Minimal change disease (nil disease)

- the most common form of nephrotic in children.
- 25% of nephrotics in adults.
- rapidly developing oedema (days usually) that is noted first in the face .
- increase in body weight (up to 3% may be) can be the presenting problem.
- some times precipitated by an upper RTI(common), vaccination, pollen allergy, insect bite (bee).
- History of atopy , asthma, Eczema (personal & family)
- Hodgkin disease, mycosis fungoidis, chronic lymphocytic leukemia (usually associated with membranoproliferative GN) are malignancy that may triger MCD
- NSAIDs, interferon alfa/beta, pamidronate ,lithium(rare usually interstitial nephritis), gold (usually MN).
- Male: female 2:1 in children and equal in adolescence and adulthood
- Generalized oedema, ascitis are common. Pericardial effusion and pulmonary oedema uncommon
- Diarrhoea : due to enteritis, ischemic collitis due to oedema and hypoalbuminemia or thrombosis, malabsorption due to bowel oedema, steroids
- Histology normal LM and effaced podocytes by EM

- 24 hour urine selective protienuria > 3.5 g/24h
- Selectivity index is
- IgG u X ALBUMIN s / IgG s X ALBUMIN u (< 0.01 selective & > 0.02 non selective. If selective highly indicate minimal or steroid responsive nephrotic
- Selective proteinuria usually in children
- Treatment steroid 1-2mg/kg/day ,rapid resolution
- If no response within 16 w in adult …. Steroid resistance and other therapy indicated as cyclophosphamide or cyclosporine
- Relapse…. recurrence of proteinuria 1 month after complete remission (proteinuria < 200mg/day and albumin > 3.5 g/dl)
- Frequently relapsing 2 relapses within 6 months.
- Steroid dependent 2 consecutive relapses during therapy or 14 days after discontinuation of treatment
- Biopsy indicated in adults usually (>=13 years)

Membranous nephropathy

- Histology :Thickened capillary walls and spikes by LM & by IF & EM diffuse finely granular subepithelial (beneath podocytes) immune deposits only IgG4 subclass (pathognomonic for idiopathic MN).
- Causes : idiopathic (most), immune (lupus and type I DM), hepatitis BV, gold penicillamin, NSAIDs, miscellaneous (tumors …solid as CA colon, kidney transplant)
- Uncommon causes : RA,graves disease, hashimotos. DH, small bowel enteropathy, hepatitis CV ,syphilis , hydatid
- Nephrotic in 60 %, most common cause of adult nephrotic (caucasian > 60 years) , FSGS now increasing especially in blacks
- Hypertension 10 % & is mild
- Hematuria in 30 %
- Thromboembolism in up to 40 %
- Males > females
- Treatment by steroids and cyclophosphamide for three months especially in severe nephrotics or renal impairement (hemorrhagic cystitis, infertility and secondary leukemia are risk), rituximab, ACTH, cyclosporine,
- Non immune treatment (antiproteinuric) ACEI & / ARB with statins +/- CCB +/- spironolactone
- High risk increase BU & s creatinine / proteinuria > /= 8g > 3-6 months
- 1/3 spontaneous remission, 1/3 renal failure, 1/3 persistant nephrotics

FSGS

- ***Histololgy*** : focal (< 50% of glomeruli) seclerosed, if > 50% of glomeruli affected by pathology this is diffuse lesion. S= sigmental part of the glomerulus affected. If all the glomerulus affected this is known as global seclerosis.the lesion is hyalinization and seclerosis
- Some biopsies are normal and diagnosed as minimal CD because the process is focal
- ***Causes***: Primary (ideopathic) mediated by circulating factor, secondary causes are familial, viral (HIV, parvovirus B 19, CMV) , drugs (herion, pamidronate, lithium), obesity, nephrectomy or single kidney(the remaining kidney will develop sclerosis), anabolic steroids, sickle cell disease
- ***Presentation*** : nephrotic in 50 %. Leg odema is the most common, hypertension in 30-50 % . Aminoaciduria,glucosuria,phosphaturia can happen due to associated tubular fibrosis
- ***Poor prognosis*** *nephrotic range , black race, increasing creatinine, no response to initial therapy with prednisolone*
- ***Treatment*** non specific (anti proteinuric measures) with steroid if poor response to nonspecific treatment. Alternative cyclosporin or tacrolimus, cyclophosphamide, mycophenolate mofetil

