
EXPERIMENTAL
PATHOLOGY

IMMUNE COMPLEX-MEDIATED DISEASE

(ACUTE GLOMERULONEPHRITIS)

INTRODUCTION

Acute Glomerulonephritis is an example of an Immune complex-mediated disease, which is a Type III Hypersensitivity, caused by excess antigen and insufficient antibody to properly remove the antigen. Instead, the antibodies bind to more antigen and form pathogenic immune complexes that get deposited in organs where blood flows at high pressure:

- Glomeruli (Glomerulonephritis)
- Joints (Arthritis)
- Serial membranes (Pleuritis / Pericarditis)
- Skin (Skin lesions / Rash)
- Blood vessels (Vasculitis — Inflammation of blood vessel lining)

KIDNEY OVERVIEW

The functional unit of the kidney is the nephron (left), which filters blood to excrete waste, retain nutrients, and regulate plasma volume. Filtration occurs in the glomerulus (right), where blood is filtered at high pressure, and is thus the site of immune complex deposition in glomerulonephritis.

Parts of the glomerulus

- ***Mesangial Cells***: Support capillaries & secrete components to maintain the mesangium.
- ***Fenestrated Endothelium***: Endothelial lining of the capillaries with holes for filtration.
- ***Glomerular Basement Membrane***: -ve charged ions, porous to water & some solutes.
- ***Podocytes***: a.k.a. visceral epithelium, podocytes have foot processes key to the filtration unit. Also secrete components to maintain GBM components.
- ***Urinary space***: Ordered by podocytes, GBM, and parietal epithelium
- ***Filtration barrier***: Foot processes + Fenestrated endothelium + GBM

PATHOLOGY

Acute glomerulonephritis (AG) occurs when a person is immunocompromised and unable to produce enough antibodies to remove the antigens present in the body. The 2 main etiologies of acute glomerulonephritis being studied is Post-streptococcal infection, and Systemic Lupus Erythematosus (SLE). In both cases, the immune complexes produced may deposit in various parts

of the glomerulus to cause AG: subepithelial, mesangial, in the mesangium (matrix), in the GBM, or between GBM & endothelial cells.

Post-streptococcal infection

Streptococcal infections affect the throat and skin, and anti-strep[illegible]ibodies are produced by the immune system to combat the infection. However, as the infec[illegible]s are [illegible] aggressive, there is often more antigen than antibody, and this causes the form[illegible]n of i[illegible]ne com[illegible]es. These complexes are usually cleared by the spleen. However, i[illegible]se[illegible] Group [illegible]haemolytic streptococcus, immune complexes may be pathogenic, depos[illegible] the g[illegible]ruli, causing glomerulonephritis.

Systemic Lupus Erythematosus (SLE)

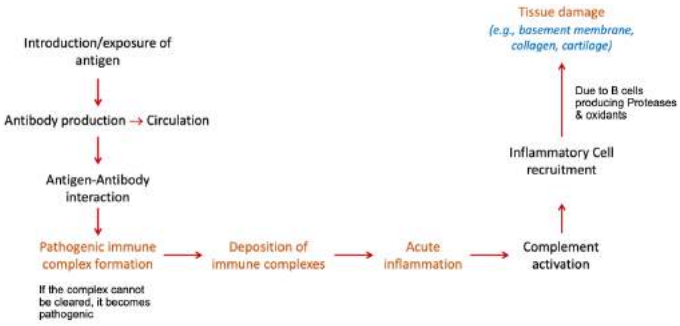
SLE is an autoimmune disease where the body pr[illegible]anti-nuclear ant[illegible]ies, targeting nuclear antigens. Immune complex deposition is common in[illegible]h the co[illegible]xes being deposited in various sites in addition to those listed above:

- Lungs (pleuritis)
- Heart (pericarditis / endocarditis)
- Brain vessels (hemorrhage & infar[illegible])
- Skin (Rash especially on face wi[illegible]da[illegible]e causes necrosis & nuclear proteins are exposed to the immune system)

PATHOGENESIS

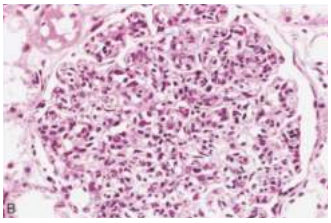
The deposition of the immune comple[illegible]in th[illegible]rulus will trigger complement activation, and recruit various immu[illegible]lls: Neutr[illegible] monocytes, macrophages, T cells, and platelets. These cells then produc[illegible]oxi[illegible] which cause glomerular cell damage, which ultimately leads to degradat[illegible]e GBM a[illegible]overall filtration unit.

