Student Handout: Hematologic Malignancies & Kidney Disease

Andrew Bland, MD, FACP, FAAP

July 2026

Student Handout: Hematologic Malignancies & Kidney Disease

> **Learning objective:** Understand renal complications of blood cancers, focusing on myeloma kidney, MGRS, lymphoma/leukemia effects, and stem cell transplant-related nephropathy

---

Overview

Blood cancers have unique mechanisms of causing kidney disease due to high protein production, immune dyscrasia, and treatment-related complications. This handout covers the major entities:

1. **Multiple Myeloma** → Myeloma kidney (cast nephropathy)
2. **Monoclonal Gammopathy of Renal Significance (MGRS)**
3. **Lymphomas** → Immune complex disease, TLS
4. **Acute Leukemias** → TLS, blast lysis
5. **Stem Cell Transplantation** → TLS, thrombotic complications

---

MULTIPLE MYELOMA & MYELOMA KIDNEY

Epidemiology

- **Incidence:** ~200,000 new cases/year in US; 10–20 cases/million/year
- **Renal involvement:** 20–50% of patients at diagnosis have AKI or baseline CKD
- **Clinical significance:** Renal impairment = adverse prognostic factor; impacts chemotherapy dosing & prognosis

Pathophysiology of Myeloma Kidney

The mechanism (step-by-step):

1. **Clonal plasma cell proliferation** → Produces large amounts of **monoclonal immunoglobulin (usually IgG or IgA)**
2. **Free light chain production** → Clones make excess κ or λ light chains (>20 mg/dL)
3. **Glomerular filtration** → Small light chains (22 kDa) filtered by glomerulus

4. **Proximal tubule uptake** → Light chains reabsorbed via endocytosis
5. **Tubular cast formation** → Light chains precipitate with **Tamm-Horsfall protein (THP)** to form refractory casts
6. **Tubular obstruction** → Casts occlude tubular lumen → AKI
7. **Interstitial inflammation** → Lytic lesions trigger innate immunity
8. **Result: Acute tubular necrosis + interstitial nephritis**

Clinical Presentation

Feature	Details
Acute presentation	Rapid ↑ Cr (days to weeks); oliguric AKI possible
Chronic	Progressive CKD over months; proteinuria <1 g/day (not nephrotic)
Labs	↑ Cr, ↑ BUN, normal anion gap often; abnormal SPEP/UPEP
Urinalysis	**Crystal-like casts**, epithelial cells; NOT typically hematuria/RBC casts
Light chains	Serum free light chain ratio abnormal (κ/λ >100 or <0.01)

Diagnosis

The gold standard: Kidney biopsy

Modality	Finding
Light microscopy	**"Waxy" or "brittle" casts** (refractile, crystalline); dense, eosinophilic; usually in distal tubules/collecting duct
Electron microscopy	Casts composed of light chain proteins; fibrillary or organized substructure
Immunofluorescence	Casts stain with **κ or λ light chain antibodies** (usually one predominates)

Supporting labs: - SPEP: M-spike (monoclonal paraprotein) - UPEP: Bence Jones protein (free light chains in urine) - FLC assay: ↑ Involved light chain; abnormal ratio

Management of Acute Myeloma Kidney

Medical Management:

1. **Hydration:** Aggressive IV hydration (3–4 L daily) to ↑ GFR and dilute tubular fluid → ↓ cast precipitation
2. **Loop diuretic:** Furosemide to maintain high urine flow (200–300 mL/h goal)
3. **Alkalinization:** Sodium bicarbonate to alkalinize urine (target urine pH 6.5–7) — inhibits light chain precipitation

4. **Avoid contrast, NSAIDs:** ↓ GFR further
5. **Anti-myeloma therapy:** Prompt initiation of chemotherapy (bortezomib, lenalidomide, etc.) → ↓ light chain production → Resolution of casts

