Pathology – Nephritic Syndrome

Renal block

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7] Lupus nephropathy

(a) This is the renal component of SLE; the severity of the renal lesion often determines the overall prognosis in patients with SLE. It is often manifest as the nephrotic syndrome but many cases also have major nephritic features. You can find "full house" deposits of IgA, IgG, IgM and other immunoglobulins.

The pathogenesis of all forms of glomerulonephritis in SLE involves deposition of DNA and anti DNA complexes within the glomeruli. This causes an inflammatory responses that may cause proliferation of the endothelial, mesangial and/or epithelial glomerular cells and in severe cases necrosis of the glomeruli.

The World Health Organization has divided SLE glomerular disease into five classes:

Class one: Normal by light, electron and immunofluorescence microscopyc. (This is seen in less than 5% of SLE patients).

Class two: Mesangial lupus glomerulonephritis is seen in 10 to 25% of cases and is associated with mild clinical symptoms and immune complex deposits in the mesangium

Class three: Focal proliferative lupus glomerulonephiitis is seen in 20 to 35% of patients. Here one or two foci within an otherwise normal glornerulus show swelling and proliferation of endothelial and mesangial cells with neutrophilic infiltration or fibrinoid deposits and capillary thrombi.

Class four: Is diffuse proliferative glomerulonephritis and is seen in 35% to 60% of SLE patients. The histological features are similar to the one described in class 3 but are more diffuse. In this condition, immune complexes deposition create an overall thickening of the capillary walls which resemble rigid "wire loops" on light microscopy.

Class five: Is membranous lupus glomerulonephritis occurs in 10 to 15% of cases. In class 5, the patients have severe nephrotic syndrome and there is thickening of the capillary walls due to deposition of basement membrane like material as well as immune complexes.

B] Nephritic syndrome is characterized by inflammatory rupture of the glomerular capillaries, with resultant bleeding into the urinary space; proteinuria and edema may be present but usually are mild.

(1) Clinical findings:

(a) Oliguria
(b) Azotemia (which is elevation of blood urea nitrogen and creatinine levels due to decreased glomerular filtration rate/GFR).
(c) Hypertension is a result of fluid retention and augmented rennin release.
(d) Haematuria results from leakage of red cells, sometimes of irregular shape, directly from glomerular capillaries into the Bowman space. Many of the red cells are aggregated into the shape of the renal tubules and embedded in a proteinaceous matrix forming red cells casts that can be observed in the urine.
(e) The patient often reports having "smoky brown urine". Red cell casts can degenerate and become pigmented granular casts.
(f) The Patient may also have some degree of proteinuria, that may even enough to cuase edema and cause some aspects of the Nephrotic syndromes. However it is rare for patients to develop hyperlipidemia or lipuria.

(2) Posstreptococcal glomerulonephritis (acute proliferative glomerulonephritis) is the prototype of the nephritic syndrome. It is immune complex disease with the antigen being of streptococcal origin.

(a) This disorder most often follows or accompanies recurrent infections (tonsillitis, streptococcal impetigo, infected insect bites) with nephritogenic that produce toxins. strains of group A B-hemolytic streptococci, part of SLE, or in rare cases after staphylococcal infections.

(b) Complete recovery in almost all children and many adults follow. A very minority develop rapidly progressive glomerulonephritis.
(c) Several laboratory abnormalities are characteristic, including urinary red cells and red cell casts, azotemia, decreased serum C3 (Hypocomplementemia, which is due to activation by the immune deposits at a rate greater than that at which new complements can be synthesized in the liver) and increased titers of anticationic proteinase as an evidence of recent streptococcal infection.
(d) An intense inflammatory reaction involving almost all glomeruli in both kidneys result in:

1. Innumerable punctuate hemorrhages on the surface of both kidneys.
2. Diffuse, Enlarged, hypercellular, swollen, blood less glomeruli with proliferation of mesangial and endothelial cells and sometimes neutrophilic infiltration. Thrombosis formation with necrosis can also occur the vessel walls.

3. Glomerular basement membrane of normal thickness and uniformity despite the extensive inflammatory changes.
4. Characteristic electron-dense "humps" on the epithelial side of basement

membrane with subepithelial localization.

