ACUTE POSTSTREPTOCOCCAL GLOMERULONEPHRITIS

This disease is a classic example of the acute nephritic syndrome characterized by the sudden onset of gross hematurea, edema, hypertension, & renal insufficiency. It is one of the most common glomerular causes of gross hematurea in children, preceded only by Ig A nephropathy.

Etiology & epidemiology

It follows infections of the throat or the skin by certain " nephritogenic " strains of group A β-hemolytic streptococci. The factors which allow only certain strains of streptococci to be nephritogenic remain unclear. It follows streptococcal pharyngitis during cold weather & follows skin infection (pyoderma) during warm weather.

Pathology

Like most forms of acute glomerulonephritis, the kidneys appear symmetrically enlarged. On light microscopy, all glomeruli appear enlarged & relatively bloodless & show diffuse mesangeal cell proliferation with ↑ mesangeal matrix. Immunofluorescence microscopy reveals lumpy-bumpy deposits & immunoglobulins & complements on the glomerular basement membrane & in the mesangium. On electron microscopy, electron dense deposits (humps) are observed on the epithelial side of the glomerular basement membrane.

Pathogenisis

It may be mediated by immune complex formation (with ↓ C3), although the precise mechanism remain to be determined.

Clinical presentations

- It is most common in children aged 5-12 years & uncommon below the age of 3 year.
- Symptoms usually develop 1-2 weeks after an antecedent streptococcal pharyngitis or 3-6 weeks after streptococcal pyoderma.
- The severity of renal involvement varies from a symptomatic microscopic hematurea with normal renal functions to acute renal failure.
- Depending on the severity of renal involvement, patients may develop various degrees of edema, hypertension & oligurea. Patients may develop encephalopathy &/or heart failure owing to hypertension or hypervolemia.
- Encephalopathy may also result directly from the toxic effects of streptococcal bacteria on the CNS.

- Edema typically results from salt & water retention & nephrotic syndrome may develop in 10-20% of cases.
- Specific symptoms as malaise, lethargy, abdominal or flank pain, & fever are common.
- Acute subglottic edema & airway compromise may be reported.
- The acute phase generally resolves within 6-8 weeks.
- Although urinary protein excretion & hypertension usually normalize by 4-6 weeks after the onset, persistent microscopic hematurea may persist for 1-2 years after the initial presentation.

Diagnosis

- GUE → RBC , RBC casts, proteinurea, & polymorphnuclear leukocytes.
- There may be mild normochromic anemia due to hemodilution & low-grade hemolysis.
- C3 is usually ↓ in acute phase & return to normal level after 6-8 weeks.
- The diagnosis is confirmed by the clear evidence of invasive streptococcal infections :
  1. +ve throat culture may support diagnosis or represent carrier state.
  2. A rising antibody titer to streptococcal antigens confirms a recent streptococcal infection. These include :
     - ASO titer is commonly ↑ after pharyngeal infection but rarely ↑ after streptococcal skin infection.
     - The best single antibody titer to document cutaneous infection is the deoxyribo-nuclease (DNAase) B antigen.
     - The streptozyme test is alternative study which detects antibodies to streptolysin O, DNAase B, hyaluronidase, & streptokinase using a slide agglutination test.
- ↓ C3.
- Renal biopsy should be considered in :
  - Acute renal failure.
  - Nephrotic syndrome.
  - Absence of evidence of streptococcal infections.
  - Normal level of C3 or ↓ C3 level > 2 months after the onset.
  - It is considered with hematurea, proteinurea, or ↓ renal functions.

Differential diagnosis

It includes several causes of *hematurea* as :

• Ig A nephropathy • Alport syndrome • Membranous nephropathy • Membranoproliferative glomerulonephritis • SLE nephritis • Acute exacerbation of chronic glomerulonephritis • Acute glomerulonephritis following other infections like staphylococci, streptococcus pneumonia, G-ve bacteria, & bacterial endocarditis • Pyelonephritis

Complications

- Hypertension : seen in 60% of cases & may → hypertensive encephalopathy in 10%.
- Acute renal dysfunction : hyperkalemia, hyperphosphatemia, hypocalcemia, acidosis, seizure, & uremia.
- Heart failure.

Prevention

- Early systemic antibiotic treatment for streptococcal throat & skin infection does not eliminate the risk of glomerulonephritis.
- Family members of the patient should be cultured for group A β-hemolytic streptococci & treated if culture is +ve.

