

Immunopathology

Q) SLE. CF - 20y female
butterfly rash on face,
knee joint pain, chest pain,
photosensitivity.

Q) diagnosis? SLE.

Q) etiopathogenesis?

Q) specific diagnostic criteria

Q) morphology of kidney. ~~spleen~~

Q) Anti nuclear ab.

Q) AntiPL ab. (a) LE Bodies & LE cell.

(b) morphology of other organs in SLE.

Etiopathogenesis

SLE is a chronic autoimmune d/s involving multiple organs, characterized by presence of vast array of Auto Ab particularly Anti nuclear ab (ANA), in which myxoid is mainly caused by deposition of Immune complexes & binding of Ab to various cells & tissues.

• chronic + remitting + relapsing.
• predominantly affects women (9:1)
• age - 20s - 30s.

• can affect any organ.
mainly - skin, kidney, joints, heart,
serous membrane.

Etiopathogenesis

The fundamental defect in SLE is failure of mechanism that maintains self tolerance.

① Genetic factors

② Immunologic factors.

③ Environmental factors;

HLA.

Genetic factors:

① * familial association - family members have ↑ risk of SLE.

• high rate of concordance in monozygotic than dizygotic twins.

② * HLA association → risk of SLE when

HLA-DR2
HLA-DR3

alleles are there.

③ * Genetic deficiency → of early

complements

C1q, C2, C4

lead to.

• defective phagocytic clearance of apoptotic cells.

• impaired removal of immune complexes by mononuclear phagocytic system.

④ * polymorphism in FcγRIIIb inhibitory receptor

↓
inadequate control of B cell activation

② Immunological factors.

① failure of self tolerance in B cells due to defective elimination of self reactive B cells.

• due to defects in central & peripheral tolerance.

↓
↑ autoreactive B cells.

② activation of CD4+ T cells.

specific for nuclear Ag, that has escaped tolerance.

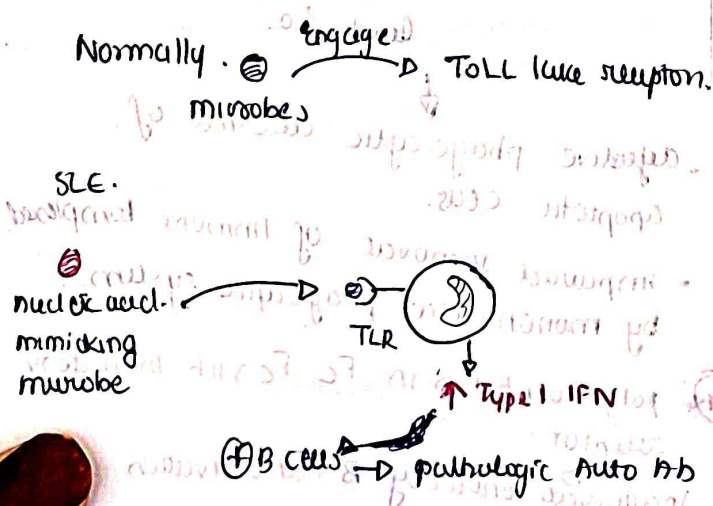
③ Type I interferon - IFN-α is ↑ in SLE, produced in dendritic cell.

④ Nuclear DNA/RNA in IC

↓
via engagement of TLR

↓
further activation of B cells.

↓
↑ production of antinuclear autoantibodies.



Environmental.