5. 'Lumps-bumpy" immunofluorescence (extremely coarse granular imnuinofluorescence for IgG or C3), unlike the deposits in membranous glomerulonephritis which present with a “spike and dome appearance”

Clinical Course of Acute Proliferative Glomerulonephritis:

- Can be accompanied by malaise, fever, nausea.
- Clinical presentation of nephritic maybe mild to moderate or maybe very sever.
- Only the macroscopic Hematuria can be seen even when the symptoms are mild.
- The Proteinuria may start out mild but may progress until it causes one of the characteristics of the nephrotic syndrome.
- They are usually treated with corticosteroids and supportive therapy.
- Prognosis is variable and includes: almost full recovery especially in children, rapidly proliferative Glomerulonephritis, or even Chronic Renal failure.

(3) Rapidly progressive (crescentic) glomerulonephritis (RPGN).

Rapid Proliferative Glomerulonephritis can be:

1. Idiopathic which are
2. Associated with disease and can be classified as:

Type I: associated with Anti-basement membrane antibodies that encompass a number of diseases, most notably being Good Pasture Syndrome: a disease in which antibodies attack the glomerular and alveolar basement membranes.
This type is important to dignose because patients can benefit from plasmaphoresis: plasma is separated from the cells in the blood, the cells are suspended in saline, a plasma substitute or donor plasma), and the reconstituted solution may be returned to the patient. The procedure is used to remove excess antibodies from the blood

Type II: is associated with diseases of immune-complex deposition and include:

- SLE
- Postinfectious glomerulonephritis.
- IgA nephropathy
- Hench-Sholien purpora: HSP is a systemic vasculitis (inflammation of blood vessels) and is characterized by deposition of immune complexes containing the antibody IgA, that may hit the kidney. the disease causes palpable purpura (small hemorrhages); often with joint and abdominal pain.

Type III: Pauci-immune where ANCA tests positive with no immune complexes only the antibodies, as opposed to the previous types. This type can be the renal component of diseases like: Wegener granulomatosis (C-ANCA), and Microscopic polyangiitis (P-ANCA).

(a) RPGN usually presents with the nephritic syndrome that progresses with a fulminant course, rapidly to renal failure within weeks or months. The disorder is histologically defined by the formation of crescents between the

Bowman capsule and the glomerular tuft which result from deposition of fibrin, maybe even RBC can leake in the Bowman space and from proliferation of parietal epithelial cells of the Bowman capsule, which are caused by constant irritation of cellular infiltration and cellular deposition. Cells of monocytic origin are often involved.

(b) The etiology is posts treptococcal in approximately 50% of cases with immune complex deposition; other immune complex forms of RPGN include, among others, lupus nephropathy and IgA nephropathy.

(c) Antiglomerular basement membrane antibodies (non streptococcal) are characteristic in approximately 10% of cases; these cases often present clinically as Goodpasture syndrome.

-Clinical Course of Rapidly Progressive Glomerulonephritis:

- It exhibits the characteristics of nephritic syndrome but a more sever case of oliguria and azotemia.
- These individuals become severely anuric and require transplantation or dialysis.
- The Disease is treated with corticosteroids but generally have a bad prognosis.

(4) Good pasture syndrome (antiglomerula basement membrane disease).

(a) The cause is the formation of antibodies (antiglomerular basement membrane antibodies) which are directed against antigen in the glomerular and pulmonary alveolar basement membranes.

(b) Flourescent antibody studies for IgG demonstrate positive linear immunofluorescence, in contrast to the granular manner found in membranous glomerulonephritis and APGN.

(c) The patient is usually young, maybe even 20 years. Clinical manifestations include:

1. Nephritic syndrome.
2. Pneumonitis with hemoptysis (hemorrhagic pneumonitis).
3. Peak incidence in men in their mid-20s.
4. RPGN crescentic morphology with linear immunofluorescence.

Alport syndrome.

a) This disease is a hereditary nephritis associated with nerve deaflines and ocular disorders, such as lens dislocation and cataracts.

b) Clinical characteristics include the nephritic syndrome, often progressing to end stage renal disease by 30 years of age.

c) The causes is mutation in the gene for the 5 chain of type IV collagen.

d) Irregular glomerula basement membrane thickening, where some parts are thick and some parts are thin, with foci of splitting of the lamina densa are seen by electron microscopy.

e) Proteinuria and Hematuria may also occur

C] Other glomerular diseases

(1) IgA nephropathy (Berger disease) is an extreme common entity defined by deposition of IgA in the mesangium. Where there is overproduction of IgA immunoglobulin that ultimately causes deposition in the basement membrane.

