LESSON
ON THE THEME:
“ACUTE AND CHRONIC GLOMERULONEPHRITIS IN CHILDREN”
DEPARTMENT OF PEDIATRICS

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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 reversible lesion.

2. Chronic glomerulonephritis
   • Chronic glomerulonephritis with insidious onset or acute in some cases, non responding to treatment more than 2 years.
   • Is common proteinuria, 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
• Membranous 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, lumbar pain, renal or extrarenal signs.
• Nonspecific symptoms: weakness, fever, abdominal pain, malaise.
• Puffiness of the face and symmetrical edema.
• Hypertension to fluid overload, 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 (i.e. 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.

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 immunuity
    • 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

Isolated urine syndrome- asymptomatic evolution
• Microscopic hematuria >5 red cells/10ml of urine.
• Microproteinuria
• 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.

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.