

### Post-streptococcal glomerulonephritis

Age/Sex: Childhood, 2:1 male predominance

Renal Presentation: Hematuria, Proteinuria, Red cell casts, oliguria

Systemic findings: Edema, hypertension, fever, malaise, abdominal ache, nausea, hypocomplementemia

Pathology: Immune complexes, swelling of glomerular tufts, hypercellularity of glomeruli, proliferation of mesangial/epithelial/endothelial cells

Pathogenesis: Immune complex deposition in the glomeruli causing a decrease in GFR

Natural Course: Most recover w. no or mild therapy

Treatment: Antibiotics, maintain Na and H<sub>2</sub>O balance

### Membranous glomerulopathy:

Age/Sex: Adults, 2:1 M:F

Renal Presentation: proteinuria

Systemic findings: nephrotic syndrome – massive proteinuria, hypoalbuminemia, edema, hyperlipidemia / lipiduria

Pathology: Thickening of the capillary walls. Irregular dense deposits between basement membrane and epithelial cells on electron microscopy. Irregular spikes protruding from BM w. silver stain.

Pathogenesis: Immune complex deposition activates complement (C5b-C9) leading to destruction of capillary wall and leakage of proteins from the blood. Commonly caused by drugs (penicillamine, captopril, gold, NSAID), tumors, SLE, infections (HepB, C, syphilis, schistosomiasis, malaria), metabolic (diabetes, thyroiditis), idiopathic

Natural course: Irregular but generally indolent

Treatment: low salt diet, diuretics, ACE-inhibitors in general treat underlying symptoms. Do not use corticosteroids except in severe cases.

### Membranoproliferative Glomerulonephritis (Type I)

Age/Sex: Young Adults, Older children

Renal Presentation: nephrotic syndrome with hematuria and mild proteinuria

Systemic findings: nephrotic syndrome, hypocomplementemia, mild HTN

Pathology: Hypercellular, lobular glomeruli with proliferation of mesangial cells and increased mesangial matrix. Glomerular capillary wall has a “double-contour” appearance. Sub endothelial electron dense deposits. C3 deposited in a granular pattern and early complement (C1-C4) and IgG is present.

Pathogenesis: Immune complex activation of classic and alternative pathways

Natural course: Slowly progressing and unremitting

Treatment: Corticosteroid, immunosuppressive, anti-platelet drugs have been tried w. varying degrees of success.

### Dense Deposit Disease (MPGN Type II)

Age/Sex: Young Adults, Older Children

Renal Presentation: nephrotic syndrome with hematuria and mild proteinuria

Systemic Findings: nephrotic syndrome, hypocomplementemia, mild HTN

Pathology: Hypercellular, lobular glomeruli with proliferation of mesangial cells and increased mesangial matrix. Glomerular capillary wall has a “double-contour”

appearance. Deposition of dense material within the glomerular basement membrane. C3 is present in irregular foci in the GBM but not in the dense deposits. IgG and early complement components are absent.

Pathogenesis: Activation of only the alternative complement pathway. Early components (C1-C4) of the classical pathway are not decreased in the blood. C3 nephritic factor (C3NeF) circulates in the blood and stabilizes the alternative C3 convertase (C3b,Bb) which serves to activate the alternative pathway and diminish plasma concentrations of C3. Nature of dense deposits is unknown.

Natural course: Slowly progressing and unremitting

Treatment: As in Type I. High incidence of recurrence in transplant patients.

IgA Nephropathy:

Age/Sex: Children, young adults -- Congenital

Renal Presentation: Recurrent hematuria and sometimes proteinuria

Systemic findings:

Pathology: Histology is variable ranging from normal glomeruli to mesangial proliferation to focal proliferation. Characteristic picture is mesangial deposition of IgA. Early complement components are usually absent.

Pathogenesis: Hypersecretion of IgA and entrapment of the Ig complexes in the glomeruli with subsequent activation of the alternative pathway. IgA hypersecretion by mucosal cells is caused by an acquired abnormality of immune regulation combine with exposure to antigens. Celiac disease predisposes as does liver disease due to decreased clearance of IgA complexes

Natural course: Many patients maintain normal renal function. Some progress to chronic renal failure.