(a) Most frequently, the disease is characterized by benign recurrent hematuria in children, usually following an infection where there is an excessive production of IgA in response to environmental elements or more commonly pathogens, lasting 12 days, and usually of minimal clinical significance.

(b) Focal glomerulonephritis may be the presenting feature. The entrapped IgA in the mesingium activates the alternative complement pathway causing damage and injury to the glomeruli.

(c) IgA nephropathy can be a component of the Henoch-Schonlein vasculitis disease.

(2) Membrane proliferative glomerulonephritis

(a) Clinical characteristics include slow progression to chronic renal disease.

(b) Histological characteristics include both basement membrane thickening and cellular proliferation.

(c) The disease is marked by reduplication of the glomerular basement membrane into two layers due to expansion of the mesangial matrix into the glomerular capillary loops; this results in a characteristic tram-track appearance best seen with silver stains.

(d) Disease occurs in two forms:

1. Type I lobar glomerulonephritis is an immune complex nephritis deposited in the subepithelium and mesingium associated with an unknown antigen. It has a striking tram-track appearance.
2. Type II (dense deposit disease) has a tram-track appearance that is not as apparent as that of type I, where the depositions are intramembranous.
   a. Irregular electron-dense material deposited within the glomerular basement membrane is characteristic. C3 is demonstrable adjacent to but not within the dense deposits and serum C3 is characteristically markedly reduced, with a tram track appearance.
   b. The possible cause is an IgG autoantibody (C3 nephritic factor) with specificity for the C3 convertase of the alternate complement pathway.

Nephrotic Syndrome	Nephritic Syndrome
Increased Basement membrane permeability	Inflammatory rupture of the glomerular capillaries
- Proteinuria >3.5 g - Hypoalbumineia - Generalized edema - Hyperlipidemia (fatty casts)	- Oliguria - Azotemia (↑ blood urea nitrogen & creatinine levels due to ↓ GFR) - Hypertension - Haematuria - Smoky Brown Urine (RBC casts can degenerate and become pigmented granular casts)

RENAL FAILURE

A] General considerations

(1) Renal failure can be acute or chronic and can result from any of the glomerular or tubulointerstitial lesions diseased in the preceeding sections.
(2) Azotemia (elevated urea and creatinine) of renal origin is always an associated feature.
(3) In advanced stages, renal failure results in uremia; the term uremia denotes the biochemical and clinical syndrome characteristic of symptomatic renal disease.

B] Major clinical characteristics of uremia

(1) Azotemia (elevated urea and creatinine)
(2) Acidosis resulting from the accumulation of sulfates, phosphates and organic acids.
(3) Hyperkalemia.
(4) Abnormal control of fluid volume.

(a) An early characteristic is the inability to concentrate urine, a later manifestation is the inability to dilute urine.

(b) Sodium and water retention can result in congestive heart failure.

(5) Hypocalcemia caused by failure to synthesize the active form of Vitamin D, hypocalcemia can lead to renal osteodystrophy.
(6) Anemia caused by decreased secretion of erythropoietin.
(7) Hypertesnion caused by hyperproduction of rennin.

C] Other clinical characteristics of uremia include anorexia, nausea and vomiting; neurologic disorders, ranging from diminished mental function to convulsions and come; bleeding caused by disordered platelet function; accumulation in the skin of urochrome and other urinary pigments and fibrinous pericarditis.

NON-RENAL CAUSES OF AZOTEMIA

A] Pre-renal azotemia. This condition results from decreased renal blood flow due to blood loss, decreased cardiac output, systemic hypovolemia (as in massive burns), or peripheral pooling of blood due to marked vasodilatation (as in grame-negative sepsis). It is characterized by increased tubular reabsorption of sodium and water, resulting in oliguria, concentrated urine and decreased urinary sodium excretion.

(1) Measurement of urinary sodium is diagnostically significant in the delineation of the oliguria of shock.
   (a) Oliguria may be caused by decreased renal blood flow with consequent decreased glomerular filtration rate, in which case tubular reabsorption of sodium is maxrmaly increased and urinary sodium is low.
   (b) Oliguria may be a manifestation of acute tubular necrosis, in which case tubular reabsorption is greatly impaired and urinary sodium is not decreased.

(2) The BUN: creatinine ratio is characteristically greater than 15 due to a combination of both decreased glomerular filtration and increased tubular reabsorption of urea.

B] Post-renal azotemia results from mechanical blockage (obstruction) of urinary flow.

BUN is an abbreviation of Blood Urea Nitrogen.