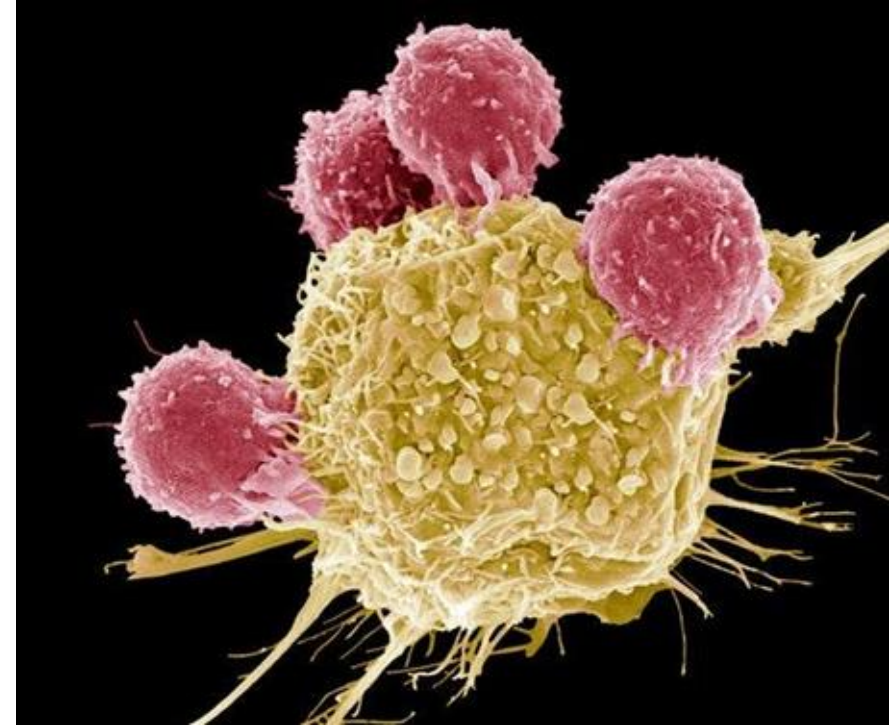


Pre-Transplant Plasma Cell Dyscrasias – Can we optimize patient outcomes?

Chris Blosser

September 18, 2026



Disclosures

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- Advisory Board Member – Pierre Fabre Pharmaceuticals, Apellis/Biogen
- Editorial Board Member -American Journal of Transplantation

Case Introduction

- 68yo healthy male
- Cavernoma, resected
 - Seizures, controlled
- May 2025: Inguinal hernia repair
 - Serum creatinine: 2.14mg/dl
- June 2025: Scr 4.0
- Aug 2025: Scr 13.3 ->HHD

August 2025

- **SPEP/IF:** glycosylated kappa monoclonal, unable to quantitate
- **Serum FLCs:** kappa 52.7 mg/dL, lambda 4.87 mg/dL, ratio 10.8
- **CBC:** Hgb 7.3 g/dL, Plt 157
- **Urine:** UPEP: Bence Jones, 24 hr protein: 430.9 mg/24 hrs

