LESSON
ON THE THEME:
“ACUTE AND CRONIC GLOMERULONEPHRITIS”
DEPARTMENT OF PEDIATRICS

Elaborated by associate professor Angela Ciuntu

Definition

- Glomerulonephritis refers to a specific set of renal diseases which an immunologic mechanism triggers inflammation and proliferation of glomerular tissue that can result in damage to the basement membrane, mesangium, or capillary endothelium .

Pathophysiology

- Glomerular lesions are the result of glomerular deposition or in situ formation of immune complexes.
- On gross appearance the kidneys may be enlarged up to 50%.
- Histopathologic changes include swelling of the glomerular tufts and infiltration with polymorphonucleocytes.
- Immunofluorescence reveals deposition of immunoglobulins and complement C3.
    - C3 increase vascular permeability and chemotactic factors C5a-
    - Neutrophils and macrophages release substances that damage basement membrane.
- A streptococcal neuramidase may alter host immunoglobulin G (IgG).
- IgG combines with host antibodies. IgG/anti-IgG immune complexes are formed and then collect in the glomeruli.
- In addition, elevations of antibody titers to other antigens, such as antistreptolysin O or antihyaluronidase.
- DNAase-B and streptokinase, provide evidence of a recent streptococcal infection.

Causes of preponderance deposition of immune complexes

- High renal blood flow -25% from cardiac ejection fraction
- Big glomerular surface area for filtration.
- Oncotic pressure in glomerular capillary are 4 time higher than in other body capillary.
- Fenestrations of endothelial cells improve toxin and antibody damage of structural integrity of the podocyte foot and slit diaphragms.
- Affinity of antigens to basement membrane ("nephritogenic"strains of group A beta-hemolytic streptococci.
- Normal negative ionic carges of basement membrane may change by different cells mediators, toxins.

Predisposing factors

- HLA genetic predisposing (HLAB8,B13,DWQ2, DQB10301 and DR7)
- High family receptivity to streptococcus
- Chronic foci of infection, parazits.
- Cold and humid weather (winter, spring)
- Social-economy and ecological factors.
- Age- particularly of immune response.
- Sex- androgens favour glomerular proliferation

Immunologic injury in glomerulonephritis

- Membranoproliferative glomerulonephritis is due to the expansion and proliferation of mesangial cells as a consequence of the deposition of complements.
- Type I refers to the granular deposition of C3,is an antiglomerular basement membrane disease-1-1.5% of chronic glomerulonephritis ;
- Type II is mediated by immune complexes -5-10% of chronic disease..
- Berger disease (IgG-immunoglobulin A(IgA nephropathy) glomerulonephritis results from a diffuse mesangial deposition of IgA and IgG
- Type IV immune vasculitis- 2% of chronic glomerulonephritis.
- Type III- is identified by antineutrophil cytoplasmic antibody.

- Idiopathic rapidly progressive glomerulonephritis is a form with glomerular crescents.
- Crescents contain fibrin, the proliferating epithelial cells of Bowman space, basement membrane-like material, frequently associated with glomerular cell death (necrosis)

Clinical classification

- Primary glomerulonephritis: acute with nephritic, nephrotic and isolated urine syndrome.
- Chronic nephritic, nephrotic, mixt.
- Rapidly progressive (crescents) glomerulonephritis.
- IgA nephropathy (Berger`s disease, IgA mesangial deposition

1. Acute glomerulonephritis
   - Acute starting (days-weeks), spontaneous resolve completely, maximum in one year.
   - Morphologic- proliferative and exudative reversibile lesion.
2. Chronic glomerulonephritis
   - Chronic glomerulonephritis with insidious onset or acute in some cases, non responding to treatment more than 2 years.
   - Is common proteinurea, glomerular damage and renal failure, difficult to establish the onset of chronic process.
3. Rapidly progressive
   - Rapidly progressive glomerulonephritis- acute onset, primary severe evolution with nephritic syndrome, edema, hypertension, acute renal failure onset in weeks/months, lead to death in 2 years from starting.
   - Morphologic: crescent formation with fibrin inside of Bowman space, proliferation of epithelial cells, disruption of the capillary walls and its necrosis. Serum C3 are normal

Pathology classification of glomerulonephritis

Nonproliferative

- With minimal lesion of glomeruli
- Focal segmental glomerulosclerosis
- Membraneous glomerulonephritis

Proliferative

- Endocapillary proliferative
- Membranoproliferative
- Mesangial proliferative
- Extracapillary with crescents
- Glomerulosclerosis

Clinical manifestation

Acute **nephritic syndrome**-acute onset after 10-21 days of streptococcal infection: fever, headache, lombar pain, renal or extrarenal signs.

- Nonspecific symptoms: weakness, fever, abdominal pain, malaise.
- Puffiness of the fase and simetrical edema.
- Hypertension to fluid overlood, secondary headache.
- Onset of acute nephritis typically 1-2wk after pharyngitis, 2-4wk post pyodermia.

Laboratory data in acute nephritic syndrome

Urinalysis

- Proteinuria <2.5gr/dl, nonselective.
- Oliguria- urine flow <300ml/24h.
- Gross hematuria brown or cola colored, granular casts

Serology and complement levels

- ASLO >200un, CRP>6mg/ml, CIC >75un;
- ESR, blood urea and creatinine rises..
- Circulated blood cryoglobulins increase.
- Serum complement (C3,C4), antinuclear antibody- differentiation systemic diseases.
- Low C3 also may be in membranoproliferative poststreptococcal nephritis.

