Chapter 9

NEPHRITIS

Term originally applied to diffuse, bilateral, non bacterial inflammatory parenchymal disease of kidney has been extended to cover focal and segmental disease.

NEPHRITIC SYNDROME

Clinical syndrome in which haematuria, proteinuria, casturia and leucocyturia is usually present. Systemic hypertension, oliguria, oligosaluria, hypervolaemia, hypocomplementaemia or encephalopathy may or may not be present.

NEPHROTIC SYNDROME

Clinical syndrome in which gross proteinuria, always selective but to variable degree, is always present with mirror image hypoproteinaemia, edema, ascites and hyperlipaemia are usually present. Systemic hypertension, azotemia, erythrocytouria and hypocomplementaemia are sometimes present. Oliguria and oligosaluria may be extreme.

Many children with nephritis suffer from immune complex deposition with few resulting from antibodies to glomerular basement membrane and others related to immunologic deficiency. Immune complex diseases are characterized by circulating immune complex in plasma and antibodies antigen complex may be eluted. Usually antigen is not identified specifically and glomerular immunofluroscence reveals granular pattern. Anti GBM disease is rare in children but occurs in some rapidly progressive crescentic nephritis and Goodpasture syndrome. Antibodies are found in plasma. GBM is attached to antibodies. Subsequently C3 complement is deposited and polymorphs deposition follows.

MORPHOLOGICAL CLASSIFICATION

A. Minimal Change:

On light microscopy glomeruli are normal or at most show minimal, focal, mesangial hypercellularity or increased amount of fibrillar basement membrane like material which forms mesangial matrix. Occasional glomeruli may appear

to be completely sclerosed without accompanying tubular atrophy and probably represent involutional process which occurs during early childhood.

Minimal change is seen in more than 80% of nephrotic children and often with symptomless proteinuria when immunofluroscence is negative and only significant change on electron microscopy is fusion of glomerular epithelial cell foot process, reversible change which resolves following disappearance of proteinuria.

Similar light microscopy changes are seen in most cases of benign recurrent haematuria and also in early stages of Alport syndrome.

B. Focal Segmental Glomerulosclerosis:

Early lesion, focal one sparing some glomeruli, consists of sclerosis, with or without hyaline deposits, involving individual segments of glomerular tufts which become locally adherent to Bowman capsule. Sclerosis spreads progressively so that in its fully developed form disease is characterized by presence of partially or totally sclerosed glomeruli as well as normal ones. Unaffected glomeruli show minimal change or mild mesangial hypercellularity. Tubular atrophy develops with less glomerular change than in other forms of glomerulonephritis.

Lesion first develops in zuxtamedullary glomeruli spreading outward through cortex. Affected glomeruli show presence of IgM and C3 with small amounts of IgG on immunofluroscence.

Well developed glomerular lesions observed in Alport syndrome are similar to focal glomerular sclerosis, although interstitial foam cells appear early. However immunofluroscence is negative while electron microscopy shows irregular thickening of basement membrane with characteristic basket weave deformity of lamina densa.

C. Membranous Nephropathy:

Capillary walls show diffuse thickening. Cellular proliferation being minimal or absent. Electron microscopy shows that discrete electron dense deposits are embeded in outer side of basement membrane which reacts by extending finger like processes between them. Immunohistology shows coarse granular capillary wall deposits of IgG and C3 with diffuse distribution. Disease is rare in childhood but carries better prognosis than adulthood.

D. Proliferative Glomerulonephritis:

Diffuse proliferative exudate glomerulonephritis: There is diffuse proliferation of mesangial and endothelial cells accompanied by infiltration of tufts with polymorphonuclear leucocytes. All glomeruli are uniformly affected. Capillary walls are normal on light microscopy. Electron microscopy demonstrates subepithelial deposits (humps). This appearance is characteristic of post streptococcal nephritis and has good prognosis.

Pure mesangial proliferation: Diffuse proliferation is confined to mesangial cells while capillary basement membranes are normal so that capillary patency is maintained. This is typically seen in resolving post streptococcal glomerulonephritis. This form also occurs in some cases of nephrotic syndrome, benign recurrent haematuria and anaphylactoid nephritis. Serial biopsy suggests spontaneous healing in majority of cases but when associated with nephrotic syndrome it may herald development of focal glomerulosclerosis.