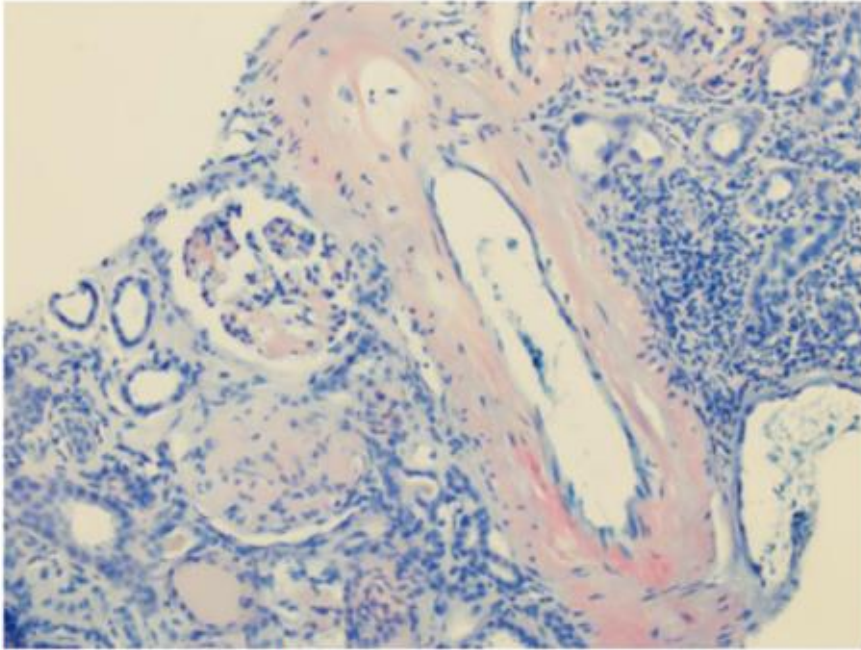
September 2025

- **Kidney biopsy: No kidney tissue**
 - Retroperitoneal hemorrhage
- **Bone marrow biopsy:** 15-20% plasma cell involvement by CD138 IHC. FISH: gain 1q and atypical t(11;14). Negative for amyloid deposition
- **TTE:** LVEF 55-60%, mildly reduced GLS (-16.8%). Mild-moderate mitral regurgitation. Mild tricuspid regurgitation. Moderately dilated left atrium.
- **PET/CT:** no suspicious bony lesions or abnormal focal areas of activity
- Diagnosed with **kappa light chain deposition disease vs myeloma cast nephropathy vs AL (kappa)-type amyloidosis involving the kidneys**
- **Systemic Therapy** 9/24/25 – 3/4/26: Dara-Vd x6 cycles
- **Serum FLCs (2/10/26):** kappa 9.87 mg/dL, lambda 3.22 mg/dL, ratio 3.0

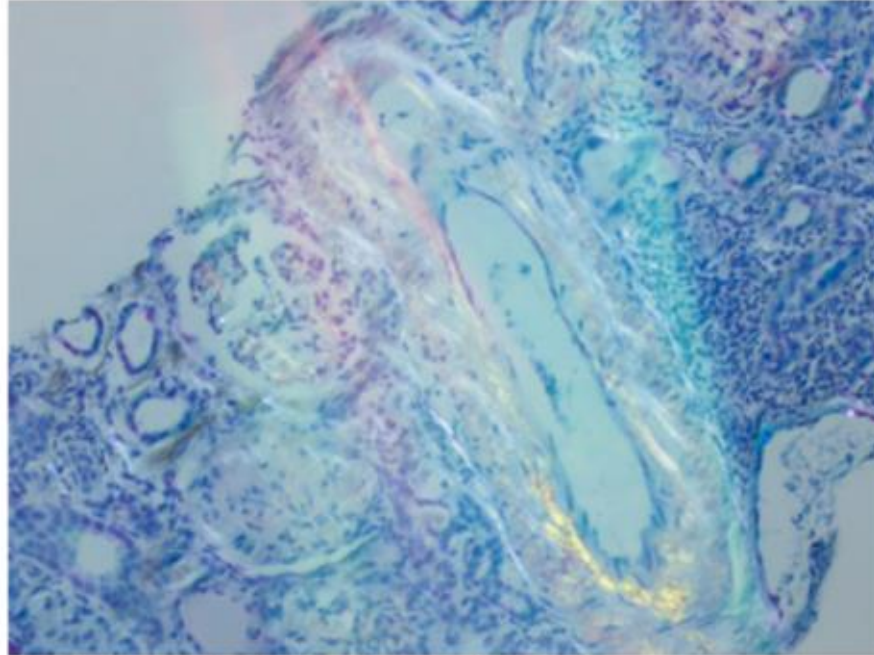
February 2026

- **Fred Hutch Second Opinion (1/5/26)**
 - Suspected kappa light chain AL Amyloidosis vs. SMM + CKD of alternate etiology
- **Abdominal fat pad biopsy (2/19/26):** Negative
- **MRI cardiac (2/22/26):** No evidence of infarction, scarring, or infiltrative process.