Treatment: Monitor patients, treat HTN aggressively, prednisone? Omega-3?

Alport's syndrome:

Age/Sex: Hereditary, Childhood, Males more than females. Most inheritance is X-linked, however dominant and recessive modes exist too.

Renal presentation: Hematuria with erythrocyte casts

Systemic Findings: Nerve deafness and eye disorders (lens dislocation, posterior cataracts, corneal dystrophy)

Pathology: Segmental glomerular proliferation or sclerosis. Increased mesangial matrix and persistence of fetal-like glomeruli. Foamy appearance of epithelial cells. Foci of thickening and thinning of GBM on electron microscopy. Absence of alpha-3, alpha-4, and alpha-5 collagen on staining.

Pathogenesis: Defects in genes coding for collagen type IV fail to produce a normal GBM.

Natural course: Progression to renal failure within a few decades.

Treatment: No definitive treatment. ACE inhibitors?

Thin GBM disease:

Age/Sex: Hereditary. Heterozygous for the alpha-3, alpha-4 collagen mutations. Have normal alpha-5 in skin unlike alport's

Renal presentation: familial asymptomatic hematuria

Systemic presentation:

Pathology: Thin GBM

Pathogenesis: Inadequate amounts of collagen IV due to gene abnormalities

Natural course: Excellent prognosis, normal renal function

Treatment: none

Minimal change disease:

Age/Sex: Children

Renal presentation: highly selective (mostly albumin) and extreme proteinuria without hematuria or HTN

Systemic findings: Sometimes associated with Hodgkins disease or other lymphomas and leukemias. May follow NSAID therapy.

Pathology: Normal glomeruli on light microscopy. On electron microscopy the GBM is normal. Effacement of epithelial foot processes.

Pathogenesis: Some immune dysfunction that causes release of a cytokine-like substance that destroys the foot processes.

Natural course: Prognosis is excellent with therapy.

Treatment: Corticosteroids

Focal Segmental Glomerulosclerosis:

Age/Sex: Children and adults

Renal presentation: severe proteinuria (nonselective), hematuria, HTN

Systemic presentation:

Pathology: Focal (not all glomeruli), segmental (not the entire glomerulus) collapse of BM and increase in the matrix and deposition of hyaline. On EM sclerotic and non-sclerotic glomeruli show loss of foot processes (a-la Minimal change Dz) but there is also focal detachment of epithelial cells and denudation of underlying GBM. IgM and C3 are present in the sclerotic areas. Hyaline thickening of afferent arterioles. In time sclerosis of all glomeruli and interstitial fibrosis.

Pathogenesis: Might be a severe form of Minimal change dz. Epithelial damage is the hallmark. Sclerosis and hyalinosis are the result of entrapment of proteins in hyper permeable foci.

Natural course: Better prognosis in children. Response to therapy variable. Some follow very rapid course. Progression to renal failure is variable.

Treatment: corticosteroids

Goodpasture's Syndrome:

Age/Sex: Young adults. Male predominance

Renal presentation: severe oliguria, hematuria, red cell casts (nephritic)

Systemic presentation: Pulmonary involvement i.e. hemoptysis

Pathology: Crescents in most glomeruli. Linear deposits of IgG and C3. Ruptures in the GBM on EM

Pathogenesis: antibodies directed against the alpha-3 chain of the glomerular basement membrane

Natural course: very quick progression to renal failure.

Treatment: plasmapheresis, steroids, cytotoxic agents.

ANCA-associated small vessel vasculitis/ necrotizing glomerulonephritis:

Lupus nephritis:

Age/Sex: Young adult females

Renal presentation: hematuria, red cell casts, proteinuria, sometimes nephrotic syndrome

Systemic presentation: many including butterfly rash, arthritis, fever, photosensitivity, pleuritic pain,

Pathology: Highly variable including mesangial, focal proliferative, diffuse proliferative, membranous with deposits present in mesangial, subendothelial, subepithelial. Wire loop lesions representing a thickening of the capillary wall can be seen especially in subendothelial. Tubulointerstitial lesions are also present.

Pathogenesis: An autoimmune disease with antibodies against DNA forming immune complexes which deposit in the kidney.

Natural course: Variable and unpredictable.

