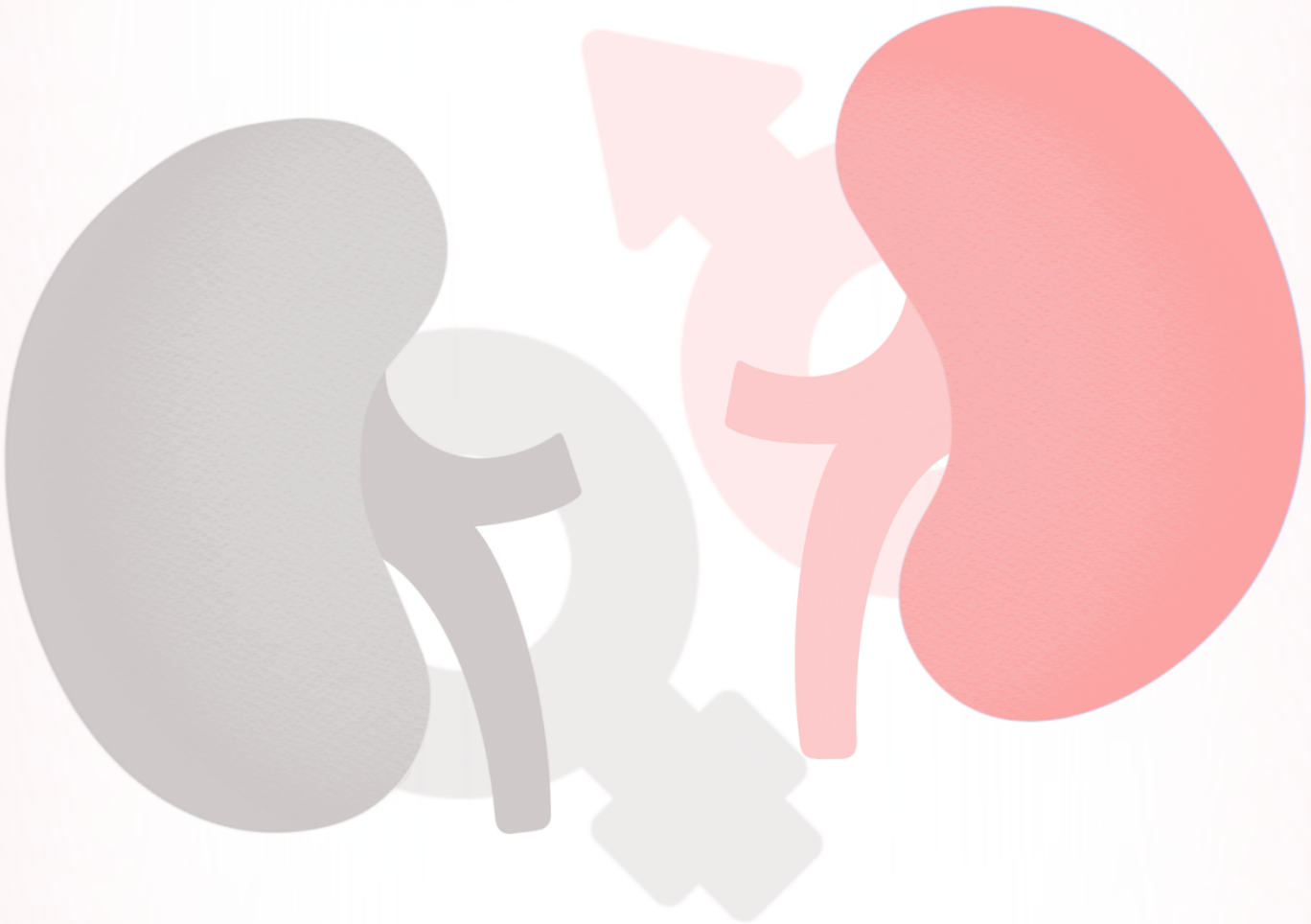
G.U.S.

4.