Kidney biopsy (2/26/26): Amyloidosis, AL (kappa)-type

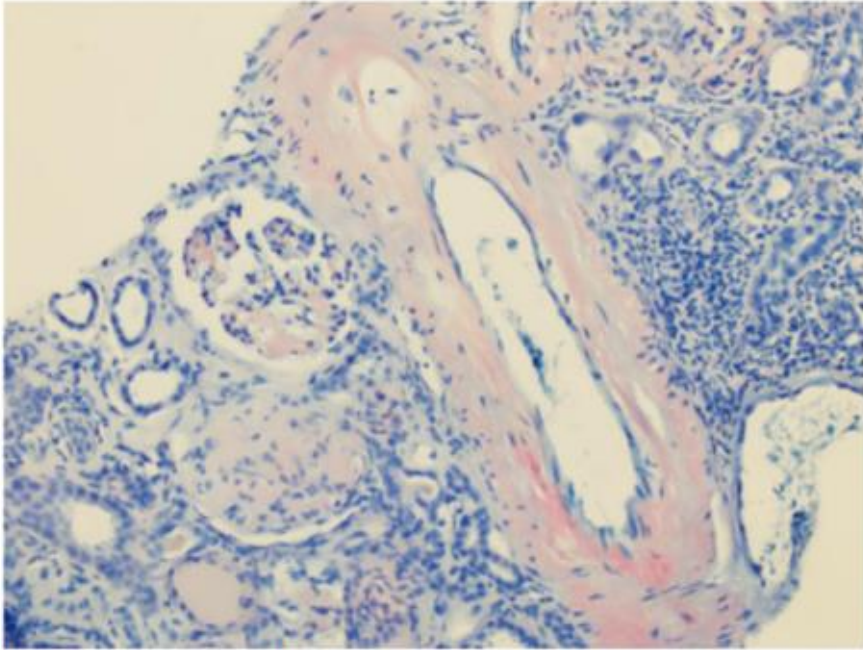


Positive Congo red in a glomerulus and vessel

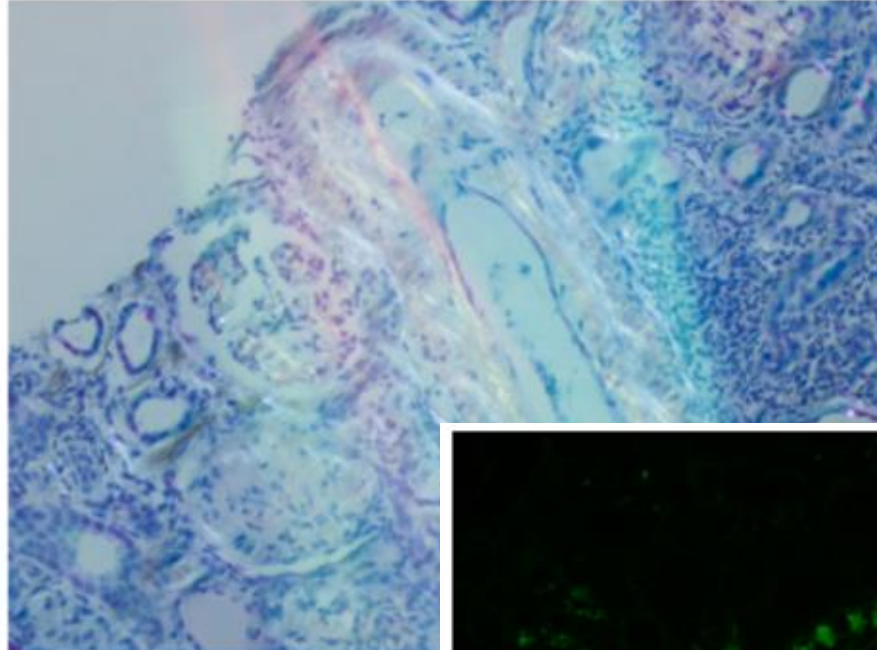


Birefringence visible under polarized light

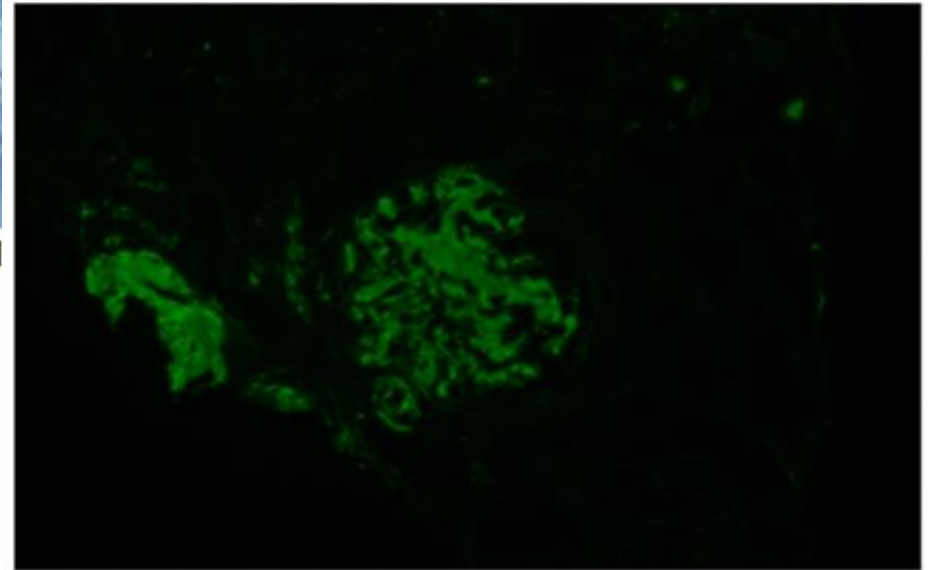
Kidney biopsy (2/26/26): Amyloidosis, AL (kappa)-type



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Birefringence visible under pol