Manegment of proteinuria

- Restrict protein diet to 0.8 -1 g/ day and some will recommend adding the protien amount lost in urine
- ACEI &/ ARBs (response assessed in three months).
- If no response (protienuria not decreased by 50%, or not < 3.5 g /24 h which is partial remission) add CCBs (diltiaze m or verapamil) if no response add spironolactone 25 -100 mg/day if no response add statins
- Salt restriction (salt use increase oedema and decrease effectiveness of ACEI & ARBs

For nephrotic oedema management is by :

- Increasing doses of furosemide starting with 80 mg / day increase gradually till diuresis or ceiling dose reached (250 mg X 2) if no response add hydrochlorothiazides or metolazone, if no response change to IV furosemide if no response give 20 % human albumin followed by bolus IV furosemide if no response do mechanical ultrafiltration
- In all these treatment check K level and cardiac status and quit when necessary

Prophylaxis with anticoagulants in

Added risk as immobilization, previous thrombotic episode , serum albumin less than 2 g/dl 0r 24 h urinary protein > 10 -15 gs

Dose of warfarin require reduction because it is a protein bound drug

IgA nephropathy (berger disease in 1968)

- is the most commonly type of glomerulonephritis
- . Haematuria is the earliest sign and is almost universal,
- proteinuria a later feature,
- hypertension very common. (so pt present with hematuria and hypertension)
- There may be severe proteinuria or in some cases progressive loss of renal function. The disease is a common cause of ESRD.
- A particular hallmark in young adults is acute self-limiting exacerbations, often with gross haematuria, in association with minor respiratory infections. This may be so acute as to resemble acute post-infectious glomerulonephritis, with fluid retention, hypertension and oliguria with dark or red urine.
- Characteristically, the latency from clinical infection to nephritis is short: a few days or less.
- Occasionally, IgA nephropathy progresses rapidly and crescent formation may be seen.(present as RPGN)
- The response to immunosuppressive therapy is usually poor.
- The management of less acute disease is largely directed towards the control of blood pressure in an attempt to prevent or retard progressive renal disease.
- alternating steroids and cytotoxic) If protein > 1g/24h or renal dysfunction
- Histo : deposition of IgA Ab predominantly in the mesangium associated with mesangial hypercellularity present in almost all biopsies

Presentation of |IgAN|

- Macroscopic hematuria after respiratory tract infection or gastroenteritis
- Asymptomatic hematuria and proteinuria (by urine exam).
- Nephrotic syndrome
- CKD
- ARF (this is due to RPGN ie crescent formation, intra tubular deposition of huge amount of blood , and during pregnancy)

Membranoproliferative GN(mesangiocapillary GN)

Type I sub endothelial and mesangial electron dense deposits

Type II electron dense deposit in the basement membrane of glomerulus, Bowmans and mesangium

Type III sub endothelial and sub epithelial EDD

There is almost always a double contour appearance of capillary loops

- Causes
- Type I

1. chronic infections especially HCV(90%) ,chronic HBV, bacterial endocarditis…ie almost exclude secondary causes
2. CTD…..lupus erythematosus, Sjogren S
3. Malignancy……..chronic lymphocytic leukemia. non Hodgkin lymphoma.

- Type II …associated with C3 nephritic factor with or without partial lipodystrophy, factor H deficiency

Presentation

1. Microscopic hematuria with non nephrotic protienuria (35%)
2. Nephrotic with decreased renal function (35%)
3. Chronic progressive GN (20%)
4. RPGN (10%)

Treatment

Steroid for 3 months if no response stop treatment and prescribe alternatives

Goodpasture syndrome (renal failure and pulmonary hemorrhage)

- Male> females, caucasian > asian & blacks
- Predisposing factors HLA DR2 & DR4
- DR1 & HLA DR7 are protective allels
- 75% present with pulmonary hemorrhage and found to have renal failure
- Factors leads to pulmonary hemorrhage are smoking, infection (pneumonia),pulmonary edema , trauma, hydrocarbons
- Exertional dyspnoea(hemorrhage leading to anemia).

- Diagnosis

Clinical + Antiglomerular basement membrane AB are +ve in all cases (false positive in inflammatory diseases) + linear deposition of antibody in renal biopsy.

DDx of lung hemorrhage + Acute RF

1. Acute renal failure with pulmonary odema
2. Vasculitis (wegner ,microscopic polyangitis,SLE,)

Treatment

IV steroid(methylprednisolone) + oral cyclophosphamide + plasma pheresis + treatment of associated conditions as sever infection