Pathology



Sheet: #4 Nephritic Syndrome

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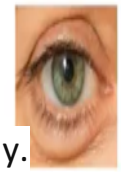
Nephritic syndrome



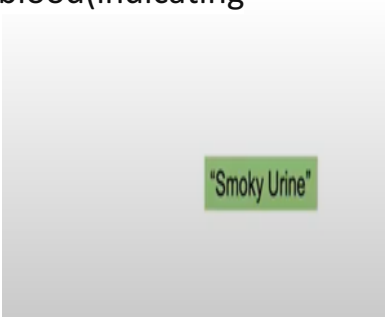
Clinical presentation (PHAROH):

-**P**roteinuria: (not as heavy as in nephrotic syndrome) less than 3.5g/1.73m2/day.

-**H**ematuria: the presence of RBCs in urine (abrupt onset).

Peripheral Edema/Puffy Eyes

-**A**zotemia: Increased concentration of creatinine and urea in the blood(indicating impairment of the renal function).



-**R**BC casts: indication of glomerular origin of hematuria.

-**O**liguria: (which means decreased urine output)

a manifestation of renal impairment.

-**H**TN: caused by fluid retention and azotemia.

Pathogenesis:

•Inflammation (inflammation of the glomerulus) causes leukocytic infiltration → which stimulates proliferation of cells in the glomeruli.

• Proliferation causes damage to the capillary walls → escape of RBCs into urine (hematuria and RBC casts).

• Eventually, this will cause reduction in the GFR → oliguria, fluid retention (edema), and azotemia (reduction of renal clearance to toxic substances).

• Hypertension (a result of both the fluid retention and increased renin release from kidneys).

• Proteinuria may occur but not as heavy as in nephrotic syndrome.

Glomerular diseases mostly presenting with Nephritic syndrome:

1-Membranoproliferative Glomerulonephritis (MPGN)

As the name implies, there is abnormal proliferation of glomerular cells, as well as inflammation, patients usually have nephritic syndrome, others have a combined nephrotic-nephritic picture.

Types of MPGN:

1- **Type I :** (80% of cases): immune complex mediated injury of the glomeruli (the inciting antigen is not known), Circulating immune complexes reach the kidneys and get deposited in the glomeruli initiating an inflammatory reaction which will start the cascade of changes of the nephritic syndrome.

Many **diseases can be associated such as**: hepatitis B and C, SLE (systemic lupus erythematosus), infected A-V shunts.

2- **Type II:** (aka dense-deposit disease DDD) :

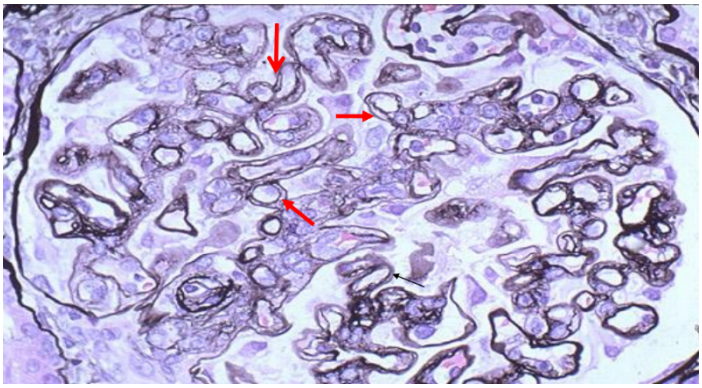
- The cause of this disease is excessive complement activation.
- Patients have autoantibodies against C3 convertase called C3 nephritic factor (it stabilizes the enzyme and lead to uncontrolled cleavage of C3 and activation of the alternative complement pathway) .
- Resulting in consumption of C3 complement and hypocomplementemia.

Morphology of MPGN:

• **LM:** both types of MPGN are similar under the LM.

Glomeruli are large with accentuated lobular appearance and show proliferation of mesangial and endothelial cells as well as infiltrating leukocytes.

GBM (glomerular basement membrane) is thickened (double contour or "tram track"), this is mainly because of the inflammation, injury of the membrane, and the deposition of immune complexes.