The immune cells recruited also relea[illegible]th factors that inflammatory mediators meant to encourage immun[illegible]proliferation but also causes glomerular cell proliferation and glomerular cell swelling.

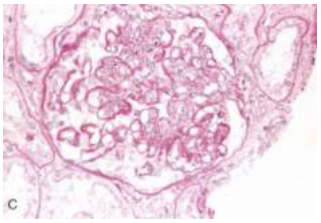


PATHOLOGY

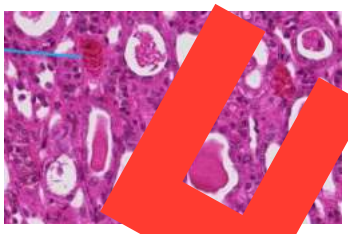
Microscopic



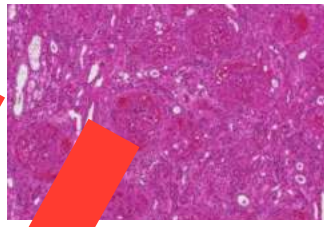
Hypercellularity
- Increased glomerular cell proliferation
- Infiltration of immune cells due to inflammatory response



Dark Staining
- Dark pink staining indicative of complex deposition



Red Cell Cast *(left bla*
- Red blood cell leakage in
  tubules



f Urinary Space
l space filled up due to
ypercellularity within the

DIAGNOSIS

Clinical Syndromes

Nephritic (inflammation)	Nrotic (capillary wall derangement)
Haematuria (Blood in urine, RBC leakage)	N moturia
Oliguria (low urine production)	ly normal urine production
Decreased Glomerular Filtration Rate	Norm
Azotemia: High nitrogen-containing com ds blood, ***SC***(Serum creatinine) & ***BUN***(blood ure ogen)	***erlipidaemia***
Hypertension	***Lipiduria***
Red cell cast in the urine	***poalbuminemia***
	nuria, esp. in Nephrotic
	dema
	Sodium & water retention

Electron Microscopy

This method pinpoints th ion of immune complex deposits, which tells us about the charge of the an resent. The rular Basement Membrane (GBM) is polyanionic (-ve charged), and s ationic tigens uld be deposited past the GBM, and antigens unable to pass thro the GB ely anionic.

Imm cence M oscopy

This method uses sp antibodies to visualize immune complexes. Type III Hypersensitivity will produce a more staining whereas the Type II Hypersensitivity will produce more consistent staining. This is because Type II Hypersensitivity is due to an endogenous self-antigen, which would consistently be found throughout the structure.

ELISA

Coat plate with the target antigen, perform blocking, and add patient serum sample to detect presence of disease-specific antibodies. (More details on ELISA in Topic 1)

Complement Fixation Test

Step 1: Incubate patient sample to deplete complement in the p t seru

Step 2: Add antigen + complement.

In the presence of an antibody (Ab), the Ab will bind to the dded the C' will be fixed by binding to the Ab-Ag complex. If antibody is absent, n mplex will be formed and thus the C' will remain free in the serum.

Step 3: Add opsonized RBC

In the **absence** of Ab, C' is free in the serum, a ind to th C due to the Ab-Ag complex. Once bound, it will form the membrane at MAC), and cause lysis of the RBC (hemolysis).

In the **presence** of Ab, C' is fixed a on't b to bind to the RBC (no lysis)

Step 4: Centrifuge the sample

Centrifugation will bring intact RB om of the plate, forming observable pellets, and liquid will be clear. If ly the liquid ht pink and no pellets will be formed.

Video link for explanation: https:/ /w

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ult Analysis

Antibody of interest	C' Fixa	Haemolysis	Colour	Pellet
Present (+ve)	Yes	No	Clear	Yes
Absent (-ve		Yes	Light red / Pink	No