Immunoglobulin A Nephropathy (Berger's disease)

IgA nephropathy, also known as **Berger's disease**, is the most common primary glomerulonephritis worldwide. It is characterized by the **deposition of IgA1-containing immune complexes in the glomerular mesangium**, leading to **mesangial proliferation, inflammation**, and subsequent **glomerular injury**.

The hallmark of the disease is **mesangial deposition of IgA**, often accompanied by complement component C3, leading to a form of **immune complex-mediated glomerulonephritis**.

Pathophysiology

IgA nephropathy is a **multi-hit immune-mediated disease** with the following mechanisms:

1. **Increased synthesis of aberrantly glycosylated IgA1** in mucosal immune sites (especially after infections).
2. **Formation of autoantibodies** (usually IgG or IgA) against galactose-deficient IgA1.
3. **Immune complex formation** and deposition in the **glomerular mesangium**.
4. **Mesangial cell activation**, cytokine release, and **complement activation (especially via the alternative and lectin pathways)**.
5. Resulting in **inflammation, cellular proliferation**, and eventually **glomerular fibrosis and sclerosis**.

Etiology & Risk Factors

The exact cause remains unclear, but several contributing factors are recognized:

Immunological Factors

- Overproduction of galactose-deficient IgA1.
- Autoantibody formation against IgA1.
- Defective mucosal immune regulation.

Genetic & Environmental Factors

- **Familial clustering**—suggests genetic predisposition.
- Common in **East Asians and Caucasians**; rare in Black populations.
- **Males are affected more frequently** (2:1 ratio).
- Most common in **teens to early 30s**.

Associated Conditions

- **Liver diseases** (e.g., cirrhosis).
- **Celiac disease**.
- **Infections** (especially respiratory or gastrointestinal).
- **Dermatitis herpetiformis**.

- **HIV and other immune dysregulation syndromes**.

Clinical Presentation

Common Symptoms

- **Recurrent episodes of gross hematuria**, often following **upper respiratory tract infections (synpharyngitic hematuria)**.
- **Asymptomatic microscopic hematuria** with or without mild proteinuria.
- **Coca-Cola or tea-colored urine**.
- **Foamy urine** (indicating proteinuria).
- **Peripheral edema** (due to nephrotic-range proteinuria).
- **Hypertension**.

Other Presentations

- **Rapidly progressive glomerulonephritis (RPGN)** in severe cases.
- Flank pain and fever may occur during gross hematuria episodes.

Diagnosis

Laboratory Investigations

- **Urinalysis**:
  - Microscopic hematuria (with dysmorphic RBCs and RBC casts).
  - Mild to moderate proteinuria (<1 g/day; nephrotic-range in severe cases).
- **Serum studies**:
  - Normal complement levels (C3 and C4).
  - Elevated serum IgA in ~50% of patients.

Definitive Diagnosis

- **Renal biopsy**:
  - **Mesangial proliferation** and expansion.
  - **Granular mesangial deposits of IgA** and **C3** on **immunofluorescence**.
  - Possible presence of crescents in progressive disease.

Prognostic Indicators of Poor Outcome

- Persistent proteinuria > 0.5–1 g/day.
- Hypertension.
- Elevated serum creatinine at diagnosis.
- Microscopic hematuria > 6 months.
- Histological findings: **glomerular sclerosis**, **interstitial fibrosis**, and **crescent formation**.

Treatment and Management

General Approach

- **No definitive cure**—management aims to slow disease progression and control complications.
- Patients with isolated microscopic hematuria and preserved renal function may only require observation.

Pharmacologic Therapy

- **ACE inhibitors (ACEIs)** or **ARBs**:
  - First-line in patients with **proteinuria >0.5–1 g/day**, hypertension, or reduced renal function.
- **Corticosteroids**:
  - Considered in patients with **persistent proteinuria >1 g/day** despite optimized supportive therapy.
- **Immunosuppressants** (e.g., cyclophosphamide or mycophenolate mofetil):
  - Reserved for rapidly progressive disease or crescentic nephritis.
- **Fish oil (omega-3 fatty acids)**:
  - May have anti-inflammatory benefits in mild cases.

Renal Transplantation

- May be required in end-stage renal disease (ESRD).
- Recurrence of IgA nephropathy in the transplanted kidney can occur but usually with a milder course.

Complications

- **Hypertension**: due to chronic glomerular injury.
- **Chronic kidney disease (CKD)**: slow progression over years.
- **Acute kidney injury (AKI)**: in severe cases, especially RPGN.
- **Nephrotic syndrome**: in patients with heavy proteinuria.
- **Cardiovascular disease**: due to associated hypertension and dyslipidemia.
- **End-stage renal disease (ESRD)**: occurs in 20–40% within 20 years in high-risk patients.

High-Yield Clinical Pearls

- IgA nephropathy commonly follows an upper respiratory infection **within 1–2 days**, distinguishing it from post-streptococcal glomerulonephritis (which occurs 1–3 weeks later).
- Normal complement levels help differentiate from other immune complex-mediated glomerulonephritides (like lupus nephritis).
- Renal biopsy is **essential for diagnosis**.
- Persistent proteinuria is the most **important modifiable risk factor** for progression.
- Use **RAAS blockers** early in patients with proteinuria to reduce glomerular damage.