Renal Replacement Therapy: - **Indications:** Oliguric renal failure unresponsive to hydration, severe hyperkalemia, fluid overload - **Modality:** CRRT or hemodialysis (some argue CRRT preferred because continuous) - **Outcome:** 30–50% of oliguric patients recover renal function with supportive care + chemotherapy

Prognosis: - **Early treatment:** ~50–70% recover renal function if caught early - **Delayed treatment:** ~10–20% recover if AKI prolonged - **Late diagnosis:** Often results in permanent dialysis dependence

Long-Term Monitoring

- Serial Cr, FLC assay (response to therapy reflected in ↓ FLC)
- Suppress light chain production aggressively
- Avoid nephrotoxic drugs
- ACEi/ARB if proteinuria >1 g/day

MGRS (Monoclonal Gammopathy of Renal Significance)

What is MGRS?

Definition: Kidney disease caused by monoclonal immunoglobulin OR light chains deposited in glomeruli in the absence of overt hematologic malignancy. Usually a precursor to lymphoproliferative disorder.

Key distinction: MGRS ≠ Myeloma (no plasma cell clones >10% in marrow); MGRS is a renal-dominated disease

Pathology Patterns

Pattern	Mechanism	Presentation
Membranoproliferative GN	Monoclonal Ig deposits in capillary wall	Hematuria, proteinuria, hypertension
AL Amyloidosis	Misfolded light chain fibrils	Nephrotic syndrome, proteinuria >3 g/day
Light chain deposition disease	Linear deposits of light chains in GBM	AKI, hematuria, nephrotic
Monoclonal IgA/IgM GN	Monoclonal deposits mimicking IgA-N	Hematuria, proteinuria, progressive CKD

Clinical Presentation

- **Proteinuria:** 0.5–5 g/day (often >1 g, sometimes nephrotic)
- **Hematuria:** Often present (RBC casts, dysmorphic RBCs)

- **Renal function:** Normal to impaired; variable AKI vs CKD
- **Blood counts:** Normal (no cytopenias; distinguishes from frank malignancy)

Diagnosis

Kidney biopsy is essential: - Light microscopy: GN pattern (MPGN, FSGS, or linear deposits) - Immunofluorescence: **Monoclonal Ig or light chain deposition** (κ or λ only, not polyclonal) - Electron microscopy: Confirms pattern (amyloid fibrils, electrodense deposits, etc.)

Supporting labs: - SPEP/UPEP: Small M-spike or absence thereof - FLC assay: Usually abnormal ratio (elevated involved light chain) - Bone marrow: <10% plasma cells (by definition)

Management

1. **Treat underlying clone:**
   - Chemotherapy if light chain/myeloma-like (bortezomib, lenalidomide)
   - Rituximab if B-cell proliferation
2. **Supportive:** ACEi/ARB for renal protection, BP control
3. **Monitor renal function & proteinuria closely**
4. **Long-term surveillance:** 10–20% progress to frank myeloma over 5 years

---

LYMPHOMA & KIDNEY DISEASE

Types & Mechanisms

Lymphoma Type	Renal Complication	Mechanism
Hodgkin Lymphoma	Immune complex GN, FSGS	Circulating immune complexes, nephrotic syndrome common
Non-Hodgkin (Burkitt)	**TLS** (high risk), immune complex GN	Massive cell turnover → hyperkalemia, hyperuricemia, AKI
Non-Hodgkin (Indolent)	Cryoglobulinemia, MPGN	Monoclonal Ig deposition similar to MGRS
Post-transplant lymphoproliferative	Glomerular disease, interstitial nephritis	EBV-driven; responds to reduction of immunosuppression

Clinical Features

High-grade (Burkitt, aggressive): - Peak risk: TLS (see prior handout) - AKI common (20–30% of patients) - Monitors: K+, uric acid, PO_4 closely

Indolent (Low-grade): - Gradual proteinuria, hematuria - CKD progression over years - May have cryoglobulinemia (RNP, C4 ↓, Cr, mixed cryoglobulins)