Glomerulonephritis with crescents: This type of lesion may be seen in anaphylactoid purpura, SLE, PAN and Goodpasture syndrome. It may also occur as illness presenting as mixed nephritic nephrotic syndrome.

Dominant feature is epithelial crescent because aggregation of proliferating epithelial cells binding glomerular tuft to capsule assumes this shape in section. Rarely mesangial proliferation is absent and tufts are collapsed showing linear capillary wall deposits of IgG. In childhood there is more often mesangial proliferation and immunohistology reveals granular capillary wall deposits of IgG and C3 or mesangial IgA in case of Henoch Schonlein nephritis. Crescents themselves may contain fibrin.

Crescents undergo fibrous organization. Encircling crescents involving more than 80% of glomeruli usually denote rapidly progressive course, whereas occasional small crescents seen typically in focal proliferative glomerulonephritis will merely leave few scars. Minority of patients will have slowly progressive glomerulonephritis.

Focal proliferative glomerulonephritis: Mesangial proliferation is focally distributed throughout kidney and also affects individual glomeruli segmentally. Overlying epithelial cells proliferate to form small crescents which heal with local scar formation. Lesion is typical of anaphylactoid nephritis but also occurs in nephrotic syndrome and mild lupus nephritis.

Membranoproliferative glomerulonephritis: Lesion is characterized by diffuse capillary wall thickening in addition to variable and extreme mesangial proliferation.

In type 1 deposits seen on electron microscopy occupy subendothelial position and are discrete. They are associated with mesangial interposition in which mesangial cells and matrix extend in wedge like manner between capillary basement membrane and lining endothelium causing double contour seen on light microscopy.

In type 2 electron microscopy reveals continuous replacement of lamina densa with extremely dense homogeneous material, so called dense intramembranous deposits. This variety is sometimes associated with partial lipodystrophy.

Coarse granular capillary wall deposits of C3 and other complement components and immunoglobulins are found. Disease most often occurs primarily presenting clinically with mixed nephritic and nephrotic features and is frequently

associated with hypocomplementaemia. Similar lesion occurs with infected ventriculo atrial shunt.

RENAL BIOPSY

A. Differential Diagnosis of Various Forms of Glomerulonephritis Which May Present Clinically in Similar Manner:

Nephrotic syndrome: 80% of children with nephrotic syndrome have minimal changes on biopsy. This is dominant lesion in preschool child. Hypertension and haematuria are transient and minimal and proteinuria highly selective. Other two lesions found are focal segmental glomerulosclerosis and membranoproliferative glomerulonephritis.

Acute nephritic syndrome: Diagnosis of acute post streptococcal nephritis is supported by finding diffuse proliferative exudative glomerulonephritis. Low ASO titre and persistent abnormal C3 pattern will suggest different underlying cause. Heavy proteinuria is generally transient in post streptococcal glomerulonephritis while blood pressure, renal functions and serum protein levels rapidly return to normal. Persistence of any of these abnormalities beyond one month from onset would suggest need for renal biopsy.

Asymptomatic proteinuria: Isolated excessive proteinuria can only be regarded as of pathological significance when it has been shown to persist for several weeks and effect of posture has been eliminated. Associated microscopic haematuria is indication for immediate renal biopsy.

Recurrent haematuria: Most children in this category are suffering from benign recurrent haematuria in which biopsy changes are minor and nonprogressive consisting mainly of segmental or diffuse mesangial thickening and sometimes hypercellularity with or without IgA deposit. Familial nephropathy presents with recurrent haematuria. Mesangial IgA deposits are absent. Characteristic changes on electron microscopy in capillary basement membrane consisting of localized but often widespread splitting and layering of lamina densa with corresponding widening of whole membrane.

B. Assessment of Severity:

In anaphylactoid nephritis glomerular lesion is always proliferative but varies in severity from minimal, focal and segmental mesangial hypercellularity which is capable of complete healing to diffuse proliferative glomerulonephritis with extensive crescents involving more than 80% of glomeruli which is associated with rapid downhill course.

Lesion of SLE can also take form of either focal or diffuse proliferative glomerulonephritis often with excessive crescents in later. In addition there is membranous type which carries worse prognosis than that of primary membranous

nephropathy in childhood. EM may reveal extensive deposits both within and on either surface of basement membrane when light microscopy shows little evidence of abnormality of capillary wall. This would indicate very active disease with prospect of deterioration calling for intensive therapy.