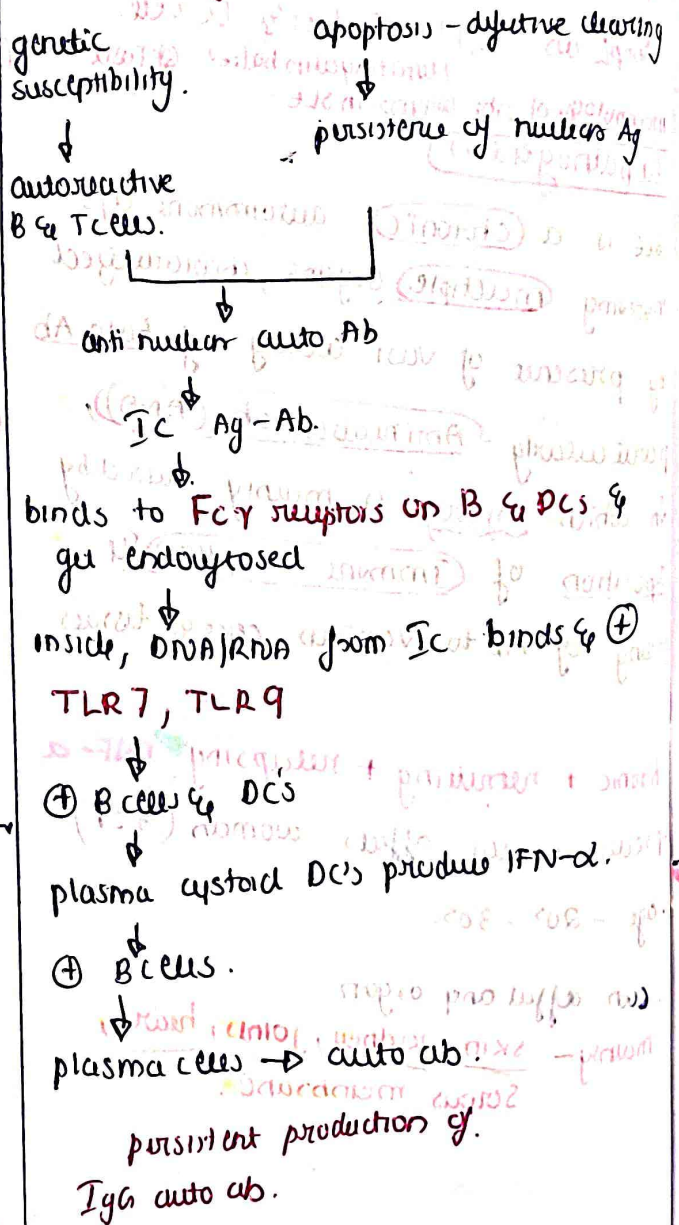
• UV exposure.

• sex hormones - 10x in women of reproductive age than men.

• drugs - Isoniazid & procainamide.

• cigarette smoking.

Pathogenesis - Explanation.

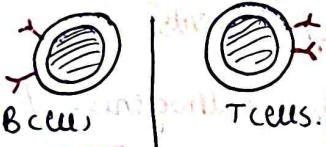


Robbins

Genetic factors.

HLA associated. Susceptibility gene. [HLA DR2, 3].

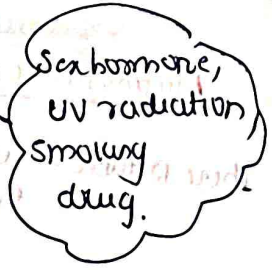
failure of self tolerance



B & T cells specific for self nuclear Antigen.

Environmental factors.

normal tissue.

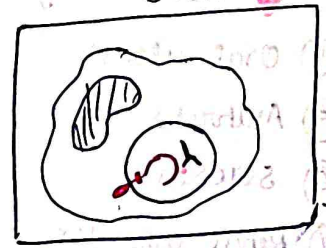


apoptosis

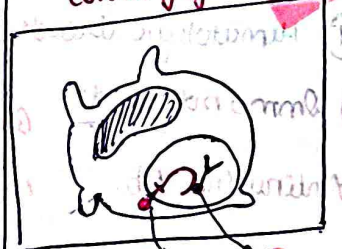
defective clearance of apoptotic bodies.

increased burden of nuclear Antigen.

B cell.



correct figure DC



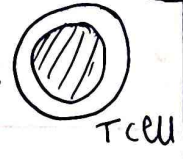
antinuclear antibodies.

Immune complex.

Dendritic cell.

(plasmacytoid DC.)

INF-d



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Endocytosis of Ag-Ab complex.

TLR engagement by nuclear Antigen.