Kappa light
chains

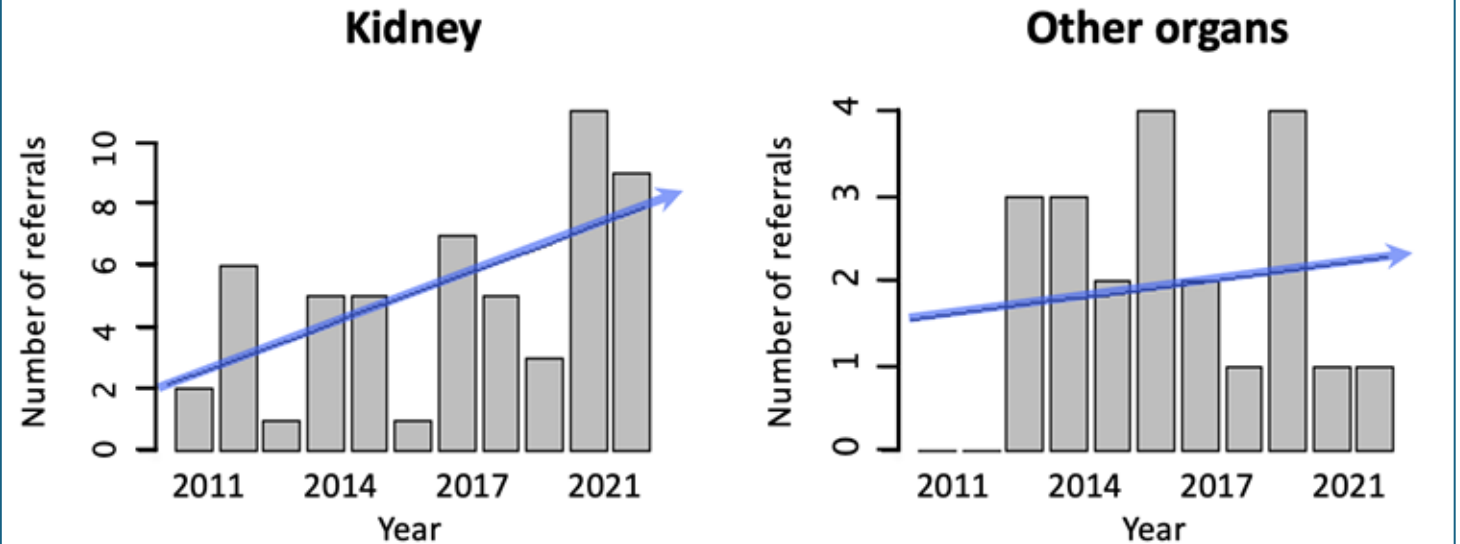
April – Sept 2026

- **Dara-Vd x6 cycles** (9/24/25 – 3/4/26)
- **Serum FLCs (3/31/26):** kappa 11.3 mg/dL, lambda 2.93 mg/dL, ratio 3.86
- **4/8/26 -> Daratumumab** maintenance therapy
- **Serum FLCs (7/6/26):** kappa 13.6 mg/L, lambda 3.54 mg/L, ratio 3.84
- **PET/CT:** No significant interval change, no evidence of recurrent metastatic disease.
- **24-hr urine (7/13/26):** IgG kappa monoclonal
- **Bone marrow biopsy (7/15/26):** 1-2% plasma cells with kappa light chain restriction consistent with residual plasma cell neoplasm.
- **Central therapeutic goal (Sept):** eradication or maximal suppression of residual amyloidogenic plasma cell clone before kidney transplant
 - Preferred next-line strategy: teclistamab plus daratumumab
 - Second-choice option: carfilzomib, cyclophosphamide, and dexamethasone (Car-Cy-Dex)