C. Monitoring Progress:

Serial biopsy study is of value in children with persistent disease in whome measurements of GFR remain normal. GFR may show little or no decline until both kidneys are already irreversibly damaged. Comparison of two biopsy specimens taken at interval of 2-5 years may afford useful information regarding progression of lesion and long term prospect of reaching maturity before requiring dialysis or renal transplant.

D. Research:

It is possible to explore 'normality' in form of patients with relapsing nephrotic syndrome in whom biopsy has been performed prior to considering cyclophosphamide therapy but while in steroids induced remission.

Much of research based upon renal biopsy has utilized material obtained primarily for clinical purposes.

ACUTE NEPHRITIS

Upto 85% cases occur in relation to streptococcal infection usually of throat but occasionally of skin or elsewhere. Lancefield group A beta haemolytic streptococcus concerned is most likely type 12 but other types such as 4, 25 or 49 are occasionally involved.

It is misnomer to call it post streptococcal because continuing streptococcal illness is infact present in considerable proportion of cases unless antibiotic has been given. Elevation of ASO titre to 200 Todd units per ml is most reliable test.

ASO titre is normal at first in 15% cases particularly when there is skin primary but may become positive if repeated late in illness.

Anti streptokinase and anti hyaluronidase titres may be abnormal when ASO titre is not.

In skin cases anti streptococcal deoxyribonuclease B test is more frequently positive. C3 nephritic factor may provide useful information.

Not all cases of acute nephritis are streptococcal in origin. Precipitating cause can sometimes be viral infection such as varicella, mononucleosis, echovirus or hepatitis B.

Although most cases of acute nephritis are sporadic, local epidemics of streptococcal skin infection or respiratory infection may produce local epidemics.

Microscopic haematuria can occur during any streptococcal infection and is not necessarily followed by acute nephritis. Type specific antibodies appear one to two months after streptococcal infection.

Pathogenesis:

Acute nephritis is immunological consequence of extraneous infection usually by Lancefield group A type 12-beta haemolytic streptococci.

It is immune complex disease due to cross reaction of antibodies produced in response to exogenous antigen with endogenous basement membrane. Antibodies active against renal tissue are found in circulation. Hypocomplementaemia occurs. Immunofluroscence demonstration of IgG and C3 as granular capillary wall deposits is possible. Plasma C3 level is low.

Acute streptococcal nephritis is diffuse inflammatory condition usually bilaterally symmetrical and affecting glomeruli, tubules and interstitial tissue. Lesions are proliferative and exudative to varying degree.

Clinical Features:

Presentation usually results from observed haematuria following upper respiratory infection. Swollen, tender cervical glands may have been noted.

Atypical presentation may be with myocardial involvement, acute left heart failure, acute hypertension, headache, hypertensive encephalopathy or acute anuria. Fever and abdominal pain are complained of but not dysuria or frequency.

Acute nephritis is commonest between 5-10 years of age but may occur even in 6 month old baby and older children. Males are more commonly affected than females. In first attack there is likely to be delay of 7-14 days between onset of respiratory infection and recognition of acute nephritis. Time interval is shorter if second attack arises precipitated by subsequent streptococcal infection.

Presenting features are haematuria, casturia, oliguria, edema and systemic hypertension. Occasionally children present with hypertension and pulmonary edema before haematuria has begun. Apparent anaemia may reflect hypervolaemia.

Swollen cervical glands or follicular tonsillitis may be present. Periorbital edema is common. Pitting edema may be generalized with or without ascites. ESR is raised. C3 level decreased. Oliguria, oligosaluria and gross haematuria are usual. Most erythrocytes in urine are lysed giving brown, smoky appearance. Specific gravity exceeds 1020 and osmolality 500 mos per litre. Casturia is marked with cellular cast common. Gross haematuria persists for 1-14 days but microscopic haematuria may persist for several months. Proteinuria varies in amount and may occasionally be so gross as to cause hypoalbuminaemia leading to nephrotic syndrome either initially or later in disease. When present initially this is called as nephrotic nephritis.

There are two phases:

Initial phase is period of oliguria with hypervolaemia, azotaemia, hypertension and pulmonary congestion which gives way to diuresis and natriuresis usually within one to two weeks.

Oliguric phase is product of glomerulo tubular imbalance with less filtration and adequate reabsorption. Systemic hypertension is usually present. Acute nephritis associated with skin lesions has higher incidence of edema and hypertension. Hypertensive encephalopathy occurs in 10% of such cases and is typified by convulsions, vomiting, aphasia and hemiparesis. Headache may be warning sign, reinforced by confusion and disorientation prior to seizures.