TLR of B cells &

DCs.

of B cells & T cells by INF-d.

plasma cell



persistent production of

IgG autoab.

Auto Antibodies.

• Hallmark of SLE is the production of auto Ab.

Importance.

- 1) we feel for diagnosis & management of patients.
- 2) responsible for pathogenesis of tissue damage.

Types

auto ab are against →

① plasma proteins → complement components, clotting factors.

② proteins, phospholipid complex.

③ cell surface Ag → Lympho, neuro, RBC, platelet

④ Intracellular cytoplasmic. — microfilaments, microtubules, lysosome etc..

⑤ nuclear DNA, RNA, histone.

Antinuclear Antibody (ANAs.)

These are directed Against nuclear self antigens

4 categories, based on their specificity to:

- ① DNA
- ② Histone
- ③ Non histone protein, bound to RNA
- ④ Nuclear Ag.
- ⑤ Ribonucleo protein.

most widely used method for detection of ANA's is

↓
Indirect Immunofluorescence

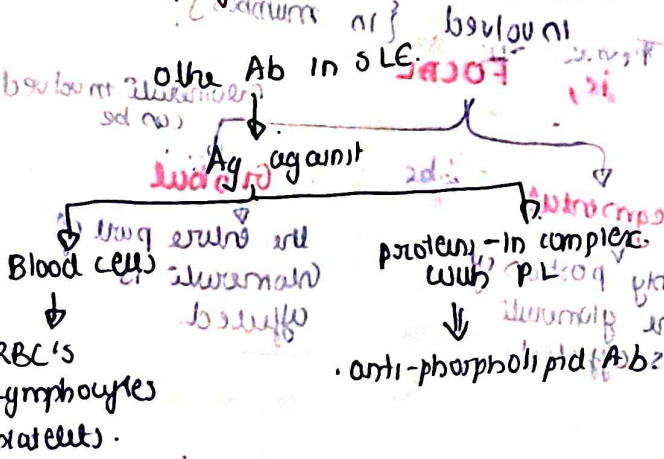
↓ ↓
Pattern of nuclear fluorescence suggest type of Ab present in serum.

• Homogenous / diffuse nuclear staining → Common in SLE.
• reflects Ab to: ds DNA, chromatin, Histone, nucleosomes.

• speckled pattern → m/c pattern, least specific.
Ab to (non-DNA) nuclear components like Sm Ag; RNP; SSA & SSB Ag.
• seen in SLE

Others: centromeric, peripheral / rim, Nucleolar patterns.

★ Ab to ds DNA & Sm Ag (classical) most specific & diagnostic of SLE



Type of ANA

Ag recognized

Anti-ds DNA	ds DNA	most sensitive & specific
Anti-Sm	non histone proteins	most specific bound to RNA
anti-histone Ab	Histone associated DNA	
Anti-RO (SSA)	U1 RNP	specific Ab in neonatal Lupus with congenital Heart Block.

ANA's → Most Sensitive Antibodies

Mechanism of Tissue Injury

- Immune Complex deposition { Type III HSR }
 - most systemic lesions are caused by Immune complexes deposition.
 - ↓ granular deposits of IC, complement
- Auto-Ab mediated destruction of Blood cells. { Type II HSR }
 - blood cells are tagged by autoab.
 - ↓ phagocytosis & destruction { cytopenia }
 - m/c → ITP
- Anti-phospholipid Antibody sx.
 - ✓ recurrent thrombosis
 - ✓ recurrent spontaneous miscarriage
 - ✓ cerebral / Ocular / Ischemic.