- Normal serum C3 suggests systemic vasculitis, renal immune complex disease, idiopathic rapidly progressive nephritis or Berger nephropathy.
- Cultures of throat and skin lesions- role out Streptococcus species.
- Anti-DNA antibodies, antineutrophil cytoplasmic antibodies (ANCA), c-ANCA

Imaging Studies

- Chest X-ray in patients with cough, with or without hemoptysis (ie.Wegener granulomatosis, Goodpasture syndrome, pulmonary congestion).
- Abdominal X-ray or computed tomography if visceral abscesses are suspected.
- Renal ultrasonography evaluate kidney size, the size <9cm is suggestive of scarring.
- Echocardiography in patients with a new cardiac murmur or positive blood culture to role out endocarditis or a pericardial effusion.

Consideration for renal biopsy

- Consideration for renal biopsy includes the development of renal failure, persistence of hematuria; low C3 more than 3mo after onset; family history of renal disease.
- Pathology- diffuse endocapillary proliferation, lesion >50% of nephrons, immune depositions
- 95%of cases resolve completely, microhematuria my persist months/years, around 1-5% pass on to chronic glomerulonephritis

Treatment of nephritic syndrome

- Hospital treatment, restricted the activity in the acute phase.
- A strict intake of fluids in patients with significant edema. Vegetal proteins 0.5g/kg/day increase to the 2-3 weeks(1-2g/kg) selective butter, curds, eggs and carbohydrates, minimal calories 400/m2/day.
- Eradication of etiological factors- antibiotics 10-14days, if necessary repeat.
- Antihistaminic drugs in allergic processes.
- Nonsteroid or pulse- steroid drugs in systemic vasculitis with renal disorders.
- Treating hypertension with beta-blockes, angiotensin-converting enzyme (ACE) inhibitors, vasodilators and diuretics-drugs, monitor serum potassium level.

Isolated urine syndrome- asymptomatic evolution

- Microscopic hematuria >5 red cells/10ml of urine.
- Microproteinurea
- Asymptomatic clinical manifestation
- Benign evolution.

Mixt glomerulonephritis

- Moderate edema, persistent, my be anasarca.
- Persistent severe arterial hypertension unresponsive to drugs.
- Persistent of hematuria, red custs, nonselective proteinuria.
- Different grade of anemias, rises ESR.
- High level of blood creatinin and urea lead to chronic renal failure.

Nephrotic syndrome

- Common pediatric problem, generally resolve completely.
- 90% of children have some form of idiopathic nephrotic syndrome.
- Onset in the first year (3-12mo) may be genetic.
- Causes of nephrotic syndrome:
- Abnormality in T-cell lymphocyte function and humoral immunyti
- Key role of vascular endothelial growth factor, maintaining normal glomerular integrity
- Hypoproteinemia, fundamentally hypoalbuminemia <25g/l.
- Elevated all serum lipid levels (cholesterol, triglycerides) and lipoprotein.
- Patology: the essential lesion is the thickening of the foot-plate of the basement membrane with minimal lesion (80%). As a result, there is increased permeability of glomerulus to plasma proteins. In 10-12% focal glomerulosclerosis, 1-5% membrane damage

Clinical manifestation NS

- Males often suffer between 3-8 years.
- Insidious starting with general signs, skin allergy, digestive disorders, hepatomegaly.
- Edema around the eyes and the lower extremities, “pitting” in nature.
- Massive edema, anasarca, oliguria, weight gain, respiratory distress
- Blood pressure may be low (intravascular volume depletion), or elevated (neurohumoral responses.

Laboratory Evaluation

- Diagnosis of nephrotic syndrome is confirmed by the triad of generalized edema, proteinuria, albuminuria (> 2+ on dipstick or urine protein/creatinine ratio (>2mg/mg), and hypoalbuminemia (serum albumin < 2,5 g/dl)
- Hypercholesterolemia is also commonly present
- In patients with a typical presentation, serum studies should include an evaluation of complete blood count, electrolytes, blood urea nitrogen (BUN), creatinine, and albumin levels.
- For patients at an older age or with atypical presentation, additional serum studies to exclude secondary causes of nephrotic syndrome should include C3 and C4 complement levels;
- Antinuclear antibody (ANA) and possibly anti-double-stranded DNA;
- HIV antibody; hepatitis A, B, and C serologies, and consideration of other viral serologies

Treatment of NS

- Specific Therapy
- The initial treatement for new-onset nephrotic syndrome erally includes 60mg/m2/day (maximum 80 mg/d) of prednisone for 4 to 8 weeks, followed by 40mg/m2 every e day for 4 to 8 weeks, and then a gradual taper until discontinued.
- In patients, FRNS and SDNS, alternative agents with potential steroid sparing effects are often used, including cyclophosphamide, levamisole, cyclosporine, tacrolimus, and mycophen mofetil.
- In patients with SRNS, may be used agents include cyclosporine, tacrolimus, high dose intravenous methylprednisolone, and mycophenomofetil (MMF).

Prognosis

- The single most important prognostic factor for maintenance of long-term normal renal function in nephrotic syndrome is the patient's initial response to corticosteroids.
- Although children who enter complete remission during an 8-week initial course of oral corticosteroids have an excellent prognosis, the prognosis for those who fail to enter remission is more guarded.
- Overall, close to 80 % of newly diagnosed children treated with corticosteroids will achieve complete remission.