Lupus Nephritis

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What is Systemic Lupus Erythematosus (SLE)?

- An Autoimmune Chronic Inflammatory Disease
  - Immune System produces proteins called autoantibodies that turns against a part of the body it is designed to protect → Inflammation → Damage.

- Lupus can affect joints, skin, heart, blood vessel, kidneys, lungs & brain

- It is characterized by periods of illness (flares) & periods of wellness (remissions)
What is Systemic Lupus Erythematosus (SLE)? (Cont’d)

• Understanding how to prevent flares & how to treat them when they do occur helps SLE patients maintain better health.

• More common in Women; African American & Hispanic & Asian.
What is Lupus Nephritis?

- A type of Kidney Inflammation (a common complication of SLE)

- It is histologically evident in patients with SLE even if no clinical involvement is yet detected.

- Autoantibodies attack glomeruli of kidneys (waste filters) → blood in urine (hematuria), Proteins in Urine (proteinuria), high BP & Kidney failure.
Classification of Glomerulonephritis in Lupus

As per Kidney Biopsy findings:

- **Class I disease** *(Minimal Mesangial LN) ➔ NL*
  Urine Analysis & Serum Creatinine concentration

- **Class II disease** *(Mesangial Proliferative LN) ➔ Microscopic hematuria &/or proteinuria. HTN, Nephrotic Syndrome and renal insufficiency are rare.*

- **Class III disease** *(Focal LN) ➔ Hematuria & proteinuria (most patients). Elevated Cr conc. HTN, Nephrotic syndrome (only some). Progressive renal dysfunction is less common.*
Classification of Glomerulonephritis in Lupus (Cont’d)

- **Class IV disease** *(Diffuse LN) →* Hematuria & Proteinuria (in all pts with active LN). Nephrotic Syndrome, HTN & Renal Insufficiency is common.

- **Class V disease** *(Lupus Membranous nephropathy) →* Nephrotic Syndrome mainly. Creatinine level is NL-slightly elevated.

- **Class VI disease** *(Advanced Sclerosing Lupus Nephritis) →* ‘healing of prior inflammatory injury’ slowly progressive renal dysfunction.
Symptoms of Lupus Nephritis

- **Active SLE symptoms:**

  **Brain** → Persistent headaches, memory loss or confusion.
  **Mouth & Nose** → Sores
  **Lungs/Heart** → Shortness of breath, Chest Pain.
  **Fingers/Toes** → may turn blue/white on cold exposure/stress
  **Fatigue & Unexplained Fever**
  **Eyes** → Dry or puffy
  **Skin** → Butterfly malar rash on face, worsen with sun exposure.
  **Stomach** → Nausea, vomiting, recurring Abdominal pain.
  **Bladder** → Persistent Infections and blood in urine.
  **Joints** → Persistent pain and swelling
Symptoms of Lupus Nephritis (Cont’d)

- **Asymptomatic Lupus Nephritis** detected in Lab results during regular follow up → more typical of mesangial or membranous LN

- **Active Nephritis**: Peripheral edema 2ry to HTN or Hypoalbuminemia.

- **Diffuse Lupus Nephritis**: Headache, dizziness, visual disturbances, symptoms of cardiac decompensation
Physical Findings

- **Focal & Diffuse LN: Generalized Active SLE**
  - Rash
  - Oral & Nasal Ulcers
  - Synovitis or Serositis

- **Active LN**
  - HTN
  - Peripheral edema
  - Cardiac decompensation occasionally.

- **Membranous LN**
  - No HTN
  - Peripheral edema
  - Ascites, Pleural & pericardial effusion.
Diagnosis of Lupus Nephritis

- **Tests Conducted:**
  - **Urine Analysis** → check for Protein, Red Blood Cells, & Cellular casts.
  - **Blood Test** → Blood Urea Nitrogen <BUN>, Creatinine <Cr>.
  - **Spot Urine Test** → for protein and Cr concentration. Calculate Urine Albumin/Creatinine Ratio.
  - **24 hr. urine test** for Cr clearance & Protein excretion.
  - **Kidney Biopsy** → in any pt with clinical/lab evidence to classify disease.

- Most common abnormality is **Proteinuria** (protein in urine)

- Hematuria & Proteinuria with or without elevated Creatinine level is observed in most SLE patients.
Diagnosis of Lupus Nephritis (Cont’d)

• Lab tests to detect SLE disease Activity:
  ▫ Antibodies to double stranded DNA (dsDNA)
  ▫ Complement (C3, C4 & CH50)
  ▫ Erythrocyte Sedimentation Rate (ESR)
  ▫ C-reactive protein (CRP)
There is no cure for lupus nephritis. Treatment goals aim to:

- Induce remission of the active disease.
- Keep the disease from getting worse.
- Reduce symptoms (remission).
- Avoid the need for dialysis or kidney transplantation.
- Maintain remission.
Treatment of Lupus Nephritis (Cont’d)

• Diet Alterations (according to HTN & Hyperlipidemia)
  ▫ Salt Restriction
  ▫ Restrict Fat Intake
  ▫ Restrict Protein Intake (if renal function significantly impaired)

• Lipid Lowering Therapy
  ▫ Statins for hyperlipidemia 2ry to Nephrotic Syndrome.
Treatment of Lupus Nephritis (Cont’d)

- **Corticosteroid Therapy (1st line of therapy)**
  
  If the patient has clinically significant renal disease.

- **Immunosuppressive Agents; Cyclophosphamide, Azathioprine, or Mycophenolate mofetil**
  
  If pt has aggressive proliferative renal disease or no response to corticosteroids.
Treatment of Lupus Nephritis (Cont’d)

- **Hydroxychloroquine** → decreases flare rates
  (background therapy in all pts unless contraindicated).

- **Angiotensin Converting Enzyme Inhibitors (ACEIs) & Angiotensin Receptor Blockers (ARBs)** → ttt HTN
  (maintain BP below 130/80) and proteinuria in lupus nephritis
Treatment of Lupus Nephritis (Cont’d)

- **Calcium Supplementation** → for Osteoporosis 2ry to long term Corticosteroid therapy.
- **Biphosphonates**
- **Avoid NSAIDs** and other drugs that affect renal function.
- **Avoid Pregnancy** during active lupus → worsens renal disease & medication are teratogenic.
- **ESRD, Sclerosis** patients → unlikely to respond to aggressive therapy → focus therapy on extra-renal manifestations & possible kidney transplant.
Investigational therapies for lupus nephritis & SLE:

- Rituxmab
- Other anti-CD20 monoclonal antibodies
- Belimumab
- Atacicept
- Abetimus
- Anticytokine therapies (monoclonal antibodies directed against interferon alpha, Interleukin 1,6,10 and TNF alpha.)
References