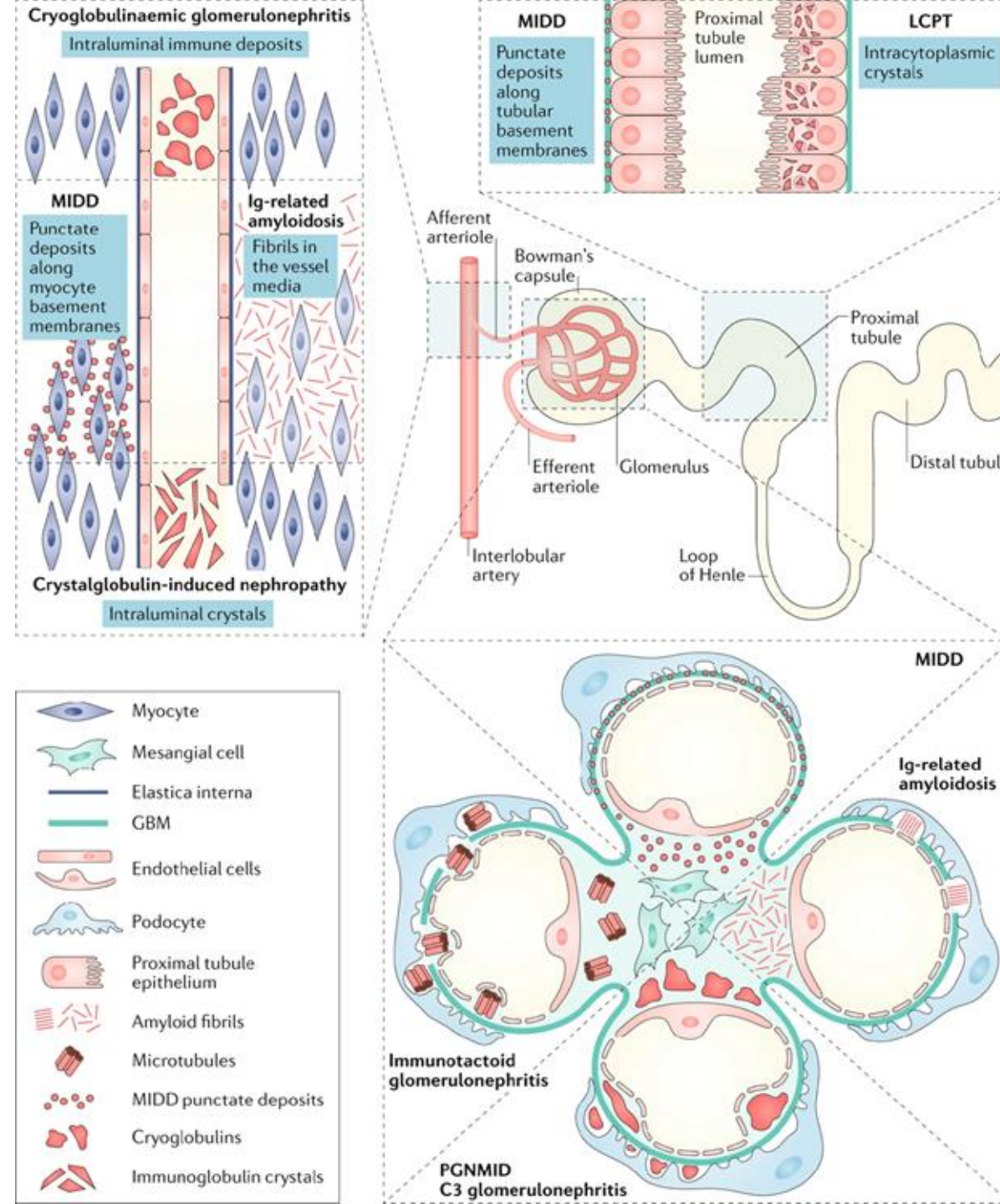
Prevalence of Plasma Cell Dyscrasias in Patients Referred to UW for Organ Transplants (2011-2021)

- Plasma cell dyscrasias cause kidney injury via multiple MOAs.
- ~50% of patients with PCD develop kidney disease but historically have rarely been referred for transplant out of concern for prognosis, PCD progression, or transplant injury.
- New PCD therapies have enabled improved transplant access, yet data does not encompass contemporary referral and transplant

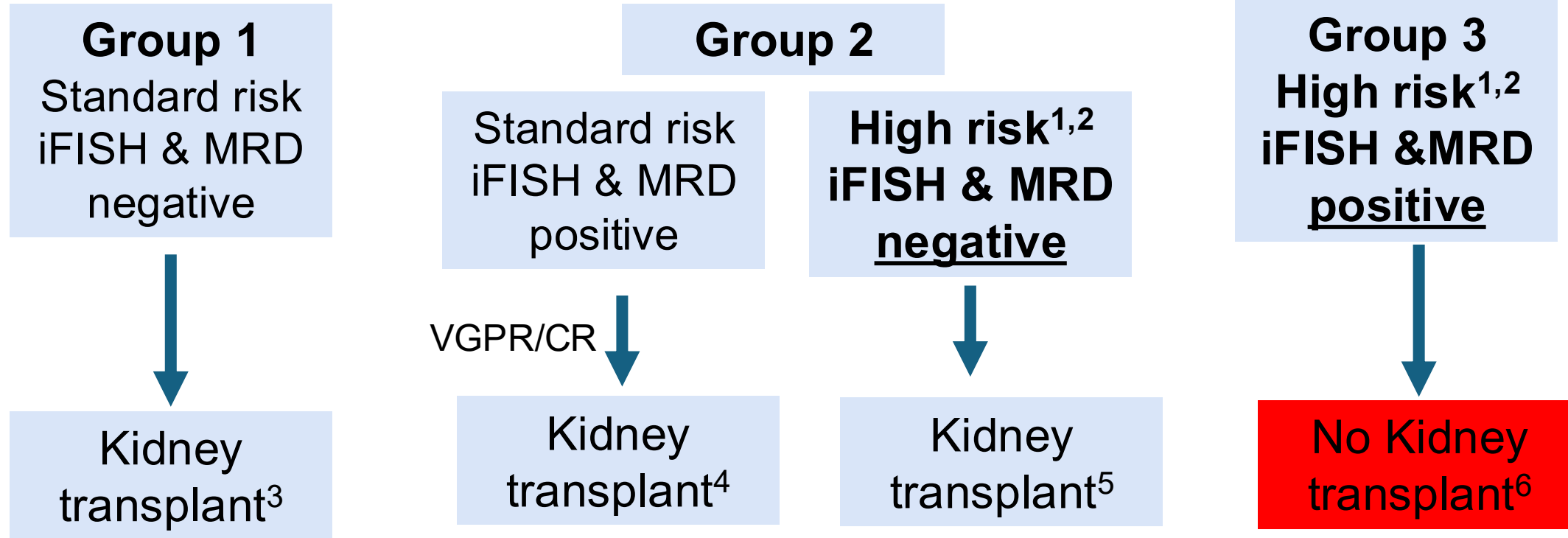
Figure 1. Number of referrals for kidney and organ transplant in patients with PCD by year. There was an average increase of 0.6 patients per year ($p=0.05$) for kidney transplants and 0.1 patients per year ($p=0.62$) for other organ transplants from 2011-2021.