Acute hypertension may produce left ventricular embarrassment with pulmonary edema, basal crepitations and raised JVP with peripheral edema.

During period of sodium retention, whether or not hypertension is present, there tends to be hypervolaemia with increased cardiac size and gross increase in pulmonary vascular pattern.

Electrocardiographic changes reflect electrolyte imbalance sometimes in association with depression of T wave.

Blood urea ranges from normal to grossly elevated values if anuria persists. Renal plasma flow is normal. GFR reduced. Tubular function is less affected than glomerular.

Haemoglobin may be low, partly due to hypervolaemia. Anaemia is thus normocytic normochromic and improved by diuresis. Neutrophil count may be raised or normal. ESR is raised unless congestive heart failure is present. C3 fraction of complement may be lowered.

Renal biopsy is unjustified in straightforward case of glomerulonephritis. Indications are renal insufficiency, secondary nephrotic syndrome and persisting low levels of plasma C3. When disease exists for more than one month biopsy may assist prognostication or correct wrong diagnosis but rarely influences prognosis.

DIFFERENTIAL DIAGNOSIS

A. Acute Pyelonephritis:

This may present with haematuria, frequency, dysuria, rigors, scalding on micturition and pyuria. Fever may be present. Stained urine sediments reveal bacteria and culture of urine high bacterial count.

B. Anaphylactoid Nephritis:

There is history of purpuric rash with or without polyarthritis, abdominal colic and malena. Plasma C3 is not lowered.

C. Recurrent Haematuria:

There are no signs of hypertension and hypervolaemia. ASO titre and blood urea values are normal.

D. Nephrotic Syndrome:

This may present with haematuria, oliguria and hypertension. Erythrocyturia is unlysed and transient. Gross selective proteinuria, edema with hypovolaemia are

distinctive. Biopsy is required to identify certain histologic patterns of nephritis such as membranoproliferative type which may present with nephrotic syndrome, nephritic syndrome or both.

E. Other Diseases:

- Gross hypertension.
- Paroxysmal haemoglobinuria.
- SLE.
- Schistosomiasis.
- Familial nephritis.
- Goodpasteur syndrome.
- Haemolytic uraemic syndrome.
- Calculus.
- Periarteritis nodosa.
- Trauma.
- Haemorrhagic cystitis.
- Rhabdomyosarcoma.
- Nephroblastoma.

MANAGEMENT

A. Antimicrobial Therapy:

Penicillin should be given for 2 weeks. ASO titre is estimated and test repeated in 2 weeks. If patient is sensitive to penicillin then oxytetracyclin is given.

B. Dietary Restriction:

During period of oliguria average patient should be given one litre of fluid per day. One easy regime is 500 ml of milk and 500 ml water daily supplemented by carbohydrates ad lib. This amounts to 17 gm of proteins daily. Sodium intake is reduced to 20-50 mmol per day. When diuresis occurs then sodium, water and proteins content of diet should be increased.

C. Bed Rest:

This is not beneficial to patient in absence of gross hypertension. Proteinuria and haematuria may be increased using orthrograde position. This is usually transient.

D. Treatment of Complications:

When oliguria is severe and urine output is less than 400 ml per day fluid intake should be restricted to 300-500 ml plus equivalent of total volume of urine passed. Sodium intake should be restricted to 10-20 mmol per day and protein intake 15-20 gm per day. Frusemide can be given 1-2 mg per kg when acute left ventricular failure occurs. Peritoneal dialysis is indicated by climbing serum phosphorus more than 3.5 mmol per litre. Acute pulmonary edema is absolute indication.

Hypertensive encephalopathy: Diastolic blood pressure more than 100 mm Hg is indication to start phenobarbitone.

If blood pressure continues to rise intravenous frusemide 2-5 mg per kg may be given.

Diazoxide intravenous 2-10 mg per kg is drug of choice. It lasts for 12-24 hours.

Reserpine 0.05 mg per kg intramuscular reinforced by hydralazine 0.2 mg per kg intramuscular 12 hourly.

If hypertension persists treatment by aldomet may be given, initially 3 mg per kg and repeated 8 hourly. If seizures begin then midazolam intravenous 0.1-0.2 mg per kg per dose may be given until fit stops, followed by intramuscular phenobarbitone.