Treatment: Immunosuppression

Diabetic nephropathy:

Age/Sex: As per DM

Renal presentation: At first increased GFR and microalbuminuria followed later by proteinuria, loss of GFR, end stage renal dz.

Systemic presentation: As per DM i.e. hypertension, obesity (type II), hyperglycemia, etc.

Pathology: Thickening of the GBM, glomerulosclerosis (increase in mesangial matrix) can be nodular (hyaline nodule form at periphery of glomerulus and expand) or diffuse. Nodular lesion is virtually pathognomonic.

Pathogenesis: Metabolic effect of decreased insulin and increased glucose cause the glomerulosclerosis. In GBM increased synthesis of Collagen IV and fibronectin with decreased production of proteoglycan and heparan sulfate. Glycosylation of proteins. Glomerular hypertrophy brought on by hypertension lead to glomerular sclerosis.

Natural course: Leads to End stage kidney

Treatment: Dialysis, transplant, recently glycemic control and ACEI

Amyloid nephropathy:

Age/Sex:

Renal presentation: Heavy proteinuria or nephrotic syndrome and later progression to uremia:

Systemic presentation:

Pathology: Amyloid deposits in the glomeruli. Congo red amyloid positive fibrillary deposits in subendothelium and mesangium.

Pathogenesis: Deposition of amyloid in glomeruli

Natural course: Prognosis is poor

Treatment: Treat underlying symptoms. Transplantation

Acute Tubular Necrosis:

Age/Sex: Any

Renal presentation: Decrease in urine output, Rise in BUN, uremia (hyperkalemia, metabolic acidosis). Recovery phase consists of increase in urine output, loss of sodium, potassium (hypokalemia) water, return of BUN to normal. Predisposition to infection at this stage.

Systemic presentation: underlying syndromes of ischemia, shock, or toxicity.

Pathology: Focal tubular epithelial necrosis of multiple points along the nephron often with rupture of tubular BM and occlusion of lumens by casts (mostly in the distal portions of the nephron and consisting mainly of Tamm-Horsfall protein) . In toxic ATN the proximal tubule is affected most.

Pathogenesis: Necrosis of tubular epithelial cells due to ischemia or toxicity.

Clinical course: Usually reversible

Treatment: restore blood flow to the kidney or get rid of toxic agent

Allergic Interstitial Nephritis:

Age/Sex: Any

Renal presentation: Hematuria, mild proteinuria, leukocyturia (some eosinophils). In older pt renal failure w oliguria

Systemic presentation: Eosinophilia, fever, rash

Pathology: Edema and infiltration of interstitium by lymphocytes and monos. With some drugs granulomas are seen

Pathogenesis: Immune mediated hypersensitivity reaction. Allergens act as haptens and bind to components of tubular cells precipitating an immune reaction.

Natural course: Renal failure if not treated

Treatment: Remove the offending allergen

Uncomplicated UTI:

Reflux nephropathy:

Age/Sex: Children

Renal presentation: Often undiagnosed until late. Incidental diagnosis by discovery of pyuria or bacteruria. W loss of tubular function nocturia and polyuria

Systemic presentation: Hypertension. Sometimes symptoms of acute pyelonephritis – back pain, fever

Pathology: Gross – Irregularly shaped with a coarse corticomedullary scar overlying a dilated and blunted calyx. Micro – some hypertrophied and some atrophied tubules, inflammation and fibrosis of interstitium, focal segmental glomerulosclerosis in later stages (w proteinuria) otherwise glomeruli can be nl or have varying degrees of change. Small blood vessels exhibit end arteritis or hyaline arteriosclerosis.

Pathogenesis: Superimposition of UTI on congenital vesicoureteral reflux and/or intrarenal reflux.

Natural course: Loss of concentrating ability, sometimes progression to massive proteinuria and end-stage renal failure.

Treatment: Antibiotics and surgery if severe

Pyelonephritis:

Age/Sex: Until 40 more prevalent in females, evens out after

Renal presentation: dysuria, frequency, urgency, pyuria (non-specific) if with casts then tubular involvement

Systemic presentation: Costovertebral pain, fever, malaise

Pathology: patchy interstitial suppurative inflammation and tubular necrosis, glomeruli usually unaffected

Pathogenesis: Bacterial invasion of urinary tract and spread upward into the kidney, usually due to obstruction of the UT or reflux allowing for stasis of urine in bladder or reflux into kidneys.

