Antineutrophil cytoplasmic antibody associated glomerulonephritis

Patients with ANCA-associated glomerulonephritis are usually aged from 40 to70 years and most have had a flu-like illness with arthralgia and myalgia a few days or weeks prior to the onset of renal disease or vasculitis. A spectrum of vasculitis is seen, ranging from disease limited to the kidneys in about a quarter of cases to a systemic vasculitic process with pulmonary involvement in about half the patients. ANCA-associated glomerulonephritis is now the commonest form of crescentic or rapidly progressive glomerulonephritis.

The renal lesion is characterized by few or no deposits of immunoglobulin or complement in the kidney **(so-called pauci-immune glomerulonephritis)** and by necrosis and crescent formation

Two pattern of antineutrophil cytoplasmic antibody (ANCA) reactivity are important clinically: generalized cytoplasmic staining **(cANCA)** and a perinuclear pattern **(pANCA)**. Most cANCA sera react with a serine proteinase called proteinase 3 (PR3), while most pANCA sera react with myeloperoxidase (MPO). A further pattern is associated with inflammatory bowel disease, particularly ulcerative colitis, some cANCA/ Panca positive sera react with neutrophil antigens other than PR3/MPO.

Raised ANCA titres are generally detectable during active granulomatosis with polyangiitis, and rising titres may herald a relapse. There has been debate whether ANCAs are pathogenic in vasculitis or simply a marker, but there is mounting evidence that they are pathogenic. The exact pathogenesis of granulomatosis with polyangiitis is not completely understood, but T cells, B cells, neutrophils and endothelial cells have all been implicated in the process.

Lecture No. 12-13

Membranous glomerulonephritis

Membranous glomerulonephritis can occur at any age, with the peak incidence in adults aged between 30-50 years and is characterized by the formation of immune complexes on the subepithelial surface of the basement membrane. The antibodies react in situ with endogenous podocyte antigens. The majority (70-80%) of patients with primary MN have circulating autoantibodies to **M-type phospholipase A2 receptor (PLA2R),** a transmembrane receptor that is expressed in glomerular podocytes. Antibodies to thrombospondin type-1 domain containing 7A protein (THSDA7A) and neutral endopeptidase have been identified in smaller subsets of patients.

Typical features include diffuse thickening of the basement membrane with fusion of the foot processes. The inhomogeneous distribution of the IgG and C3 deposits results in

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