Digoxin is given if congestive heart failure ensues.

Peritoneal dialysis may be life saving when oliguria is profound.

PROGNOSIS

Death may occur due to hypervolaemia and pulmonary edema. Sometimes nephrotic process continues and secondary nephrotic syndrome may arise after weeks or months. This progressively downhill course may last for months or years. Eventually, condition either resolves spontaneously or goes on to renal insufficiency with metabolic acidosis, systemic hypertension and azotaemia.

With development of chronic glomerulonephritis, clinical features change. Urine contains variable but small quantity of protein and volume tends to be large. Casturia is rule and casts tend to be granular or waxy. There is occasional microscopic haematuria and excessive white blood cells excretion. Urinary osmolality on water deprivation is diminished to below 300 mOsmol and blood urea rises progressively to above 150 mg per dl. Metabolic acidosis occurs. Renal osteodystrophy may be present. Occasionally sodium or potassium losing state may arise. Anaemia of normochromic normocytic type may occur partly due to increased haemolysis and partly to decreased synthesis.

Nonstreptococcal Nephritis:

1. Subacute bacterial endocarditis.
2. Shunt nephritis.
3. Septicaemia.
4. Syphilis.
5. Hepatitis B.

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

Defined as producing renal insufficiency within 6 months of onset. Many cases follow post streptococcal nephritis. Others are due to SLE, anaphylactoid nephritis or diffuse proliferative nephrotic syndrome, focal glomerulosclerosis or membranoproliferative lesion associated with hypocomplementaemia.

Pathologically it is diffuse proliferative glomerulonephritis with high percentage of glomeruli showing epithelial crescents. Antiglomerular basement membrane antibodies may be associated.

Treatment with anticoagulants, fibrinolytics, cyclophosphamide and prednisolone have been tried.

Renal transplantation is life saving.

GOODPASTEUR SYNDROME

Rare glomerulonephritis associated with diffuse pulmonary hemorrhage. In addition to nephritis child has dyspnea, cough and haemoptysis. Pulmonary infiltrates are seen on X ray chest. Most cases progress to death in uraemia or from pulmonary hemorrhage. This is form of anti glomerular basement membrane antibodies disease with linear capillary wall deposits of IgG and C3. Pulmonary alveoli may be antigenically similar and therefore vulnerable to this reaction. Anaemia due to iron sequestration in lungs and haemoptysis may occur.

This clinical picture is not specific and may be produced by polyarteritis nodosa, anaphylactoid purpura, pulmonary haemosiderosis and Wegner granulomatosis.

Most promising treatment is repeated plasmapheresis.

ANAPHYLACTOID NEPHRITIS
(Henoch Schonlein nephritis)

Nephritis that occurs in course of severe anaphylactoid purpura presents insidiously with purpura, proteinuria, microscopic haematuria and later gross haematuria and casturia with or without nitrogen retention and systemic hypertension. Overt renal symptoms occur in 40% of children with anaphylactoid purpura. Boys are affected more commonly than girls. Histological abnormalities are likely to be detected in 70% of cases on renal biopsy.

Urinary manifestations are indistinguishable from acute post streptococcal nephritis and only preceding, concomitant or subsequent signs of anaphylactoid purpura make clinical differentiation possible. Such signs are specifically distributed purpura, polyarthritis and gastrointestinal manifestations. Majority have mild signs such as transient proteinuria lasting for few days, beginning several days after rash and arthritis. Haematuria may complicate picture as may gross proteinuria (more than 1 gm per day). Such children are likely to progress to secondary nephrotic syndrome.

Child with mild proteinuria is likely to recover completely. Haematuria may persist for many months and then disappear. Daily loss of more than 2 grams of protein per day in urine indicates underlying diffuse proliferative lesion and rapid downhill progression often with nephrotic phase.

Signs of beta haemolytic infection should be sought by throat swab, ASO titre.

If haematuria persists for 1 month, proteinuria exceeds 1 gm per day, malignant hypertension arises or renal insufficiency sets in then renal biopsy is indicated.

Range of histology is varied from pure mesangial proliferation through focal proliferative glomerulonephritis to less common extracapillary glomerulonephritis.

Prognosis is not good in extracapillary glomerulonephritis if crescents are present in more than 50% of glomeruli. Deposits of immunoglobulin IgG, complement and fibrinogen can be found in most glomeruli irrespective of histology present.