The tram track appearance is caused by "splitting" of the GBM.

SILVER stain is used to show the elastic fibers of the basement membrane.

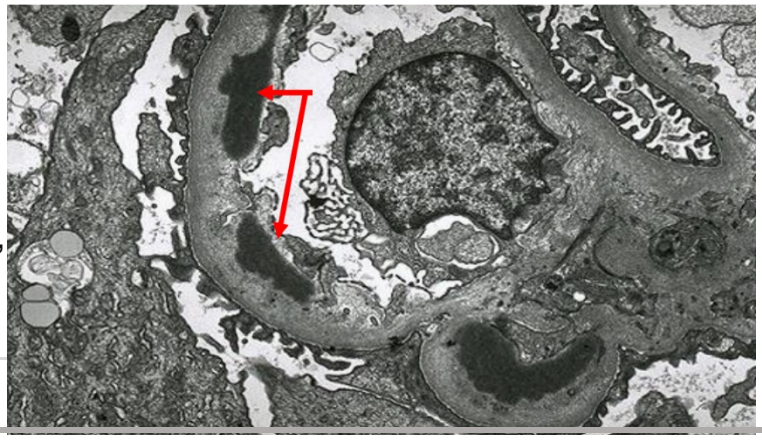
->The red arrows in the picture show the tram-track appearance (double contour) which is a characteristic of MPGN.

• **Immunofluorescent** test shows differences between type 1 and type 2 due to the different pathogenesis of each disease.

Type I : subendothelial electron-dense deposits (IgG, complement C1q and C4)

Type II : C3 alone in the GBM

• **EM** picture of MPGN II, Red arrows show dense immune deposits within the GBM composed of C3 without IGs.
-Because of the heavy dense black area, it was called dense deposit disease.



Clinical Course

• Poor prognosis .

• No remission.

• 40% progress to end-stage renal failure within years.

• 30% had variable degrees of renal insufficiency.

• Dense-deposit disease (type II) has a worse prognosis and tends to recur in renal transplant recipients. (because the problem is within the immune system, not the glomeruli)

2- Acute Postinfectious (Poststreptococcal) Glomerulonephritis (PSGN)

Produced by : Deposition of immune complexes + inflammation and proliferation of glomerular cells and leukocytes (mainly neutrophils).

**Not direct infection of the kidney (post infectious).

Pathogenesis

- Immune-mediated reaction to a previous infection of pharynx or skin.
- Post-streptococcal GN (most common) ,other organisms as pneumococci and staphylococci can be as well a cause for post-infectious GN.

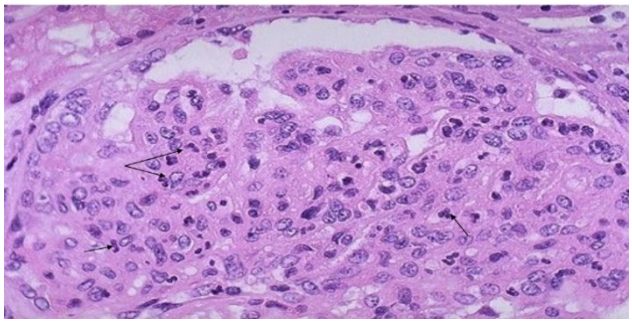
Clinical presentation of Poststreptococcal GN :

1-4 weeks after recovery from a group A streptococcal infection (pharynx or skin), patient will start to develop clinical manifestations related to inflammation of glomeruli.

**A few strains (3%) of β-hemolytic streptococci are capable of this disease.

Mechanism:

Binding of immune complexes (that were formed against streptococcal antigens) to GBM proteins or the binding of antibodies to bacterial antigens “planted” in the GBM. Which will activate the inflammatory cascade in the glomeruli causing the nephritic syndrome.



