Ep 13 Glomerulonephritis - Dr Chua Horng Ruey

How common is glomerulonephritis? 00:17

- 2nd commonest cause of ESRF in Singapore – accounts for 14-15% of all ESRF patients
- IgA nephropathy commonest GN of biopsied GNs
- Likely to be an increasing trend
- Less infection related, more immune mediated and metabolic syndrome related
- Can be fairly asymptomatic – hence pick up rates depends on aggressiveness of screening

When should we be suspected glomerulonephritis? 03:07

- 3 groups of patients: 1) Frank nephrotic/nephritic syndrome 2) Incidental haematuria/proteinuria noticed on health screening and subsequently worked up 3) Asymptomatic – Overtime, often go on to develop hypertension and then present
- Suspect GN in patients with microscopic haematuria or proteinuria especially if associated with:
    - Hypertension
    - Tenuous kidney function – caution with the many patients labeled as AKI due to dehydration
    - Absence of DM
- Is hypertension the cause of CKD or is it a sequelae of GN?
    - Hypertensive kidney disease usually requires long standing hypertension (older patients), has concomitant complications like left ventricular hypertrophy and macrovascular complications, scarred and shrunken kidneys
    - Proteinuria in hypertensive kidney disease tends to be mild, UFEME should not be active unless patient is in hypertensive urgency

What does the initial evaluation for glomerulonephritis entail? 09:13

- Obtain basic urinary protein, haematuria and kidney function assessment early (before hospital interventions set in)
- Urinary Protein Assessment
    - Spot urine protein creatinine ratio
        - § Good screening tool despite variability with orthostatic changes, activity relation, acute illness
        - § Caution about units – always refer back to reference range
    - 24-hour urine protein
        - § Confirm and quantify urinary protein in instances when urinary protein is high
        - § Factor in practical considerations (e.g. incontinence, immobility etc)
    - Serum albumin
        - § Much of protein loss in the form of albumin
        - § Many patients will be hypoalbuminemic
- Haematuria Assessment
    - Consider urological causes: Urothelial/bladder malignancy, stones
        - § Malignancy risk factors: Older patients, smokers, toxins, cyclophosphamide, pelvic radiation
        - § Consider urological work-up with CT urogram and cystoscopy to exclude mitosis
    - Phase contrast microscopy
        - § Looking for dysmorphic cells that may suggest glomerular etiology
        - § Numerical cut-offs not well agreed upon
- Casts
    - RBC Cast: Suggestive of glomerular disease
    - White Cell Cast: Tubulointerstitial inflammation
    - Hyaline Cast: Non-specific

- Kidney Function Assessment
    - Trend renal function and focus on areas of decline in kidney function
    - Check what was happening then: New/changes in meds? Hospital admission? BP control?
    - If kidney function is tenuous, may push toward a biopsy

Nephrotic vs Nephritic Syndrome 21:08

- Nephrotic Syndrome:
    - 3.5g/day of proteinuria, hypoalbuminuria, lowish BP (due poor oncotic pressure; however, in patient with concomitant hypertension, this might not be the case), dyslipidemia
    - At risk for clotting tendencies
    - Pathophysiology: Podocyte disorder where filtration barrier is compromised causing excess protein leakage
- Nephritic Syndrome:
    - Active urinary sediment (haematuria, cast), proteinuria, renal dysfunction, usually hypertensive
    - Pathophysiology: Inflammed glomerulus causing cellular proliferation
        - § Immune Complex: Lupus, IgA nephropathy
        - § Non-Immune Complex: ANCA related vasculitis
    - Assess for life threatening extra-renal manifestations: Especially pulmonary renal syndromes (hemoptysis)

