Lecture No. 15

Lupus nephritis

Lupus nephritis is glomerulonephritis caused by (SLE) Although only 25% of patients with SLE present with renal disease as the first manifestation of lupus . clinical glomerulonephritis occurs in about 50% of cases of SLE at some time, and evidence of renal involvement can be detected in most patients, even in the absence of proteinuria.

Clinical Features

Asymptomatic hematuria or proteinuria may be the presenting features, but they often progress to nephritic and/or nephrotic syndrome. Hypertension, azotemia, nephritic urine sediment (with hematuria and cellular casts), hypocomplementemia and high anti–double-stranded DNA (dsDNA) titers are more commonly found in patients with proliferative lupus nephritis.

Pathophysiology of lupus nephritis

Pathophysiology involves immune complex deposition with development of glomerulonephritis. The immune complexes consist of

- Nuclear antigens (especially DNA)
- High-affinity complement-fixing IgG antinuclear antibodies
- Antibodies to DNA

Deposition of immune complexes from the circulation into the kidney appears to be the initiating event in proliferative lupus nephritis; however, only a subset of immune complexes appears to be nephritogenic.

DNA and anti-DNA antibodies are known to be concentrated in glomerular deposits in the subendothelial location and are likely to play a central role in the pathogenesis of proliferative lupus nephritis.

Classification of lupus nephritis is based on histologic finding

Class I. Minimal mesangial lupus nephritis: normal glomeruli under light microscope, but with minimal mesangial deposits in immunofluorescence. (**Normal serum creatinine and urine laboratory results. Incidental finding**)

Class II. Proliferative mesangial lupus nephritis: hypercellularity and mild mesangial expansion under light microscope, with mesangial deposits evident in immunofluorescence; there may be subepithelial or subendothelial deposits visible in an electron microscope or with immunofluorescence.

Class III. Focal lupus nephritis :lesions present in less than 50% of glomeruli with diffuse subendothelial deposits, with or without mesangial alterations. (Proteinuria and haematuria)

Class IV. Diffuse lupus nephritis : Damage that amounts to more than 50% (Haematuria, proteinuria, nephrotic syndrome, renal failure, arterial hypertension. Associated with elevated anti-nDNA titre and hypocomplementaemia May evolve towards renal failure)

Class V. **Membranous lupus nephritis**: thickening of the basal glomerular membrane with global or segmental immune deposits on the subepithelial wall of the basal membrane; may be associated with mesangial expansion.

Class VI. Sclerosing lupus nephritis, with involvement of over 90% of glomeruli, with no residual activity.

Diagnosis

1. Urinalysis and serum creatinine (all patients with SLE)
2. Renal biopsy
3. Diagnosis is suspected in all patients with SLE, particularly in patients who have proteinuria, microscopic hematuria, red blood cell (RBC) casts, or hypertension. Diagnosis is also suspected in patients with unexplained hypertension, elevated serum creatinine levels, or abnormalities on urinalysis who have clinical features suggesting SLE.
4. Elevated anti–double-stranded-DNA (anti-dsDNA) antibody titers and low complement (C3 and C4) levels often indicate active lupus nephritis and support the diagnosis.
5. If the aforementioned studies are abnormal, **renal biopsy** is usually done to confirm the diagnosis and classify the disorder histologically.
6. Histologic classification helps determine prognosis and direct treatment.

Henoch-Schonlein nephritis

Henoch–Schonlein nephritis (Henoch–Schonlein purpura or anaphylactoid purpura) is a common form of systemic vasculitis in which small blood vessels in a number of organs are involved.

It is usually a disease of children, with a peak age of onset between 4 and 10 years. The syndrome is characterized by nonthrombocytopenic purpura of the skin (particularly around joints) arthralgia, gastrointestinal pain and glomerulonephritis. Kidney disease is the most important manifestation of HSP as renal failure is the main cause of death.

The **prevalence of renal disease** varies from 40% to 100% but in most patients this is mild; progression to renal failure occurs in fewer than 10%. Those with the most severe clinical presentation have the worst outcome: about 40% of those with nephritic or nephrotic syndromes at onset show long-term impairment of renal function.

Immunohistology of the renal biopsy shows irregular,granular deposits of IgA, C3 and fibrin in the glomeruli. Deposits of IgA and C3 are also found in the skin, even in non-affected areas, and are diagnostic of the condition.

As in IgA nephropathy, the available evidence suggests an IgA dominant immune-complex pathogenesis with complement activation occurring via the alternative pathway. A variety of bacterial or viral antigens could be involved, as there is an association with preceding upper respiratory tract infection. In addition, HSN is a seasonal disease: most patients present during the winter. The clinical and immunological similarity between HSN and IgA nephropathy suggests that IgA nephropathy is a renal limited form of HSN.

Lecture No. 16

Anti-glomerular basement membrane disease

Acute glomerulonephritis mediated by anti-glomerular basement membrane (anti-GBM) antibody account for about 1-2% of all cases of glomerulonephritis. Anti-CBM nephritis is more common in men and in those who possess HLA-DR2. Patients present with nephritis alone or, more commonly, with glomerulonephritis and lung haemorrhage, a combination termed Goodpasture's syndrome. However, rapidly progressive nephritis and pulmonary haemorrhage can occur in other multisystem disorders such as SLE or Wegener's granulomatosis so the combination of renal and lung involvement is not synonymous with anti-GBM disease.

The target antigen is the α3 chain of type IV collagen, a major constituent of the GBM. Lung damage results from antibodies to antigens common to both alveolar and glomerular basement membranes. In Goodpasture's syndrome, respiratory symptoms often precede renal disease by 1 year or longer. Haemoptysis, usually leading to anemia, is a prominent feature and the sputum typically contains haemosiderin-laden macrophages. Lung biopsies show intra-alveolar haemorrhage and necrotizing alveolitis.

Etiology

Although the cause is unknown, anti-GBM disease follows upper respiratory tract infections in 20-60% 0f patients, or exposure to certain hydrocarbons. These agents may damage alveolar basement membrane, generating new and potent antigens able to stimulate autoantibody production. Alternatively, the agent responsible (e.g. a virus may cross-react with basement membrane antigens. Pulmonary haemorrhage in anti-GBM disease is strongly associated with cigarette smoking.