Treatment:

Streptococcal infection may or may not be present. Benzyl penicillin therapy should follow immediate culture of throat or other specific nidus of infection.

Bed rest is indicated for early active anaphylactoid purpura since this diminishes cropping of purpura and reduces proteinuria.

If gross albuminuria leads to secondary nephrotic syndrome then this should be dealt with diet and diuretic therapy. This would necessitate low sodium intake (25-50 mmol per day) high protein intake (2.5 gm per kg per day) and frusemide (1-2 mg per kg per day).

Occurance of acute severe glomerular dysfunction would occasion use of diet low in sodium (25-50 mmol per day) low protein (0.5 gm per kg per day) and restricted fluid intake (500-1000 ml per day or urinary volume plus 25 ml per kg per day).

Severe hypertension should be treated with restricted sodium intake, intravenous methyldopa or hydralazine.

Acute renal insufficiency may call for peritoneal dialysis.

In rapidly progressive glomerulonephritis combined use of corticosteroids, cytotoxic drugs (cyclophosphamide and azathioprine), anticoagulants (heparin, aspirin) is tried.

Prognosis:

Gross proteinuria exceeding 1-2 gm per day is bad prognostic sign indicating diffuse proliferative glomerulonephritis.

Chronic renal insufficiency requires renal transplant.

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS

Patients with nephritis and persistently low levels of C3 may present with proteinuria, haematuria, acute nephritic or nephrotic picture.

Onset is usually in childhood and commonest above 6 years. ASO titre is normal. Disease may affect several members of family.

Biopsy reveals cellular proliferation with sclerosis of mesangium. Capillary walls are irregularly thickened. Electron microscopy reveals two types: split basement membrane and those with dense deposits in basement membrane.

C3 is always deposited in capillary loops. Immunoglobulin may also be deposited in granular membrane.

Disease is associated with activation of alternative pathway as opposed to classical complement pathway. Siblings may be affected. There is also link with partial lipodystrophy and possibly with SLE and excessive vulnerability to infection. Condition may occur in mixed connective tissue disease.

Onset may be insidious or dramatic, varying from gradual increase of proteinuria or haematuria to rapid onset of acute hypertension or nephrotic syndrome, always with persistently low C3 and sometimes C4. Disease usually progresses with diminishing renal function.

Prognosis is bad with rapid downhill course.

When chronic renal insufficiency sets in long term dialysis or renal transplant may be considered.

FOCAL GLOMERULONEPHRITIS

Clinically there are recurrent minor episodes of haematuria. Pathologically variety of differing lesions which tend to be localized to small areas of kidney or to individual glomeruli such as focal embolic nephritis in bacterimia.

This term is applied to histological pattern in which only some glomeruli are affected in number of conditions such as nephrotic syndrome, proteinuria, haematuria, anaphylactoid nephritis and benign recurrent haematuria.

Classification by renal biopsy is focal proliferation, minimal change with focal glomerular fibrosis and minimal change with focal or segmental hyalinization.

Prognostically those with focal proliferation tend to do well and those with focal glomerular fibrosis and focal and segmental hyalinization tend to do badly.

In most patients hypertension, proteinuria, casturia and haematuria resolve over period of months.

Group of patients with arthritis, transient skin rash, colicky abdominal pain and anaemia in association with focal lesions has been described.

HEREDITARY NEPHRITIC SYNDROME

Group of inherited form of renal diseases which may or may not be accompanied by progressive deafness, ocular defects, platelet defects, hyperlipidaemia, hyperprolinaemia and hyperprolinuria.

Hereditary nephritic syndrome was first described by Guthrei in 1902. Term Alport syndrome is used when proteinuria, haematuria and deafness coexist.

Pattern of inheritance varies. Commonly autosomal dominant. Sometimes partial X linked dominance with male to male transmission from occasional crossing over of homologous portions of X and Y chromosomes.

Clinical Presentation:

Onset is insidious with mild proteinuria, casturia and erythrocyturia which remains undetected until coincident illness or screening programme leads to detection. Occasionally there is abrupt onset related to upper respiratory tract infection or to urinary tract infection.

Disease progresses relentlessly with exacerbations resulting in recurrent haematuria. Progress is much faster in males.

Deafness should be detected by audiogram.

Urine of parents, siblings, parental siblings and grandparents should be tested for proteinuria and haematuria and for hyperprolinuria in patient.