Treatment

- *General measures* :
  1. Bed rest : only indicated during the oliguric phase (1st week).
  2. Diet : ↑ carbohydrates diet to provide adequate calories & ↓ protein & salts during oliguric phase & with complications as severe hypertension & marked vascular congestion.
  3. Fluid balance : During the oliguric phase, measurement of the daily urinary output is important. The total daily fluid intake should be equal to the urinary output + insensible water loss.
- *Specific measures :*
  1. Eradication of streptococcal infections by 10 days penicillins to ↓ the spread of nephritogenic organisms.
  2. Control of hypertension : ↓ Na^+ intake, diuretics, Ca^{+2} channel antagonists, vasodilators, & angiotensin converting enzyme inhibitors. [captopril 0.5-1 mg/kg/day, hydralazine 1-2 mg/kg/day, propronalol 1-2 mg/kg/day, the dose of each drug is divided 3-4 times].
  3. Control of edema : In most cases, edema subsides spontaneously at the end of 1st week & with the onset of diuresis. ↓ fluid & salt intake during the 1st week is usually important. In more severe cases, -ve fluid balance is required. Diuretics as furocemide may be used.
- *Treatment of complications :*
  1. Severe hypertension (hypertensive crisis) : Na^+ nitroprusside infusion (0.5-10 microgram/kg/minute), Labetalol infusion (0.25-3 mg/kg/hour), Esmolol infusion (150-300 microgram/kg/minute).
  2. Heart failure.
  3. Renal failure.

Prognosis

- Complete recovery occurs in > 95% of patients.
- Mortality rate in the acute phase can be avoided by appropriate treatment of acute renal failure, heart failure, & hypertension.
- Infrequently, the acute phase may be severe & may → chronic renal insufficiency.
- Recurrences are extremely rare.

HEMOLYTIC–UREMIC SYNDROME (HUS)

It is the most common cause of acute renal failure in children < 4 years. History of preceding gastroenteritis or upper respiratory infections 5-10 days before the onset of illness is usually obtained. Shiga toxin–producing E.Coli O157:H7 is common cause. Less often, other bacteria as shigella, salmonella, streptococcal pneumonia, & viruses as coxsackievirus, influenza, & varicella. HUS may be epidemic or sporadic. The *epidemic* variety may follow an infective insult & the *sporadic* type may be a more heterogeneous group with a number of etiologies.

Clinical presentation

The onset is abrupt with manifestation of :

1. *Microangiopathic hemolytic anemia* as intense pallor. The examination of blood smear is important to identify RBC fragment, Burr cells, & schistocytes, as well as severe anemia & reticulocytosis.
2. *Acute renal failure* which is usually but not always oligoanuric with acidotic breathing & altered consciousness (↑ blood urea, ↑ serum creatinine, ↑ serum K^+, & metabolic acidosis).
3. *Throbocytopenic purpura* which may be mild (platelets count is about 120,000/mm^3) to severe (platelets count < 20,000/mm^3).

Pathogenesis

The primary event is the *endothelial cell injury*. Capillary & arterial endothelial injury in the kidneys → localized clotting. The microangiopathic hemolytic anemia results from mechanical damage of RBC^S as they pass through the altered vasculature. Thrombocytopenia is caused by intrarenal platelets adhesion or damage. Damaged RBC^S & platelets are removed from the circulation by liver & spleen → hepatosplenomegaly.

Complications

These include : • *Anemia* • *Acidosis* • *Hyperkalemia* • *Fluid overload* • *Heart failure*

• *Hypertension* • *Uremia* • *Extrarenal manifestations* which include : 1. CNS (irritability, seizure, & comma) 2. GIT (colitis, intestinal perforation, intususception, & hepqtitis) 3. Heart (pericarditis, myocardial dysfunction, & arrythmias) 4. Other rare complications as focal pancreatic necrosis, skin necrosis, parotitis,& adrenal dysfunction.

Treatment

- It is generally *supportive* treatment including treatment of fluid & electrolyte imbalance, anemia, hypertension, aggressive nutritional support, & early dialysis.
- Avoid antibiotics if gastroenteritis due to E.Coli 0157:H7 because this may → ↑ % of HUS.
- Plasmapharesis or fresh frozen plasma may be used in 1. HUS which is not associated with diarrhea & not associated with streptococcus pneumonia. 2. HUS with severe CNS involvement.
- There may be need for renal transplant.
- Synor b-PK : a silicon dioxide-derived univalent adsorbant which binds shigatoxin in the intestinal lumen (under study).