What needs to be done overnight for a patient with GN? 27:11

- Pulmonary renal syndromes are to be emphasized
- Get basic tests: Urine PCR, UFEME, FBC (looking for cytopenias) GXM, consider autoimmune screens (SLE, anti GBM, ANCA) in nephritic picture/suspect pulmonary
- Control blood pressure
- Hemoptysis measures: Yankeur suction, hemoptysis charting etc
- Caution with hydration in AKI
    - Not all AKIs are due to dehydration
    - Patients in the general ward have received a share of resuscitation
    - Risk of tipping patient into fluid overload
    - Assess based on hemodynamics, physical examination, labs (e.g. hyponatremia)

Etiological evaluation for glomerulonephritis? 33:20

- Nephrotic Syndrome
    - Metabolic Profile Screen: Hba1c, lipid profile
    - SLE screen
    - Special Serologies: Anti PLA2R (A/w membranous nephropathy; diagnostic role still being established), anti-thrombospondin (association with underlying mitotic disease)
    - Hep B and C, HIV
    - Paraproteinemia (myeloma, amyloidosis): Serum protein electrophoresis, immunofixation, free light chain ratio
- Nephritic Syndrome
    - Autoimmune: SLE screen (ANA, anti-ds DNA, complements), Anti-GBM and ANCA especially if renal function is unstable (of note, these tests are run only once a week)
    - Hep B and C, HIV
    - Anti PLA2R
- Role for imaging? - Guide biopsy planning: Scarring/cortical thickness, cysts/tumours, hydronephrosis, single vs bilateral kidneys
- Which patients should undergo a kidney biopsy?

- In principle, all patients without a certain diagnosis should be offered biopsy – in non-diabetics, threshold of biopsy is significantly lowered
- Exclusions: Severely scarred kidneys, poor functional pre-morbids
- In patients with diabetes, will have to consider in the context of other micro/macrovascular diseases
    - § If other comorbidities outweigh in significance the concern of renal disease, will have to contextualise the overall management
    - § Is this just diabetic nephropathy?
        - Associated microvascular (retinopathy, neuropathy) and macrovascular disease
        - Duration: May be unreliable especially for T2DM
        - Proteinuria decline tends to follow renal decline
        - If there is glomerular haematuria, plunge in renal function or rise in proteinuria, consider element of GN
- Risk for biopsy bleeding highest in uncontrolled hypertension and AKI state. Also if significantly azotemic or severely overloaded, may consider dialyzing first to optimize procedural conditions

<u>General Measures for Patients on Immunosuppression? 49:07</u>

- Optimise metabolic health
    - Blood Pressure Control
    - Glycemic Control: DM screening, teach glycemic monitoring
    - Lipid management
    - Smoking Cessation
- Infective complications:
    - Screen Hep B, C and HIV
        - § For Hep B, screen anti-HBcAb to pick up core mutants/occult Hep B
        - § Patients may require Hep B prophylaxis
    - TB: Chest X-ray, TB quantiferon
    - Bactrim prophylaxis for PCP - KIV check G6PD level first
- Bone Health: Calcium, Vit D, BMD
- Hyperkalemia: Especially when there is RAAS blockade, calcineurin inhibitors, bactrim
- Thromboembolic complications: Usually in patients with membranous nephropathy with severe proteinuria and hypoalbuminemia
    - May consider anticoagulation prophylaxis – but need to be temporally distant from biopsy in view of delayed bleeding risk
- Diet: Low salt diet, weight loss if overweight, avoidance of raw food
- Cost issues: Consider social worker review
- Age appropriate cancer screening

<u>Specific Immunosuppressants 56:55</u>

- Calcineurin Inhibitors
    - Cyclopsorin: More subsidies; but SE of hypertrichosis, gingival hypertrophy
    - Tacrolimus: More expensive
    - Malays may require higher doses
- Cyclophosphamide: Sterility issues
- Rituximab: High cost
- Mycophenolate: Diarrhea

<u>Take Home Points</u>

- Glomerular diseases can be complex – Consult others when in doubt

- Management of glomerulonephritis is not just about immunosuppression
- Pay attention to: Metabolic health, infective risks, medication side effects, cost