النادي الطبي

GENITOURINARY SYSTEM

SUBJECT : Pathology

LEC NO. : Summary L2

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وَقُل رَّبِّ زِدْنِي عِلْمًا

اي اشي عليه هايلايت بالنهدي هو الي الدكتورة حكت عنه مهم بالمحاضرة

Primary disease with nephrotic syndrome

1. Minimal change disease (MCD) :—

- no hypertension, selective proteinuria (albumin), treatment is corticosteroids, 5% develop chronic renal failure after 25 years, in adults the response is slower and relapses are more common, can occur at any age but it's more common in children

2. Focal and Segmental Glomerulosclerosis (FSGS) :—

- sclerosis affecting some but not all glomerulus, involving only some segments, it's the most common cause of nephrotic syndrome in adults
- Causes: 1.association with other conditions like HIV nephropathy, heroin nephropathy 2. secondary event in other forms of GN like IgA nephropathy 3. maladaptation after nephron loss 4. inherited or congenital resulting from mutations affecting cytoskeletal or related proteins expressed in podocytes (like nephrin » transmembrane glycoprotein, the major component of slit diaphragms between adjacent foot processes) 5. primary or idiopathic FSGS, accounts for 20% to 30% of cases
- How does FSGS differs from MCD in children » nonselective proteinuria, higher incidence of hematuria & hypertension, poor response to corticosteroid
- Pathogenesis » primary FSGS is unknown, nonimmune injury to the podocytes can represent the initiating event of primary FSGS and is the underlying mechanism of proteinuria, permeability-increasing factors produced by lymphocytes have been proposed in MCD & FSGS, deposition of hyaline masses in the glomerulus represents the entrapment of plasma proteins and lipids, IgM and complement proteins in the lesion result from nonspecific entrapment in damaged glomerulus
- Morphology » some segments within a G and sparing of the others (segmental), first affects only some of the G (focal), affected G exhibit: 1.increase mesangial matrix 2. deposition of hyaline masses (hyalinosis) and lipid droplets in the affected G and endocapillary foam cells 3. scarred obliterated capillary lumens with accumulations of matrix material, immunefloure scence » nonspecific trapping of immunoglobulins usually IgM and complement in the areas of hyalinosis
- Progression » leads to global sclerosis of the G with pronounced tubular atrophy and interstitial fibrosis, with progression to renal failure occurring in 50% of FSGS patients after 10 years

- Collapsing glomerulopathy » aggressive type of FSGS, at least 1 glomerulus with capillary loop collapse, worse prognosis, idiopathic or associated with viruses

3. Membranous GN (MGN) = Membranous Nephropathy (MN)
- Diffuse thickening of the capillary wall (all the glomerulus is involved), subepithelial immunoglobulin-containing deposits (inside podocytes)
- Pathogenesis » most idiopathic MGN are induced by Abs reacting in situ to endogenous or planted glomerulus Ags, chronic immune complex nephritis
- Types » 1-Idiopathic (85% of cases): second common cause of nephrotic syndrome in nondiabetic adults, diffuse subepithelial immune complex deposition, thickening of glomerular basement membrane and subepithelial deposition of immune complexes (silver stain, spike), anti-PLA2R autoantibodies, immune complex formation that activates lectin complement pathway and causes podocyte injury and proteinuria, 2 major target antigens (PLA2R) & (THSD7A) 2-Secondary membraneous nephropathy: in immuneflourescence: finely granular staining for IgG in all glomeruli
- Morphology » 1.light microscope: diffuse thickening of GBM 2.immuneflourescence: deposits of immunoglobulins and complement along GBM (IgG) 3.electron microscope: effacement of foot processes, diffuse thickening of GBM caused by subepithelial dome deposits (spike when using silver stain & dome pattern)
- Clinical course » idiopathic MGN characterized by insidious development of the nephrotic syndrome in contrast to MCD the proteinuria is nonselective and does not usually respond to corticosteroid
- Prognosis » poor

Membranoproliterative GN (MPGN)
- Both nephrotic and nephritic disease, characteristic light microscopic changes: hypercellularity and thickening of the glomerular basement membrane, hypocomplementemic, histologic lesion not a specific disease entity, mesangial and subendothelial deposits, duplicating of glomerular basement membrane, (MPGN) thought to be a diagnosis of exclusion
- Clinical features » traditional classification based on electron microscope: MPGN I (subendothelial an mesangial deposits), MPGN II (intramembranous dense ribbon-like deposits), MPGN III (subendotheli and subepithelial deposits), newer classification based on immunofluorescence
- Pathogenesis » most cases of type I MPGN are caused by circulating immune complexes, but the inciting Ag is not known, type I MPGN may occur in association with other known disorders

- Type I classical » subendothelial and mesangial electron dense deposits, immune complex deposition indicating activation of classic complement pathway & some alternative complement pathway, > 50% with nephrotic syndrome, 10 - 20% with acute nephritis syndrome, -50% with low C3
- Type II MPGN (dense-deposit disease) » ribbon-like deposits of the glomerular basement membrane now categorized under C3 glomerulopathies, autoantibody against C3 convertase called C3 nephritic factor, hypocomplementemia
- Morphology » both types of MPGN are similar by LM: {mesangial and endocapillary hypercellularity with lobular accentuation, irregular thickening of glomerular basement membrane, double contour / tram track appearance (PAS or silver stain)}, crescents in ~20% cases, tram track appearance caused by "splitting" of the GBM, Type I characterized by discrete subendothelial electron-dense deposits, by immunofluorescence C3 is deposited in an irregular granular pattern& IgG, Type II MPGN-C3 alone in GBM, type II ribbon like (dense-deposit disease), IgG & the early components of the classical complement pathway (C1q & C4) are usually absent in type II
- Clinical course » prognosis poor, 40% progress to end-stage renal failure, dense-deposit disease (type II) has a worse prognosis, recur in renal transplant recipients
- Q:What serologic test is often positive with MPGN?

  Answer : C3 Nephritic factor (C3NeF) it is an autoantibody directed into C3 convertase and found in MPGN when there is hypocomplementemia

* في كم سؤال حطتهم بالمحاضرة لا تنسوا ترجعولهم *