Natural course: Can resolve with tx or can become chronic or recurrent (papillary necrosis as in obstruction or diabetes is bad and can lead to end stage kidney)

Treatment: Antibiotics

Myeloma cast nephropathy:

Age/Sex: Older men

Renal presentation: most commonly chronic renal failure and less commonly acute renal failure, most myeloma patients have proteinuria

Systemic presentation: As per myeloma (lytic bone lesions, hyperviscosity, bence-jones bodies, etc.)

Pathology: Pink to blue amorphous masses filling and distending the tubules, some are surrounded by multinucleate giant cells, surrounding epithelium necrotic and adjacent interstitium inflamed.

Pathogenesis: Bence-jones bodies combine with Tamm-Horsfall protein to form tubular casts that obstruct tubule and cause local inflammation

Natural course: as per multiple myeloma

Treatment: as per multiple myeloma

Renovascular Hypertension:

Age/Sex: Atherosclerotic – older men Fibromuscular Dysplasia – younger women (20's/30's)

Renal presentation: Bruits over renal artery can sometimes be heard

Systemic presentation: Essential HTN, increased systemic renin

Pathology: ischemic kidney is grossly smaller and has crowded glomeruli, atrophic tubules, interstitial fibrosis, inflammation, contralateral kidney may have hyaline arteriosclerosis due to HTN

Pathogenesis: either a atheromatous plaque or a hyperplasia of blood vessel cells (most commonly media) occluding the renal artery and activating the JGA

Natural course: deadly if untreated

Treatment: ACEI, surgery to bypass occluded artery

Atheroembolic renal disease:

Hypertensive Nephrosclerosis:

Age/Sex: Younger men

Renal presentation: Proteinuria and hematuria progressing to renal failure

Systemic presentation: HTN, retinopathy, papilloedema, encephelopathy, headaches, nausea, vomiting, visual impairments, scotomas

Pathology: Petechial hemorrhages on surface of kidney “flea-bitten”, fibrinoid necrosis of arterioles, hyperplastic arteriolitis of interlobar arteries “onion-skinning”, sometimes glomeruli necrose, site distal to obstruction atrophies.

Pathogenesis: Vascular damage to kidneys (i.e. from longstanding benign HTN) causes pathological changes (above) which occlude arteries and activate the JGA, vicious cycle ensues

Natural course: deadly if untreated

Treatment: antihypertensive therapy

Hemolytic Uremic Syndrome:

Age/Sex: Variable – Classic is childhood but can occur in adults i.e. pregnancy, SLE, immunosuppressed, bacterial infection

Renal presentation: Acute renal failure, oliguria, hematuria

Systemic presentation: microangiopathic hemolytic anemia, thrombocytopenia, in classic - diarrhea and abdominal bleeding

Pathology: Gross- patchy cortical necrosis Micro – thickening of glomerular capillary walls, fibrinoid necrosis and intimal hyperplasia of afferent and interlobular arteries

Pathogenesis: Endothelial injury and platelet aggregation

Natural course: deadly if untreated

Treatment: Plasma exchange, corticosteroids, in classical dialysis is helpful

Analgesic nephropathy:

Age/Sex: Females

Renal presentation: inability to concentrate urine, development of stones, renal colic due to obstruction of ureter by papillae, often complicated by UTI

Systemic presentation: severe anemia, headaches, GI symptoms, HTN

Pathology: Gross- depressed and raised areas of cortex, *various stages* of necrosis, calcification, fragmentation of papillae Micro – various stages of necrosis and sloughing of papillae, atrophy of tubules, interstitial fibrosis and inflammation in cortex due to atrophy or superimposed pyelonephritic changes.

Pathogenesis: Injury of cells by oxidation and covalent binding of the drugs and metabolites, ischemia due to anti-vasodilatory effect of aspirin

Natural course: Chronic renal failure, small percent develop transitional papillary carcinoma even after drug withdrawal

Treatment: Stop drug

Diffuse cortical necrosis: