DEFINITION

1. **Glomerulonephritis** is inflammation of the glomerulus. It is a major cause of chronic renal failure.

2. In most tissues, inflammation is a reaction that occurs in the perivascular tissue. In the specialised structure of the renal glomerulus, there is no such tissue. The equivalent tissues are the glomerular basement membrane (which is responsible for filtration), the mesangial cells and matrix (which support the capillary loops), and the glomerular capsule with its associated connective tissue.

3. Glomerulonephritis may occur as a primary disease of the kidneys or as part of a multi-system disease. Such diseases include systemic lupus erythematosus, mixed connective tissue disease, polyarteritis nodosa, Wegener's granulomatosis, rheumatoid arthritis, or as a complication of neoplastic disease.

CLASSIFICATION OF PRIMARY GLOMERULONEPHRITIS

4. This includes the following conditions:

    4.1. Acute glomerulonephritis.

    4.2. Crescentic glomerulonephritis (rapidly progressive glomerulonephritis or "malignant" glomerulonephritis).

    4.3. Glomerulonephritis associated with antibodies to glomerular basement membrane.

    4.4. Membranous glomerulonephritis (epimembranous or extramembranous nephropathy).

    4.5. Minimal change glomerulonephritis.

    4.6. Focal glomerulosclerosis.

    4.7. Mesangiocapillary glomerulonephritis.

        4.7.1. Subendothelial mesangiocapillary glomerulonephritis.

        4.7.2. Dense deposit mesangiocapillary glomerulonephritis.

    4.8. Focal proliferative glomerulonephritis.

        4.8.1. Idiopathic focal nephritis with mesangial deposits.

        4.8.2. Henoch-Schönlein purpura.

    4.9. The hereditary nephritides.

CLINICAL MANIFESTATIONS

5. The clinical consequences of glomerular disease vary according to the tissue principally affected.

    5.1. If the glomerular basement membrane is damaged, protein will be lost in the urine. At first, low molecular weight proteins will be lost, but then proteinuria will become non-selective, and ultimately the **nephrotic syndrome** can arise.

    5.2. Damage to the glomerular capillaries causes **haematuria**.

    5.3. If both the basement membrane and capillaries are damaged, the resultant proteinuria and haematuria constitute the **nephritic syndrome**.

    5.4. A reduction in glomerular filtration rate will cause retention of salt and water, with expansion of the intravascular volume and a **rise in blood pressure**.

    5.5. **Renal failure** may develop due to intrinsic renal disease or secondary to hypertension.

6. **Acute glomerulonephritis**. Until recently, this was the major cause of human glomerulonephritis. Today, it is uncommon, except in developing countries. It occurs mainly in children and young adults, males being more often affected than females. Clinically, there is salt and water retention, with mild oedema, hypertension of variable degree and proteinuria, usually less than 5g/day. Granular and leucocyte casts appear in the urine. In a few cases serum albumin depletion leads to the nephrotic syndrome. There may be haematuria, which may be microscopic or macroscopic.

7. In children who do not develop acute-stage hypertensive encephalopathy, pulmonary oedema or acute renal failure, the prognosis is excellent. Some adults continue to have proteinuria and other abnormalities of urinary sediment for years.

8. Acute glomerulonephritis may be associated with bacterial endocarditis, infection of shunts used for the treatment of hydrocephalus, and deep seated abscesses and sepsis. There is a possible link between this condition and malaria, but the evidence suggests that such a link may not be causal because eradication of the organisms does not affect the course of the renal disease.

9. **Crescentic glomerulonephritis** consists of a group of conditions where, clinically, there is rapid progression to renal failure. It may be associated with polyarteritis nodosa, Wegener's syndrome and Henoch-Schönlein purpura. As well as renal signs and symptoms, there is often systemic upset, with fever, arthralgia and anaemia.

10. **Nephritis associated with antibodies to the glomerular basement membrane**. Two thirds of patients have lung haemorrhage and are said to have Goodpasture's syndrome. Some patients with the condition have isolated clinical nephritis. Clinically, these patients present with severe progressive glomerulonephritis. Systemic features other than lung haemorrhage and anaemia are uncommon.

11. **Membranous nephropathy**. In the UK and USA this mainly affects adults, males being more commonly affected than females, although, in other European countries, children are commonly affected. The condition commonly presents with marked proteinuria and the nephrotic syndrome. At first the blood pressure is normal. About 30% of patients remit spontaneously, a further third go on to terminal renal failure, and the rest continue with proteinuria and normal renal function or mild renal impairment.

12. There is a well documented relation between membranous nephropathy and solid tumours, especially carcinoma of the bronchus and gastrointestinal tract. In addition it may accompany lymphoma or leukaemia.

13. **Minimal change nephropathy**. This is predominantly a disease of children, who present with nephrotic syndrome which may be profound. The proteinuria resolves completely on treatment with corticosteroids. Relapse is frequent. Some patients develop acute or chronic renal failure, infection or thrombosis. The blood pressure may be normal or raised.

14. **Focal glomerulosclerosis**. This is a histological diagnosis originally found in a group of patients presenting with proteinuria who were resistant to steroid treatment. All age groups may be affected and the majority of patients proceed to terminal renal failure in ten years.

15. **Mesangiocapillary glomerulonephritis**. The two subtypes affect mainly children and young adults. They present with nephrotic syndrome and renal impairment. Progression to terminal renal failure occurs in about half the patients within 7 years. A striking but rare feature is partial lipodystrophy, which occurs with dense-deposit mesangiocapillary glomerulonephritis.

16. **Focal proliferative glomerulonephritis** is seen in subacute bacterial endocarditis, systemic lupus erythematosus, periarteritis nodosum and Wegener's granulomatosis.

    16.1. **Idiopathic focal nephritis with mesangial deposits** affects children and young adults. Proteinuria is usually slight or absent. The usual presentation is with recurrent haematuria. About 10% of patients go on to renal failure.

    16.2. **Henoch-Schönlein purpura** is characterised by skin ecchymoses, swollen painful joints, gastrointestinal pain, and bleeding and haematuria. It usually affects children and adolescents, with males being twice as frequently affected as females. The illness may be precipitated by infection or drugs. Attacks may be continuous or recurrent, with complete recovery in between. 10% go on to renal failure.

17. **The hereditary nephritides**. The commonest type is Alport's syndrome, where nephritis is accompanied by nerve deafness and other features, including ocular abnormalities. These patients usually present with haematuria or renal failure. In women, in whom the disease is usually less severe, it may come to light as hypertension in pregnancy.

AETIOLOGY

18. There are 2 major immunological mechanisms of glomerular injury:

    18.1. **Immune complex disease**. This is due to the accumulation in the glomerulus of antigen/antibody complexes.

    18.2. **Glomerular fixation of antibody directed against the glomerular basement membrane**. This results in linear deposition of antibody in a continuous distribution along the basement membrane.

19. 97-8% of cases of glomerulonephritis are due to immune complex disease.

20. Immune complex disease may complicate **infection**. Many organisms may be implicated including bacteria (streptococcus Group A, Streptococcus viridans, Staphylococcus albus, Meningococcus, Diplococcus pneumoniae, Salmonella, Mycobacteria tuberculosis, Mycobacteria leprae, Klebsiella, Treponema pallidum, Brucella and Leptospira), viruses (Epstein-Barr, Oncorna, mumps, measles, rubella, Cytomegalovirus, Coxsackie and Variola varicella), rickettsiae, fungi and parasites (Plasmodium malariae, Plasmodium falciparum and Schistosoma mansoni).

21. Other agents causing immune complex disease include **drugs and chemicals**. These range from gold, mercury and penicillamine to antibiotics (including penicillins, cephalosporins and rifampicin), thiazide diuretics and frusemide.

22. Immune complex disorders may occur in relation to **endogenous antigens**, as in systemic lupus erythematosus, mixed connective tissue disease and Hashimoto's disease.

23. **Acute glomerulonephritis**. The association between streptococcal infection and acute nephritis has been known for at least a hundred years. By far the most important infective agent causing glomerulonephritis is streptococcus Group A. Not all strains of the organism are nephritogenic. Of those that are, Types 12, 4, 1 and 49 are the most important. Following infection, affected patients have long-lasting type-specific immunity.

24. The aetiology of the other types of primary glomerulonephritis is largely unknown.

CONCLUSION

25. Glomerulonephritis is inflammation of the glomerular apparatus, which is mediated by various immunological mechanisms. The condition may occur as part of a multi-system disorder or may be a primary renal disease. Primary glomerulonephritis is caused by a wide variety of aetiological agents, including infection, therapeutic drugs and chemicals. These agents produce varied immunological responses, clinical syndromes and histological appearances.

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