PCD-related Kidney Lesions



Kidney Transplant for MM Patients based on Risk and Response to Therapy



1. High risk category defined as one of the following: High risk cytogenetics, High Beta-2-microglobulin (>5.5 mg/dl) with a normal creatinine (<1.2mg/dl), extramedullary disease, or plasma cells clones in circulation at diagnosis.
2. High risk cytogenetics (iFISH or NGS): Deletion (del) (17p) in >20% CD38+ plasma cells and/or TP53 mutation, Monoallelic del (1p32), along with +1q, or biallelic del (1p32), One of the translocations: t(4;14) or t(14;16) which must co-occur with +1q or del(1p32),
3. In standard risk, MRD negative (10e-5 or 10e-6, depending on availability) MM patient, kidney transplant can be considered within 6 months of achieving a hematologic response*
4. In standard risk, MRD positive MM patient, kidney transplant can be considered 12 months after achieving a VGPR/CR, but consider continuing/maintenance therapy*
5. In high risk, MRD negative MM patient, kidney transplant can be considered 12-24 months of achieving a hematologic response, but recommend continuing/maintenance therapy*
6. High risk patients who remain MRD positive are not considered optimal kidney transplant candidates but could be considered in selected circumstances

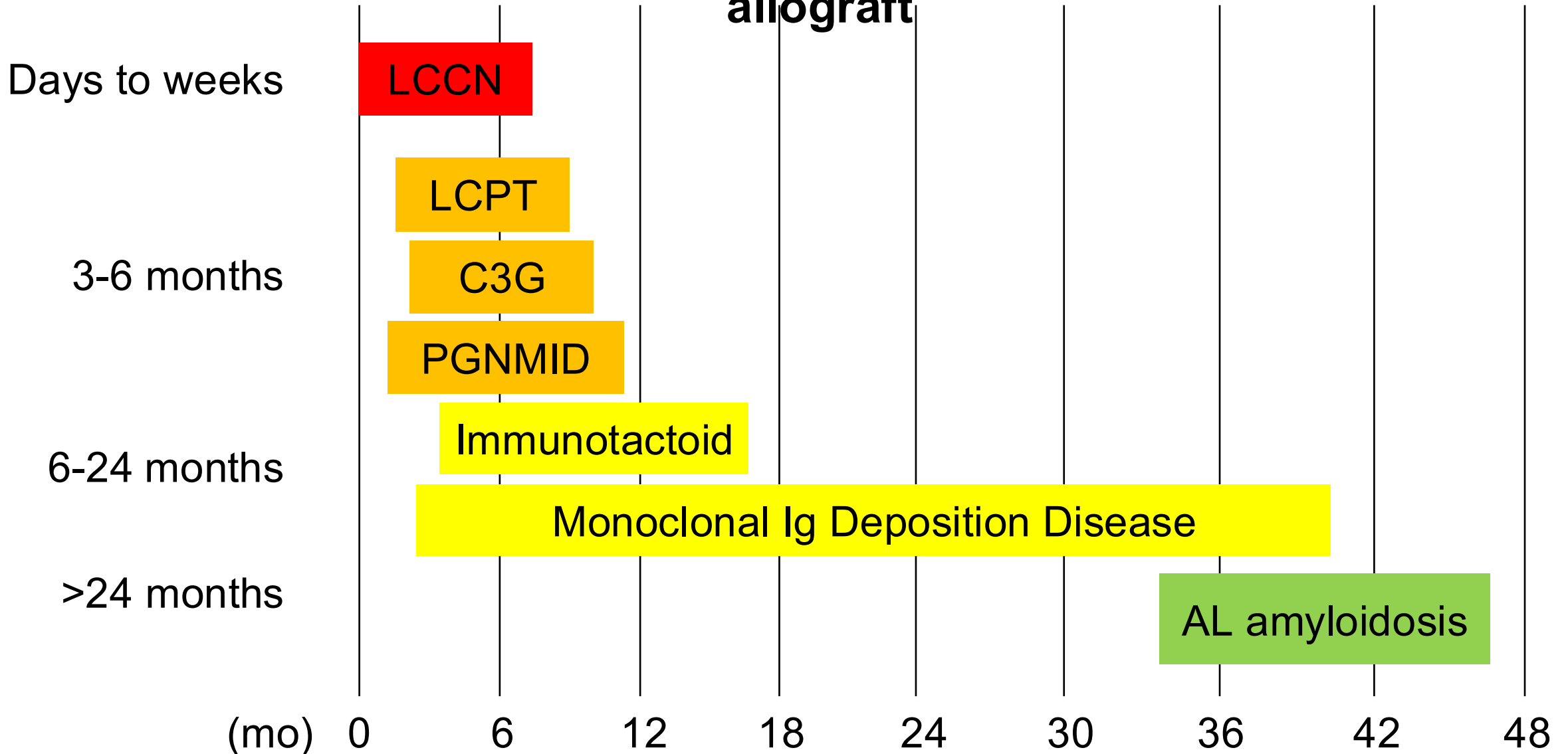
* Contingent on overall transplant candidacy and availability of a living donor

