granular pattern upon immunofluorescence. Glomerular sclerosis may occur in the latter stage of the disease. Clinically, membranous glomerulonephritis appears as a relatively mild nephrotic syndrome. Around 40% of the patients gradually develop progressive renal failure. The response to corticosteroid is poor.

Etiology

The disease is idiopathic or primary in 80% of cases; the causal antigen is never found. The remaining 20%, however, are secondary to another disease or to drugs. The most important causes are drugs (gold, penicillamine, captopril), infections (hepatitis B or C), systemic lupus erthymatosus, or carcinoma of bronchus, breast, colon or kidney.

Diagnosis

1. Renal biopsy is usually required to establish the diagnosis,
2. Serological testing for relevant autoantibodies (*i.e.*,anti–PLA2R) may be informative if renal biopsy is contraindicated.
3. Identification of PLA2R in glomerular immune deposits (by immunofluorescence or immunohistochemistry) favors the diagnosis of primary MN; mesangial deposits are often present in secondary MN.

Lecture No. 14

Postinfectious glomerulonephritis

Acute poststreptococcal glomerulonephritis is the prototype postinfectious glomerulonephritis, it is a disease of children and adolescents, but 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 sfter a throat infection or about 3 weeks after a skin infection.

Etiology and pathogenesis

Glomerular injury results from passive glomerular trapping of circulating immune complexes composed of nephritogenic bacterial antigens and IgG antibody or by the *in situ* formation of immune complexes. This is followed by immune cell recruitment, production of chemical mediators and cytokines, and local activation of the complement and coagulation cascades that drive an inflammatory response

Diagnosis

1. Increasing titres of streptococcal antibodies and a low serum C3 level. Laboratories can often test for a range of antistreptococcal antibodies including antistreptolysin (ASO), antihyaluronidase (AHase), antistreptokinase (ASKase),antinicotinamide-adenine dinucleotidase (anti-NAD) and anti-DNAse B antibodies. These antibodies

are useful in approx.95% of cases following pharyngitis and 80% in those following pyoderma.

2. Poststreptococcal glomerulonephritis is characterized by a nephritic syndrome consisting of smoky or rust-colored urine, generalized edema, hypertension, and nephritic urine sediment. Proteinuria is typically mild.
3. Patients have rising titers of anti-streptolysin and depressed C3 levels early in nephritis but normal or minimally depressed C4 levels, indicating activation of the alternative complement pathway.
4. Proliferative glomerulonephritis with polymorphonuclear leukocyte and monocyte infiltration, granular immune deposits of IgG and C3, and dome-shaped electron-dense subepithelial deposits (humps) are characteristic.
5. Kidney biopsy is rarely needed in the child but may be warranted if there is an atypical presentation or evolution.

IgA nephropathy

IgA nephropathy (mesangial IgA deposition or Bergers disease) is the most common form of primary glomerulonephritis in the world. It affects mainly older children or young adults, and present typically as recurrent episodes of macroscopic haematuria occuring after an upper respiratory tract infection or, less frequently, a gastrointestinal or urinary tract infection, or strenuous exercise. Presentation with acute nephritis, hypertension, the nephrotic syndrome or as a chance finding of microscopic haematuria is less frequent. In contrast to poststreptococcal glomeruonephritis, the period between infection and haematuria is short, ranging from hours to a few days.

Etiology and Pathogenesis

IgA nephropathy can be considered a type of renal limited vasculitis caused by an innate defect in IgA mucosal immunity in the gut or lung: repeated exposure to a variety of environmental antigens results in an abnormal IgA response, namely the generation of nephritogenic polymeric IgA antibodies with defective galactosylation of the IgA hinge region resulting in deposition in the mesangium and the induction of inflammation in genetically susceptible individual.

Diagnosis

1. On light microscopy, the glomeruli show focal and segmental mesangial proliferation and, prominent deposite of IgA are found in the mesangium of every glomerulus, together with complement components of the alternative pathway.
2. Serum IgA levels are variable but may be significantly elevated. However, this is not a specific test, as liver disease and infections may also lead to persistent elevation of IgA.