MORPHOLOGY

The most characteristic lesions of SLE are due to deposition of IC in

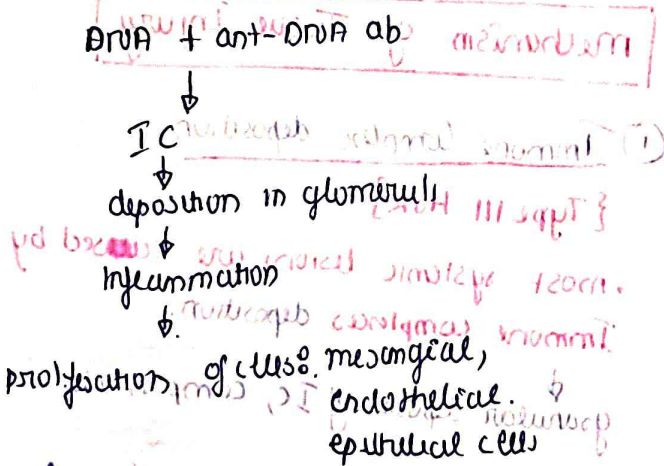
- blood vessel - read further.
- kidney ✓
- connective tissue
- skin

KIDNEY

Lupus Nephritis.

• Kidney involvement is seen in 50% of SLE patients.

Pathogenesis of glomerulonephritis in SLE



Morphological Classification of Lupus Nephritis.

• 6 patterns are recognized.

- Class I - Minimal mesangial LN
- Class II - mesangial proliferative LN
- Class III - focal LN
- Class IV - diffuse LN
- Class V - membranous LN
- Class VI - advanced sclerosing LN

My mother fights dragons, murders Aliens.

Class I Minimal mesangial

- best prognosis but least common.
- Characterized by Immune complex deposition in mesangium.

demonstrated by IF & EM (un)

★ No structural changes in (qq)

Light microscopy

Class II mesangial proliferative

- Characterised by
- mesangial cell proliferation { mild- mod}
- mesangial matrix deposition ↑

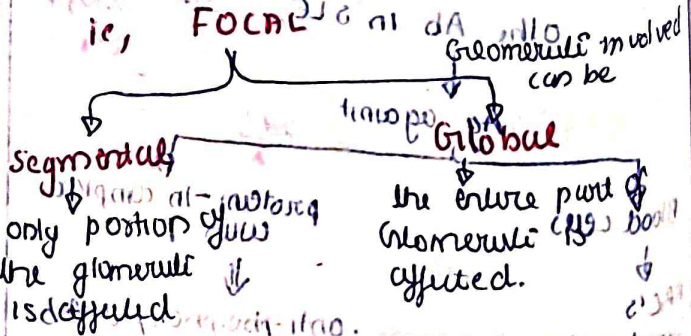
Glomerular capillaries are not involved (qq)

on (IF) → granular deposits on mesangium

IC, Ig, Complements

Class III Focal L.N.

- Less than 50% of glomeruli are involved { in numbers }
ie, FOCAL



proliferation of:

- endothelial cells
- mesangial cells.
- parietal epithelial cell → crescent formation.

- Leukocyte accumulation.
- fibrinoid capillary nerosis ✓
- intracapillary hyaline thrombi ✓

⇒ focal, necrotizing lesions & crescent formation.

Class IV - Diffuse L-N

• m/c & most severe form - poor prognosis.

• m/c pattern associated with wire loop pattern (99)

• >50% glomeruli are affected.

• Marked proliferation of: mesangial, endothelial, parietal epithelial cells. (crescent formation)

*** Sub ENDOTHELIAL** - IC deposits.

causes circumferential thickening of capillary walls

WIRE LOOP LESION - Indicates active ds poor prognosis.

• IC are diluted by IF & em.

• pt's symptomatic - hematuria, proteinuria.

• wire loop lesions are also seen in 3, 4, 5 m/c. include active ds → poor prognosis.

Class - V Membranous.

• m/c associated with Renal vein thrombosis.

• Diffuse thickening of capillary walls.

↓ due to **Sub-EPITHELIAL IC**

• ↑ production of Basement membrane.

→ (nephrotic. sx like)

severe proteinuria.

Class VI advanced Sclerosis.

• Sclerosis of >90% of glomeruli

*** WORST prognosis**

→ End stage disease.

Q **Cvs morphology** - Imp't

Other Question

MC

✓

✓

subintimal ruf. sid. angiosclerosis

arteriosclerosis