Hospital Management of Lupus Nephritis

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Epidemiology:

- Lupus nephritis occurs in ~50% of patients with lupus. Of those, 10% progress to ESRD[1]
- Lupus nephritis can be a presenting symptom of lupus in 35% cases[1]
- Race –Black, Hispanic and Asian > Caucasian

Diagnostic clues for lupus nephritis:[2] Acute renal failure, new or worsening hypertension, lower extremity edema or hypercoagulability. The following extra-renal manifestations can help with the diagnosis:

- **HEENT:** Painless ulcers on roof of mouth or nose, alopecia (scarring or non-scarring)
- **Skin:** Malar "butterfly" rash, photosensitive rash, maculopapular rash, Raynaud's phenomenon
- **MSK:** Arthralgias, arthritis
- **Neuropsychiatric:** Psychosis, transverse myelitis, seizures
- **Cardiac:** Pericarditis, myocarditis, Libman-sacks endocarditis
- **Lungs:** Pleuritis, pleural effusion
- **Hematologic:** Clotting disorders (antiphospholipid antibody syndrome), hemolytic anemia, lymphopenia, thrombocytopenia

Suggested work up for lupus nephritis:

- Complete blood count (CBC): Leukopenia (lymphopenia), low Hgb/Hct (anemia of chronic inflammation or hemolytic anemia), thrombocytopenia
- Complete metabolic panel (CMP): hypo-albuminemia, elevated creatinine, low eGFR
- Inflammatory markers: Elevated ESR/CRP
- Complement proteins: Low C3/C4
- Urine analysis: microscopy and 24-hour protein or urine spot protein creatinine ratio[3] (eg: nephrotic syndrome >3g/day; nephritic syndrome >0.5g/day with dysmorphic RBCs, RBC casts, and WBCs)
- Antinuclear Antibody (ANA) by immunofluorescence assay (IFA): negative tests essentially ruling diagnosis out (sensitivity >95%[2]), and higher titers (≥1: 160) increasing likelihood of diagnosis
- Extractable Nuclear Antigen (ENA): Anti-dsDNA, anti-Smith Ab (sometimes anti-RNP Ab, anti-SSA/Ro Ab, and anti-SSB/La Ab)
- Anti-phospholipid antibodies: lupus anticoagulant, beta$_2$-glycoprotein, and anti-cardiolipin
- Renal Biopsy**:** 1) To confirm lupus nephritis 2) Rule out mimics 3) Classify LN: important for treatment and prognostication.[3,4]

Lupus Nephritis Classification: 2018 Revision to the 2004 International Society of Nephrology and the Renal Society [2,5]

Class	**Histology**

I – Minimal Mesangial	Minimal mesangial immune complex (IC) deposits **(no therapy required)**
II – Mesangial Proliferative	Mesangial hypercellularity or matrix expansion w/ IC deposits **(no therapy required)**
III – Focal	<50% with endocapillary hypercellularity, mesangial and focal subendothelial deposits
IV – Diffuse	≥ 50% with endocapillary hypercellularity – mesangial and diffuse subendothelial IC deposits
V - Membranous	Thickening of glomeruli capillary walls with subendothelial IC deposits, +/- mesangial IC deposits
VI – Advanced Sclerosing	>90% sclerosed glomeruli (classification debated in 2018 revision as it is non-specific) **(will not benefit with therapy)**

Induction Therapy:[3]

- Class III/IV: 0.5-1gm IV methylprednisolone x 3 days → 0.5-1 mg/kg PO prednisone taper over weeks **PLUS** PO Mycophenolate Mofetil (MMF) 3gm/day x 6 months **OR** IV cyclophosphamide 500mg every 2 weeks x 6 doses.
- Class V: 0.5 mg/kg/day prednisone **PLUS** MMF (can consider addition of calcineurin inhibitors).

Additional Therapy:[3]

- Blood pressure management: ACE inhibitors or ARBs (Goal BP ≤130/80).
- Hydroxychloroquine: ≤5mg/kg a day; dose not exceeding 400 mg a day; may need to adjust according to eGFR.
- Belimumab: Can consider adding to stage III-V for increased renal response rates[6].
- Follow up on discharge: Nephrology and Rheumatology.

Clinical Pearls:

- Lupus nephritis can often be a presenting symptom of lupus.
- Suspect lupus nephritis with new or worsening hypertension, lower extremity edema, hypercoagulability, and extra-renal manifestations.
- Investigations: CBC, CMP, urinalysis, ANA, ENA, C3, C4, ESR, and CRP.
- Renal biopsy: Needed to confirm the diagnosis, rule out mimics and decide therapy (induction + BP management + hydroxychloroquine).

Resources:

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