Membranous Glomerulonephritis

MN is one of the most common causes of nephrotic syndrome. When your immune system attacks the glomeruli in membranous nephropathy, it causes changes to the filters that lead you to lose large amount of protein into the urine. is a specific type of glomerulonephritis also known as membranous glomerulopathy, Membranous nephropathy and extramembranous glomerulonephritis . is a slowly progressive disease of the kidney affecting mostly people between ages of 30 and 50 years, usually white people (i.e., those of European, Middle Eastern, or North African ancestry) .

Symptoms

The symptoms of MGN are different for everyone, and you may not have symptoms at all. If symptoms do develop, they typically include:

- swelling of the hands, feet, or face
- fatigue
- foamy urine
- an excessive need to urinate at night
- weight gain
- poor appetite
- blood in the urine

Causes of membranous nephropathy (MN)

Most cases of MN are now known to be caused by an antibody to a protein on the podocyte called the phospholipase A2 receptor (PLA2R). In most people with MN, the body's immune (defense) system makes an antibody (a protein that normally helps fight infections). Instead of targeting an infection, these antibodies attack the podocytes. The podocytes stop

retaining the proteins in the blood stream and allow them to leak into the urine.

Pathophysiology of Membranous Glomerulonephritis

MGN is caused by immune complex formation in the glomerulus. The immune complexes are formed by binding of antibodies to antigens in the glomerular basement membrane. The antigens may be part of the basement membrane, or deposited from elsewhere by the systemic circulation.

The immune complex serves as an activator that triggers a response from the C5b - C9 complements, which form a membrane attack complex (MAC) on the glomerular epithelial cells. This, in turn, stimulates release of proteases and oxidants by the mesangial and epithelial cells, damaging the capillary walls and causing them to become "leaky". In addition, the epithelial cells also seem to secrete an unknown mediator that reduces nephrin synthesis and distribution.

Diagnosis of membranous nephropathy (MN)

- **Blood test:** Taking a sample of blood to measure levels of fat and protein.
- **Glomerular filtration rate (GFR):** Studying a blood sample to measure kidney function.
- **Kidney biopsy:** Taking a small sample of kidney tissue with a needle and having a lab examine it to see if it contains an antibody associated with MN.
- **Urine test:** Measuring levels of protein and blood in your urine.
- **Antibody levels:** blood sample to measure the levels of the antibody against the phospholipase A2 receptor.

Treatment

For treatment of idiopathic membranous nephropathy, the treatment options include immunosuppressive drugs and non-specific anti-proteinuric measures such as ACE inhibitors or angiotensin II receptor blockers. Given

spontaneous remission is common, international guidelines recommend a period of watchful waiting before considering immunosuppressive treatment.[18] Likelihood of achieving spontaneous remission is much higher if anti-proteinuric therapy with ace inhibitors or angiotensin II receptor blockers is commenced.

Post infection Glomerulonephritis

Poststreptococcal glomerulonephritis (GN) is a kidney disorder that occurs after infection with certain strains of streptococcus bacteria. is mainly seen in countries in which antibiotics for streptococcal infections are not widely available and accounts for about a third of cases of acute GMN. It is a disease of children aged 2–10 years, but adolescents and adults may be affected. Over 90% of cases are preceded by streptococcal infection of the throat or skin. Patients typically present with acute nephritis 7–12 days after a throat infection or about 3 weeks after a skin infection.

Symptoms

Symptoms may include any of the following:

- Decreased urine output
- Rust-colored urine
- Swelling (edema), general swelling, swelling of the abdomen, swelling of the face or eyes, swelling of the feet, ankles, hands
- Visible blood in the urine
- Joint pain
- Joint stiffness or swelling

Causes

Poststreptococcal GN is a form of glomerulonephritis. It is caused by an infection with a type of streptococcus bacteria. The infection does not occur in the kidneys, but in a different part of the body, such as the skin or throat. The disorder may develop 1 to 2 weeks after an untreated throat infection, or 3 to 4 weeks after a skin infection.
The condition is not common today because infections that can lead to the disorder are treated with antibiotics.

Pathophysiology

APSGN is an immune complex-mediated disease. Several mechanisms may participate in the pathogenesis of renal damage. Nephritogenic immune complexes are formed in circulation and deposited in the glomeruli; alternately, the antigen and antibody arrive separately and meet in or outside the glomerular basement membrane, causing *in situ* immune complex disease. Immune cell recruitment, production of chemical mediators and cytokines, and local activation of the complement and coagulation cascades drive an inflammatory response that is localized in the glomeruli. Glomerular deposition of circulating immune complexes depends on the antigen load, the antigen:antibody ratio, and the size of the immune complexes . *In situ* formation of immune complexes is favored by cationic antigens that have a charge-dependent facilitated penetration into the polyanionic glomerular basement membrane, and tend to occur in conditions of antigen excess

Diagnosis

Laboratory investigations are the most useful in PSGN assessment.

- Evidence of a preceding streptococcal infection is determined by measuring anti-streptolysin titer (ASO), and anti-nicotinamide-adenine dinucleotidase (anti-NAD) which tend to rise following pharyngitis. Other antibodies such as anti-DNAse B and anti-hyaluronidase (AHase) are usually elevated after both pharyngitis and skin infections. ASO titer is the most frequently used test, while the most sensitive is the streptozyme test; which includes measuring the

titers of all the antibodies mentioned above. ASO titers can be falsely low in patients treated with antibiotics for streptococcal infections.

- Serum complement level (C3) is usually low due to its consumption in the inflammatory reaction. Mostly, the decrease in C3 concentration occurs before serum ASO has risen.Complement levels usually return to normal levels in 6-8 weeks.
- Urine analysis: shows macroscopic or microscopic hematuria, RBC casts, mild proteinuria. Only 5% of patients with PSGN have massive proteinuria that indicates nephrotic syndrome. White blood cell casts, hyaline, and cellular casts are usually present in the urine analysis.
- Renal Function Tests: Blood urea nitrogen and serum creatinine typically elevate during the acute phase. These values usually return to normal later.

Renal biopsy is not recommended for diagnosing patients with PSGN and is performed only when other glomerular pathologies are suspected**.**

Treatment

There is no specific treatment for this disorder. Treatment is focused on relieving symptoms.

- Antibiotics, such as penicillin, will likely be used to destroy any streptococcal bacteria that remain in the body.
- Blood pressure medicines and diuretic drugs may be needed to control swelling and high blood pressure.
- Corticosteroids and other anti-inflammatory medicines are generally not effective.

You may need to limit salt in your diet to control swelling and high blood pressure.

IgA Nephropathy

IgA nephropathy is a chronic kidney disease. It progresses over 10 to 20 years, and can lead to end-stage renal disease. It is caused by deposits of the protein immunoglobulin A (IgA) inside the filters (glomeruli) in the kidney.It is one of the most common causes of primary glomerulonephritis in the world .

IgA nephropathy was first described by Berger and Hinglais in 1968, and is also known as Berger disease.

It accounts for about 10% of all cases of primary glomerular disease in the USA, 20% of cases in Europe and 30–40% in Asia.

Symptoms

IgA nephropathy usually asymptomatic in the early stages, so the disease can go unnoticed for years or decades. It's sometimes suspected when routine tests reveal protein and red blood cells in your urine that can't be seen without a microscope (microscopic hematuria).

Signs and symptoms of IgA nephropathy include:

- Cola- or tea-colored urine (caused by red blood cells in the urine)
- Repeated episodes of cola- or tea-colored urine, and sometimes visible blood in your urine, usually during or after an upper respiratory or other infection and sometimes after strenuous exercise
- Foamy urine from protein leaking into your urine (proteinuria)
- Flank pain :- Pain in the one or both sides of your back below your ribs
- Swelling (edema) in your hands and feet
- High blood pressure (Hypertension)

Pathophysiology

The disease derives its name from deposits of Immunoglobulin A (IgA) in a granular pattern in the mesangium (by immunofluorescence), a region of the renal glomerulus. The mesangium by light microscopy may be hypercellular and show increased deposition of extracellular matrix proteins.

There is no clear known explanation for the accumulation of the IgA. Exogenous antigens for IgA have not been identified in the kidney, but it is possible that this antigen has been cleared before the disease manifests itself. It has also been proposed that IgA itself may be the antigen.

The exact pathogenesis of IgA nephropathy is still not well defined. Current data implicate an important genetic factor, especially in promoting the overproduction of an aberrant form of IgA1. The immunochemical aberrancy of IgA nephropathy is characterized by the undergalactosylation of O-glycans in the hinge region of IgA1. However, such aberrant glycosylation alone does not cause renal injury. The next stage of disease development requires the formation of glycan-specific IgG and IgA antibodies that recognize the undergalactosylated IgA1 molecule. These antibodies often have reactivity against antigens from extrinsic microorganisms and might arise from recurrent mucosal infection. B cells that respond to mucosal infections, particularly tonsillitis, might produce the nephritogenic IgA1 molecule. With increased immune-complex formation and decreased clearance owing to reduced uptake by the liver, IgA1 binds to the glomerular mesangium via an as yet unidentified receptor. Glomerular IgA1 deposits trigger the local production of cytokines and growth factors, leading to the activation of mesangial cells and the complement system. Emerging data suggest that mesangial-derived mediators following glomerular deposition of IgA1 lead to podocyte and tubulointerstitial injury via mesangio–podocytic–tubular crosstalk. This Review summarizes the latest findings in the pathogenesis of IgA nephropathy.

Diagnosis

1- ultrasound of the kidney and cystoscopy are usually done first for an adult patient with isolated hematuria, to pinpoint the source of the bleeding. In children and younger adults, the history and association with respiratory infection can raise the suspicion of IgA nephropathy.

2- A kidney biopsy is necessary to confirm the diagnosis. The biopsy specimen shows proliferation of the mesangium, with IgA deposits on immunofluorescence and electron microscopy.

3- A urinalysis will show red blood cells, usually as red cell urinary casts. Proteinuria, usually less than 2 grams per day, also may be present.

4- Other blood tests done to aid in the diagnosis include CRP or ESR, complement levels, ANA, and LDH. Protein electrophoresis and immunoglobulin levels can show increased IgA in 50% of all patients.

Treatment for IgA nephropathy

Treatment for IgA nephropathy includes medication to:

- Control blood pressure with angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), or other medicines.
- Remove extra fluid with a diuretic.
- Control your immune system to lower kidney inflammation with prescribed steroids such as prednisone or cyclophosphamide.
- Lower your cholesterol levels with medications such as statins.