Management

- Chemotherapy → Cell destruction, monitor for TLS
- Supportive: Hydration, rasburicase (if high risk)
- Renal-specific: ACEi/ARB, BP control
- Monitor: Renal function, UA, electrolytes q 1–2 weeks during/after chemotherapy

---

ACUTE LEUKEMIA & KIDNEY DISEASE

Mechanisms

Complication	Details
TLS	**HIGH RISK** — Acute leukemias have highest TLS incidence; rapid cell death post-chemo → hyperkalemia, hyperuricemia
Leukostasis	WBC obstruction of renal vessels → AKI (rare but severe)
Uric acid nephropathy	Massive purine load from blasts → Urate crystal obstruction
Blast infiltration	Direct renal parenchymal infiltration (rare)

AML-Specific

- **Higher TLS risk** if WBC >100,000 and high LDH
- **Bladder involvement:** Hemorrhagic cystitis (from chemotherapy)
- **AKI incidence:** 20–50% of hospitalized AML patients

ALL-Specific

- **Highest TLS risk** — ALL cells most chemosensitive
- **Risk factors:** Age <10 or >50, WBC >100,000, bulky disease, elevated LDH
- **Management:** Rasburicase prophylaxis, aggressive hydration, ICU monitoring (see TLS handout)

Management

- **Prevention:** Rasburicase, aggressive hydration BEFORE chemo starts
- **Monitor:** Baseline K+, uric acid, FLC; q6h labs during first 48 h
- **RRT threshold:** K+ >6.5 OR uric acid >8 with AKI OR anuria → Dialysis
- **Duration:** Usually 5–7 days of intensive monitoring

STEM CELL TRANSPLANTATION (SCT) & KIDNEY DISEASE

Timing & Complications

Phase	Complication	Mechanism
Pre-transplant conditioning	AKI from chemotherapy (TLS-like)	Myeloablative regimen toxicity
Engraftment (days 0–30)	Acute kidney injury, sepsis	Infection, medication nephrotoxicity (aminoglycosides, amphotericin)
Early post-transplant (months 1–3)	Calcineurin inhibitor (CNI) nephrotoxicity	Cyclosporine or tacrolimus → ↓ GFR, HTN
Late post-transplant (>3 months)	Chronic kidney disease, GVHD-related	CNI toxicity, chronic GVHD, infections

Acute Kidney Injury in SCT

Incidence: 40–50% of SCT patients develop AKI; 10–15% require dialysis

Causes: - **Chemotherapy nephrotoxicity** (conditioning regimens contain high-dose cyclophosphamide, busulfan) - **Sepsis** (immune reconstitution not complete; infection risk high) - **Aminoglycoside antibiotics** (empiric for fever) - **Amphotericin B** (fungal prophylaxis) - **Calcineurin inhibitors** (graft-versus-host disease prophylaxis) - **TLS** (from rapid leukemic cell kill if allogeneic transplant for hematologic malignancy)

Chronic Kidney Disease in SCT

Long-term renal outcomes: - **5-year CKD incidence:** 20–30% - **Risk factors:** High-dose conditioning, older age, GVHD, multiple nephrotoxic drugs, TBI (total body irradiation) - **Mechanism:** CNI toxicity (cyclosporine/tacrolimus) → Hyaline arteriosclerosis, glomerulosclerosis, tubular atrophy

Management Strategies

Prevention: - Minimize CNI exposure; use lowest effective dose - Alternate CNIs with sirolimus if tolerated - Avoid concurrent nephrotoxic drugs (NSAIDs, contrast agents) - Monitor BP closely (control with ACEi/ARB)

Monitoring: - Baseline renal function before conditioning - Daily Cr during conditioning & early engraftment (first 30 days) - q 1–2 week labs during months 1–3 - q 1–3 month labs long-term (look for CKD progression)