Morphology

• **LM:**

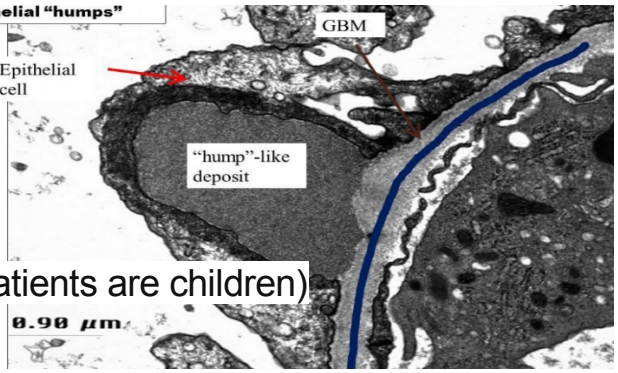
-Proliferation of endothelial, epithelial and mesangial cells.

-neutrophils in and around the capillary loops (black arrows).

•**Immunofluorescent:** deposits of IgG and complements within the capillary walls (positive because the pathogenesis is related to the inflammation and new complex formation inside the glomeruli)

IF test is positive for IG, mainly IgG as well as complements, mainly C3.

• **EM**: immune complexes “sub epithelial "humps" in GBM. Which is characteristic of PSGN.



Clinical Course

• Acute onset.

• Fever, nausea, and nephritic syndrome. (most patients are children)

• Gross hematuria.

• Mild proteinuria.

• Serum complement levels (C3 mainly) are low during the active phase of the disease.

• Serum anti-streptolysin O antibody titers. (high serum levels of anti-streptolysin O antibody titers is considered an evidence of a prior infection by streptococci)

• Recovery occurs in most children.

3- IgA Nephropathy

- One of the most common causes of recurrent microscopic or gross hematuria worldwide.
- Most commonly affects children and young adults.
- Hematuria (gross or microscopic) 1 or 2 days after nonspecific upper respiratory tract infection, lasts several days and then subsides and recur every few months.

Pathogenesis: abnormality in IgA production or clearance from circulation.

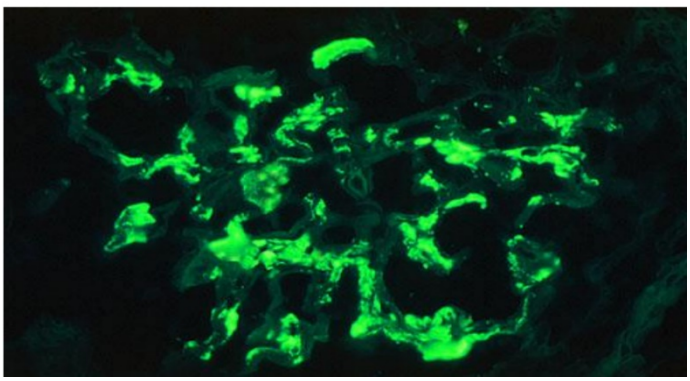
Morphology

• **LM:** variable.

• **IF:** mesangial deposition of IgA with C3. (the fluorescent areas show the mesangium inside the glomerulus) which is characteristic and diagnostic.

• **EM**: deposits in the mesangium.

IF : IgA mesangial staining.



Slides(22-27) weren't mentioned by the professor , so we didn't add them.

You can use this table to revise lecture 3 and 4.

Disease	Presentation	Age	LM	IF	EM	Prognosis
MCD	nephrotic	Children	none	negative	Effaced foot processes	good
FSGS	nephrotic	adults	Segmental sclerosis	negative	Effaced foot processes	Poor?
MNP	nephrotic	adults	Thickened GBM	IgG+ C3+	Sub-epithelial spikes and domes	Poor?
MPGN-type1	Nephritic/ nephrotic	adults	Tram track	Ig s	Subendothelial deposits	poor
MPGN-type2	Nephritic/ nephrotic	adults	Tram track	C3+	Dense deposits	poor
IgA nephropth	nephritic	Children, young adults	variable	IgA+	Mesangial deposits	variable
PSGN	nephritic	children	hypercellularity	IgG+ C3+	Subepithelial deposits (humps)	good
Alport syndrome	hematuria, hearing loss	children	variable	negative	Basket weave GBM	poor

Good luck