Summary of key cohort studies of AL amyloidosis and kidney transplantation

	Study years	Cardiac involvement	HSCT	Living donor tx	mOS (yr)	Graft survival (yr)	Recurrence (%), Estimated time	Prognosis Factors
Mayo Clinic (n=60)	1997-2018	47%	60%	80%	10.3	NR	22%, 10.2 yr	CR/VGPR: longer mOS
BU-Amyloidosis Center (n=49)	1987-2017	33%	80%	65%	10.5	8.3	29%, 3.7yr	CR/VGPR: longer mOS and lower recurrence
Memorial Sloan Kettering (n=16)	1999-2018	25%	100%	87%	13.1	11.3	25%, ND	ND
UK-National Amyloidosis Centre (n=51)	1989-2018	22%	24%	41%	7.9	NR	14%, 4.5 yr	IVSd>12mm: worse mOS and hgher recurrence
IKMG multi-center study (n=237)	1987-2020	41%	62%	54%	8.6	7.8	29%, 6.6 yr	CR/VGPR: longer mOS, lower recurrence, and longer graft survival
ND: not described, NR: not reached, HSCT: hematopoietic stem cell transplant, BU: Boston University, UK: United Kingdom, IKMG: International kidney and monoclonal gammopathy research group, CR: complete response, VGPR: very good partial response								
IVSd: interventricular septal diameter								

CR/VGPR
R →

Timing of recurrence of various PCDs in kidney transplant allograft



LCCN: light chain cast nephropathy, LCPT: light chain proximal tubulopathy, C3G: C3 glomerulopathy, PGNMID: proliferative glomerulitis with immunoglobulin deposits

PCD Management in Transplant

Pre-Transplant

Disease-related

- Establish risk-based prognosis
- Heme Surveillance (SFLC/SPEP/IFE) q3mos
- Hold Imid, PI, Dara >2 weeks

Transplant-related

- Living donor if possible
- Avoid +XM or ABOi
- Induction & maintenance
- Infection prophylaxis for both PCD +Txplt



PCD Management in Transplant

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- Infection prophylaxis for both PCD +Txplt

Post-Transplant

Disease-related

- Start maintenance therapy >2 wks for PCD type (MM, MGRS, AL)
- Heme Surveillance q2-3mos

Transplant-related

- Decrease MPA/Aza 50% w/PCD Tx
- Kidney labs (Scr, Upcr, BK)
- Consider protocol biopsy (PGNMID/C3G)
- Infection prophylaxis for both PCD +Txplt
- IVIG PRN

Questions for the Experts

- **Case Review**

- What is your interpretation of this patient's rapidly progressive course of kidney failure?

- **Diagnostic approach**

- What clues do you use to distinguish different forms of PCD-related kidney disease?
- How do you interpret serum free light chains in the setting of CKD/ESRD?

- **Management**

- How do you interpret the patient's current condition
- How would you manage his transplant candidacy based on disease progression, response to treatment and available literature?

- **Final Thoughts?**

Thank You!

- **Kara Cicero**, FHCC myeloma
- **Andrew Portuguese**, FHCC myeloma & immunotherapy group
- **Bilal Malik**, onconeurology
- **Aanand Patel**, renal pathology
- **Email:** Chrisbl@uw.edu



The Clone That Stole the Gift:

Transplant MGRS Case Review

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Vice President, American Society of Onconeurology (ASON)

Instructor, Harvard Medical School



Disclosures

None

(Not yet famous enough)

Patient Presentation & Case History

Case Overview: Post-Transplant Proteinuria

Patient Demographics & History

57 y.o. Male with IgA Nephropathy

Status post Kidney Transplant in 2014

Current Presentation & Comorbidities

Referred to DFCI Onconeurology Clinic for comprehensive evaluation of post-transplant proteinuria.