Eye changes are detectable in 10% of affected children. Myopia, cataract, spherophakia, lenticonus, retinitis pigmentosa or nystagmus.

Platelet abnormalities such as thrombocytopenia and giant platelets have been described.

Metabolic disorders include hyperprolinaemia, hyperprolinuria, hydroxyprolinuria and glycinuria.

Plasma complement levels are normal.

ASO titre is normal.

Differential Diagnosis:

Other causes of proteinuria and haematuria:

1. Benign recurrent haematuria.
2. Streptococcal nephritis.
3. Orthrostatic proteinuria.
4. Nephroblastoma.
5. Rhabdomyosarcoma of bladder.
6. Urolithiasis.
7. Urinary tract infection.
8. Bleeding diathesis.
9. Haemoglobinuria.

Normal complement fraction and ASO titre help rule out glomerulonephritis and membranoproliferative glomerulonephritis.

Intravenous urogram rules out tumors and calculi.

Urine should be cultured. Orthrostatic proteinuria can be tested for.

Renal biopsy reveals focal glomerular lesions including thickening of glomerular basement membrane and focal mesangial proliferation. Focal lesion progress to hyalinization, crescent formation and glomerulosclerosis. Periglomerular fibrosis develops. Interstitial and tubular changes occur including interstitial fibrosis. Tubules containing RBC and foam cells derived from tubular epithelium.

Prognosis:

Outlook for males is bad. Hearing deficit may progress to be bilateral. Progression of kidney disease is inexorable in males. Many die before reaching 4th decade. Females have better prognosis and normal life span.

Treatment:

Palliative nonspecific therapy of chronic renal insufficiency, long term haemodialysis, renal transplant.

Genetic counselling should be given.

MEMBRANOUS NEPHROPATHY

It complicates malaria and syphilis. Diagnosis is based on renal biopsy of child aged more than 3 years presenting with nephrotic syndrome and unexplained proteinuria.

Link between this disease and Australia antigen has been shown.

Associated crescentic glomerulo nephritis may coexist. Strong association between idiopathic membranous nephropathy and HLA DRW 3 has been reported.

Histologic examination shows thickening of glomerular basement membrane with deposits of immune complexes. Granular capillary wall deposits of IgG and C3 are seen followed by glomerulosclerosis.

Some children deteriorate in few years. Others over decades. 30-40% improve spontaneously and may recover.

Nephrotic patient will clear of edema when given steroids but proteinuria returns to normal. Prolonged low sodium diet with diuretics may be required. As chronic renal insufficiency ensues symptomatic treatment for it is required.

LUPUS NEPHRITIS

Proteinuria is rule with erythrocyturia, haematuria and casturia. Heavy proteinuria may preced nephrotic syndrome and systemic hypertension. Azotemia may occur.

Overt signs of renal disease are present in majority of children with drug induced SLE but minority of those with idiopathic SLE. It is immune complex disease with diminution of complement in plasma. Anti DNA antibodies are involved.

Histology varies: focal segmental proliferative glomerulonephritis, diffuse proliferative glomerulonephritis and membranous nephritis with diffuse thickening of capillary wall.

Tubular changes include thickening of basement membrane, hyaline droplets and tubular atrophy.

Electron microscopy reveals electron opaque deposits of antigen antibodies complexes and hyaline thrombi.

Treatment:

Steroids are given in tapering doses for 6 weeks. Azathioprin 2-3 mg daily for 2 months has been used. Low sodium diet and hypotensive drugs are required to control hypertension. If chronic renal insufficiency develops haemodialysis and renal transplant may be required.

SHUNT NEPHRITIS

Use of ventricular jugular shunt in treatment of hydrocephalus has been followed by increased number of low grade infections usually due to coagulase negative staphyllococci.

Staphyllococcal septicemia may result in fever, haemolytic anaemia, proteinuria, haematuria and nephrotic syndrome.

Histology reveals membranoproliferative glomerulonephritis, deposits of staphyllococcal antigen, IgG and C3 in glomeruli.

It is immune complex disease with low C3 in plasma.

Recovery occurs if shunt is removed.

SICKLE CELL NEPHROPATHY

Haematuria, nephrotic syndrome or defects of tubular concentration may arise. This type of nephrotic syndrome is resistant to steroids.

Renal anomalies result from ischaemia of renal papillae. Enlarged glomeruli are found in kidneys of older children.

Haematuria may be due to stasis, hypoxia and sickling relative to papillae.

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