Prognosis

This depends on the proper management of acute renal failure which → > 90% of patients survive the acute phase of HUS with diarrheal prodrome. End-stage renal disease may occur in about 9% of these patients. Patients who recover the acute phase require a long term follow up (for up to 20 years) for renal complications.

ENURESIS

Enuresis is urinary incontinence in a child who is considered adequately mature to have achieved continence. It is the most common urologic condition in children. Enuresis is classified as **nocturnal** (nighttime – majority of cases – good prognosis) or **diurnal** (daytime+ nighttime – more severe – less favorable prognosis). Daytime dryness is expected in the U.S. by age 4 years. Nighttime dryness is expected by age 6 years. Another useful classification of enuresis is **primary** (incontinence in a child who has never achieved dryness – 80% of cases) and **secondary** (incontinence in a child who has been dry for at least 6 months – 20% of cases). The prevalence of enuresis at age 5 yr is 7% in males and 3% in females. At age 10 yr, it is 3% in males and 2% in females, and at age 18 yr, it is 1% in males and extremely rare in females. Evidence suggests different rates of bed-wetting by ethnicity and culture.

Etiology: Enuresis is a symptom with multiple possible etiologic factors, including developmental difference, organic illness, or psychological distress.

A. Primary enuresis :

1. Maturational delay : Primary nocturnal enuresis due to maturational delay is by far the most common type of enuresis. It is 3 times commoner in boys than in girls & it is also commoner in the first born child & in low socioeconomic classes. A strong family history is present. The severity of enuresis is variable from one child to another but daily wetting is common in most cases & the condition may be exaggerated by parental punishment. On the other hand, understanding, encouragement & simple reward may be helpful.The prognosis for ultimate recovery is excellent.

2. Organic causes : They account for only small number of cases but they should be routinely excluded. Mental retardation, sacral anomalies(spina bifida, meningocele) & urological anomalies (bladder neck or urethral anomalies) are the main causes. In these cases, enuresis is commonly severe & diurnal.

B. Secondary enuresis : It is mostly nocturnal & caused by either emotional stress or organic causes :

1. Emotional stresses : Death of a parent, birth of a new sibling, move to a new house or marital conflicts are commonly responsible for secondary enuresis. Detailed environmental history is important in every case of secondary enuresis.

2. Organic causes : polyuria & urinary tract infection should be routinely excluded in every case of secondary nocturnal enuresis. History of dysuria or weight loss are particularly important. Urine examination should be a routine step.

Treatment : Treatment of underlying organic causes of enuresis, including UTIs, diabetes mellitus, sleep disorders, and urologic abnormalities, is essential. Elimination of underlying chronic constipation is often curative. Treatment options include **conditioning therapy**, **pharmacotherapy**, and **hypnotherapy** :

1. **Conditioning therapy :** The most widely used **conditioning therapy** for nocturnal enuresis is the **enuresis alarm**. Enuresis alarms have an initial success rate of 70% with a relapse rate of 10%. The use of an alarm requires commitment from the parent and the child. The alarm has a probe that is placed in the underpants or pajamas in front of the urethra. Children with daytime enuresis and small bladder capacity often are treated with **bladder stretching exercises**, in which the child is asked to practice holding urination for longer and longer periods. A reward system often is used in conjunction with this practice. Anticholinergic drugs, such as oxybutynin (5 mg two to three times a day for children 5 years and older) often are used for 2 to 3 months during "bladder stretching."
2. **Pharmacotherapy :** for nighttime enuresis includes tricyclic antidepressants and desmopressin acetate. **Imipramine** reduces the frequency of nighttime wetting. The initial dose for children 6 years and older is 25 mg 1 hour before bedtime. The dose may be increased to 50 mg after 1 week. The maximum dose for children younger than 12 years is 50 mg; it is 75 mg for those 12 years and older. The initial success rate is 50% with a relapse rate of 30% or more even after 6 months of treatment. The most important contraindication is risk for overdose (associated with fatal cardiac arrhythmia). **Desmopressin** is also used to treat enuresis and has proved to be safe. It is available in an oral form, which is more acceptable than the nasal spray formulation. The oral medication is started at 0.2 mg per dose (one dose at bedtime) and on subsequent nights is increased to 0.4 mg and then to 0.6 mg if needed. This treatment must be considered symptomatic, not curative, and has a relapse rate of 90% when the medication is discontinued.
3. **Hypnotherapy :** has a reported 44% success rate without relapse; an additional 31% showed significant improvement in the number of dry nights. Hypnotherapy for enuresis should be offered by health or mental health professionals who are qualified to evaluate and treat enuresis by other modalities and who have training in pediatric hypnotherapy.