Management of AKI: - Discontinue nephrotoxic drugs if possible - Hydration (unless fluid overloaded from sepsis/capillary leak) - RRT if oliguric or severe electrolyte derangements - Empiric antibiotics with renal dosing

Management of CKD: - ACEi/ARB to slow progression - BP target <130/80 - Reduce CNI to lowest dose; consider switch to alternative agent - Avoid NSAIDs - Monitor for bone disease (CKD-MBD from chronic GFR reduction)

Clinical Integration

Red Flags

- ☐ Myeloma patient with rapid ↑ Cr → Consider myeloma kidney; start aggressive hydration immediately
- ☐ High-grade lymphoma + low K+/uric acid → Think TLS; prophylactic rasburicase
- ☐ AML with WBC >100k → Highest TLS risk; ICU-level monitoring
- ☐ SCT day +5 with ↑ Cr → Could be chemo, sepsis, CNI toxicity, or TLS overlap

Key Interventions by Scenario

Scenario	Urgent Actions
Suspected myeloma kidney	IV hydration (3 L daily), furosemide, alkalinize urine, start myeloma chemotherapy, consider biopsy
High-grade lymphoma starting chemo	Rasburicase IV, aggressive hydration, baseline K+/uric acid, ICU monitoring
AML diagnosis with WBC >100k	Rasburicase, hydration, ICU admission, avoid aggressive diuresis, prepare for RRT
SCT day +3 with AKI	Hold nephrotoxic drugs, optimize hydration status, check uric acid/K+, consider RRT if worsening

---

Key Clinical Pearls

☐ **Myeloma kidney = Casts** — Crystal-like tubular casts on biopsy; light chain staining confirms ☐ **MGRS = Biopsy essential** — Distinguishes monoclonal from polyclonal immunoglobulin ☐ **Lymphoma TLS = Highest risk** — Burk lymphoma + bulky disease = ICU monitoring ☐ **AML > ALL for volume** — But ALL > AML for TLS risk per cell chemosensitivity ☐ **SCT AKI multifactorial** — Chemo + drugs + infection; needs systematic evaluation ☐ **Early treatment = Better outcomes** — Prompt chemotherapy resolves myeloma kidney; delays worsen prognosis

---

Related Content

Onconephrology Hub: - Hematologic Malignancies & Kidney Disease — Comprehensive pathology and extended management - Tumor Lysis Syndrome — Detailed TLS pathophysiology and management

Cross-Reference Student Handouts: - Student Handout: Tumor Lysis Syndrome — TLS diagnosis, risk stratification, management - Student Handout: AKI Staging — General AKI assessment framework - Glomerular Disease Algorithm — MGRS differential from primary GN

References

- **Dimopoulos MA, et al.** IMWG Consensus on Management of Acute Kidney Injury in Multiple Myeloma. Leukemia. 2016;30(11):2183–2190.
- **Nasr SH, et al.** Renal Effects of Novel Agents Used in Multiple Myeloma. Clinical Journal of the American Society of Nephrology. 2018;13(8):1232–1244.
- **Leung N, et al.** Kidney Disease in Hematologic Malignancies and Hemolytic Anemias. Clinical Journal of the American Society of Nephrology. 2016;11(11):2036–2045.
- **Alachkar N, et al.** Acute Kidney Injury in Hematologic Malignancies and Stem Cell Transplantation. Advances in Chronic Kidney Disease. 2017;24(6):379–387.
- **Fei Z, et al.** Renal Disease in Lymphomas. Current Opinion in Oncology. 2018;30(2):90–95.

Study Tips: - **Myeloma kidney:** "Waxy casts" on biopsy; bright light chain staining (κ OR λ) - **MGRS:** Monoclonal deposits on IF; no frank malignancy (BM <10%) - **Lymphoma:** Think TLS for high-grade, cryoglobulinemia for indolent - **AML/ALL:** ALL highest TLS risk; both need rasburicase prophylaxis - **SCT:** Triplet problem — chemo + drugs + infection; manage all three

Created: 2026-02-28