

SYSTEMIC LUPUS ERYTHEMATOSUS:

It is a chronic Autoimmune disease involving multiple organs. characterized by the production of various Autoantibodies - ANAs.

- Has multisystemic involvement
- Affect kidney, skin, joints, mucous membrane.
- Damage is due to the ^{deposition of immune complexes} ^{binding of} Antibodies to various cells of tissues.

Etiology:

- Autoimmune disease - defect of self tolerance
- Production of many Autoantibodies that damage the tissue either directly or indirectly by deposition of immune complexes.

Genetic Factors:

- ↑ Risk if present in Family members.
- Genetic deficiencies of early complement components (C1q, C2, C4)
 - impaired Removal of circulating immune complexes.
 - defective phagocytic clearance of Apoptotic cells.
 - failure of B cell tolerance.
- Polymorphism in the Inhibitory Fc Receptor FcγR2b
↓
Lead to inadequate control of B cell Activation.

Environmental Factors:

- Exposure to ultraviolet
- Sex hormones.
- Drugs: hydralazine, procainamide, isoniazid, D-penicillamine.
Can produce SLE.

→ Cigarette smoking.

Immunological Abnormalities:

→ Abnormality in both innate & Adaptive.

→ Type I interferons → Abnormally produced
↓
AutoAntibodies.

→ Toll-like Receptor (TLR) signals: They Recognize DNA & RNA → Regulate Response of B cells.

↓ Activated B cells produce
Antinuclear AutoAntibodies

→ Failure of self tolerance in B cells.

PATHOGENESIS:

→ Genetic Abnormalities in B lymphocytes & T lymphocytes are responsible for the failure of self tolerance.

For example, UV Radiation, smoking & hormone drugs.

↑ Apoptosis

↓

Impaired clearance of
Apoptotic Bodies

↓

Accumulation of ↑ Amount of nuclear Antigens.

↓

Production of Anti-nuclear Antibodies.

↓

Formation of Antigen-Antibody complex in the circulation

(E + VC) → RA, penicillin sensitivity

Endocytosis of immune complexes
by B cell & plasmacytoid DCs (dendritic cells)

stimulation of B cell & T cell by INP

Persistent production of IgG Antibody

Genetic factor + environmental factor

↓
Antinuclear Antibody

The Ag-Ab complexes deposit in tissues & induce inflammation
leading to characteristic vasculitis, synovitis, glomerulonephritis

SPECTRUM OF AUTOANTIBODIES:

hallmark of SLE is production of AutoAntibodies : Types are:

- Anti-Nuclear Antibodies (ANAs)

grouped as:

OA to DNA, Histone, non Histone proteins
nuclear Antigens

- Anti-phospholipid Antibodies are present in 30% of SLE
- Antibodies to dsDNA & smooth Antigens

MECHANISM OF INJURY:

- Type III hypersensitivity Rⁿ:

Most of SLE is caused by immune complex DNA-AntiDNA complex can be deposited in the glomeruli of small blood vessels

- Type II hypersensitivity Rⁿ: AutoAntibodies against cell surface Antigens
specific for RBCs, WBCs, platelets leads to opsonization,
lead to lysis

Anti-phospholipid Antibody syndrome: patients with Antithrombotic
Antibody & prone to venous & Arterial thrombosis

↓
lead to recurrent spontaneous miscarriages & focal
cerebral or ocular ischemia.

Associated with SLE → 2° APAS

Not Associated with SLE → 1° APAS

MORPHOLOGY:

Blood vessels: Auto necrotizing vasculitis → fibroid
neovasis → narrowing of lumen

Kidneys: Involvement of 50%

- Pathogenesis of Glomerulonephritis: Immune complex get
deposited in the glomeruli & Anti-inflammatory.

Divided into 3 types:

A Minimal Mesangial IgG deposits

Class I: Minimal mesangial IgG deposits

- very uncommon and characterized by immune complex deposition in mesangium

Class II: Mesangial proliferative lupus nephritis

- characterized by proliferation of mesangial cell as well as immune complex
deposition in mesangium

Class III: Focal lupus nephritis

- involvement of 50% of glomeruli
affected glomeruli exhibit swelling, reactivation of endothelial cells
associated with leukocyte accumulation

Patient present with Mild hematuria, proteinuria
Acute Renal failure.

Class IV : Diffuse lupus erythematosus nephritis.

Not common if severe form.

75% of glomeruli is affected

- Lesions may progress to scarring.
- hematuria, proteinuria, mild hypertension.

Class V : Membranous lupus nephritis. (15-18%)

subepithelial deposition of immune complexes.

thickening of capillary walls.

proteinuria.

Class VI : Advanced sclerosing lupus nephritis.

sclerosis of more than 90% of glomeruli.

EM: Shows electron dense deposits in mesangial, subendothelial, subepithelial or subendothelial locations.

CNS → Kidney (Arterio sclerosis)

Cerebral arteriosclerosis

Hypocalcaemia, hypoparathyroidism, hypocalcaemia, hypoparathyroidism.

Skin : - Butterfly Rash - erythema in face Along bridge of nose & cheeks (MALAKI RASTA)

- Vasculitis with fibrous necrosis.

BV: Acute necrotizing vasculitis.

spleen: splenomegaly, capsular thickening

Lungs: Pleuritis, pleural effusion

Joints: Non-erosive synovitis

CLINICAL FEATURES:

- more common in female 9:1 Ratio. Age 20 to 30 years.
- It is a multi-system disease.
- Renal failure is most common cause of death.
- Typical Manifestation: Butterfly rash over the face, pain more on peripheral joints, pleuritic chest pain, photosensitivity.
- They are more susceptible to infections.
- weight loss, myalgias, fatigue.

Lab Findings.

- Test for Auto Antibodies.
- Indirect Immune fluorescence assay (IFA)
- ELISA
- Multiplex flow cytometry
- Std tests for diagnosis:
 - CBC, platelet count, ESR, urinalysis.
- Urine Routine.
- Serum creatinine & Albumin
- Complement component level in serum
 - C3
 - C4

Lab Findings: