococcal glomerulonephritis

- Treatment is supportive.
- Over all prognosis is good
- Permanent renal failure is uncommon.
- Recurrent poststreptococcal GN is rare.

Rapidly progressive glomerulonephritis

- When serum creatinine rises rapidly, over few days in a pt. with nephritic syndrome.
- Crescentic glomerulonephritis is the pathologic equivalent of RPGN.
- Renal biopsy shows focal or segmental necrosis with aggressive capillary destruction by cellular proliferation & crescent formation.
- Crescents are fibrocellular collection that fill all or part of bowmen’s space.

Antiglomerular basement membrane disease.

- Auto antibody directed against glomerular basement membrane.
- The target epitopes for this antibody are normally sequestered in collagen IV hexamer, and can be exposed by infection, smoking, oxidants or solvents.

Pulmonary renal syndrome

- When glomerulonephritis present with lung haemorrhage, as in
  Goodpasture's syndrome.
  ANCA associated small vessel vasculitis,
  Lupus nephritis
- Goodpasture's syndrome present in two age groups in Twenties
  and in sixties and seventies.

Goodpasture's syndrome

- Presentation is explosive in young with haemoptysis, fever, dyspnoea & haematuria with rapid fall of Hb level.
- Urgent kidney biopsy is important for diagnosis.
- Plasmapheresis can be life saving along with steroid and cyclophosphamide.
- Kidney transplant is possible but should be delayed to avoid recurrence.

Membrano-proliferative Gn

- Characterized by thickening of GBM with mesangial proliferation.
- Type I MPGN: is most proliferative and shows mesangial proliferation and mesangial interposition between basement membrane and endothelial cells producing a double contour. C3 level is low.

MPGN

- Type II: is characterized by dense thickening of GBM containing ribbons of dense deposit & C3. there is usually no intra-mesangial or sub-endothelial deposit
- Type III: proliferation is less common, subepithelial deposits can occur along widened segments of GBM which appear laminated & disrupted.

MPGN(causes)

- Type I: most common
  - Idiopathic
  - Subacute bacterial endocarditis
  - Hepatitis B, HCV
  - Cancer: lung, breast, ovary
- Type II:
  - Idiopathic
  - C3 nephritic factor associated
- Type III: Idiopathic & Complement receptor deficiency.

MPGN

- Present with haematuria, proteinuria & pyuria with systemic symptoms malaise & fatigue.
- May present with RPGN
- 50% of patients will develop ESRD within 10 years and 90% within 20 years.

C3 level is significantly decreased in

- Poststreptococcal glomerulonephritis
- SLE
- Nephritis of chronic bacteremia
- Hepatitis B, HCV associated GN
- Type I Membranoproliferative GN (MPGN)

Lupus nephritis

- Class I: Minimal mesangial.
- Class II: Mesangial proliferation
- Class III: Focal nephritis
- Class IV: Diffuse nephritis
- Class V: Membranous nephritis
- Class VI: Sclerotic nephritis

Diabetic nephropathy

- GBM thickening
- Loss of negatively charged heparan sulphate moieties.
- Expansion of mesangium due to accumulation of extra cellular matrix.
- Mesangial sclerosis
- Nodular glomerulosclerosis.
- Vascular change.

THANK YOU