Maintenance Regimen

Mycophenolate Mofetil (MMF)

Tacrolimus (Tacro)

Prednisone

Clinical Progression

Post-Transplant Clinical Course

Phase 1: Stable Baseline

1.3 mg/dL

Serum Creatinine Settled

Initial urinalysis demonstrated a bland UA with completely negative protein and no red blood cells (RBC).

Phase 2: Acute Proteinuria Onset

3+ Protein

Detected on Urinalysis (No RBC)

Serum Creatinine **1.3–1.5 mg/dL**

Protein/Creatinine Ratio **2.7 g/g**

Microalbumin/Creatinine Ratio **1.8 g/g**

10 YRS POST-TX (11/01/2024)

Diagnostic Workup

Differential Diagnosis: Post-Transplant Proteinuria

Primary Glomerular Pathologies

Recurrent IgA Nephropathy (IgAN)

De Novo Membranous Nephropathy

Focal Segmental Glomerulosclerosis (FSGS)

Secondary & Systemic Etiologies

Monoclonal Gammopathy (MGRS)

Allograft Post-Transplant Lymphoproliferative Disorder

Calcineurin Inhibitor (CNI) Toxicity

Antibody-Mediated Rejection (AMR)

T-Cell Mediated Rejection (TCMR)

Transplant Glomerulopathy

Diagnostic Workup

Further Investigation:

Hematology Evaluation

Serum Protein Electrophoresis (SPEP), FREE LIGHT CHAINS (FLC) & BONE MARROW

SPEP: Initiated by Nephrologist, IgG lambda m-spike 1.3 g/dL.

Labs: M-Spike **1.5 g/dL (IgG κ)** | Kappa: 20.8 | Lambda: 41.0 | Ratio: 0.51 | IgG: 1931

Bone Marrow: 4% plasma cells, consistent with MGUS, no cytogenetic abnormalities.

PET-CT: Negative for active osseous lesions.

Risk Stratification: **Low-intermediate risk MGUS**

Autoimmune Evaluation

SEROLOGY & COMPLEMENT

Negative: ANA, ANCA, DS-DNA

Normal: C3, C4

Elevated: **SC5b-9 complex 518 (H)**

No circulating DSA

Infectious Evaluation

VIRAL SCREENING

Serum Negative: BK, EBV, CMV, Adenovirus

Other Negative: Hepatitis Panel, HIV

Clinical Decision Making

What is the next best step?

Option A: Allograft Biopsy

Renal Allograft Biopsy

Option B: Empiric Therapy

Optimize Supportive Care

Initiate RAAS blockade (ACEi/ARB) or consider **SGLT2 inhibitors** avoiding potential biopsy-related complications (Jehovah's Witness)

Clinical Decision Pathway

A Safer Detour: Fat Pad Biopsy

RATIONALE FOR INTERIM STEP

Patient-Centered Constraints: The patient's status as a **Jehovah's Witness** made minimizing bleeding risk and avoiding invasive procedures paramount.

Diagnostic Clue: Clinical presentation showed a strong **lambda predominance**, raising suspicion for light chain deposition.

The Detour: A non-invasive screening approach was selected to provide systemic evidence before risking a direct kidney intervention.

PROCEDURAL ADVANTAGES

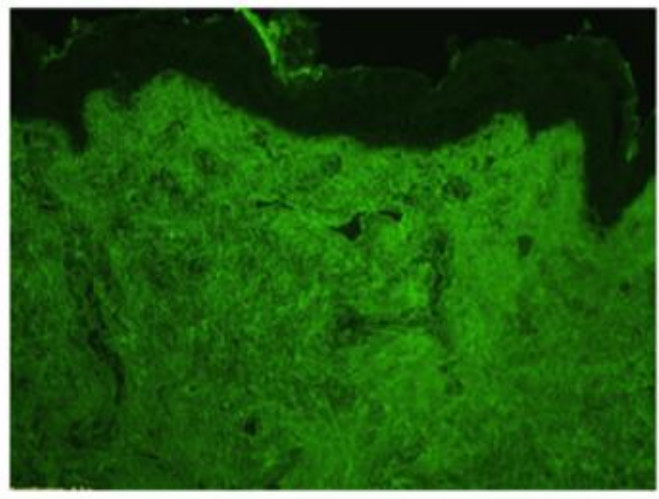
Avoids Allograft Biopsy: Bypasses the highly vascular renal transplant biopsy, eliminating major bleeding risks in a restrictive clinical context.

Minimal Risk Profile: Subcutaneous fat pad aspiration is a simple, bedside procedure with negligible complication rates.

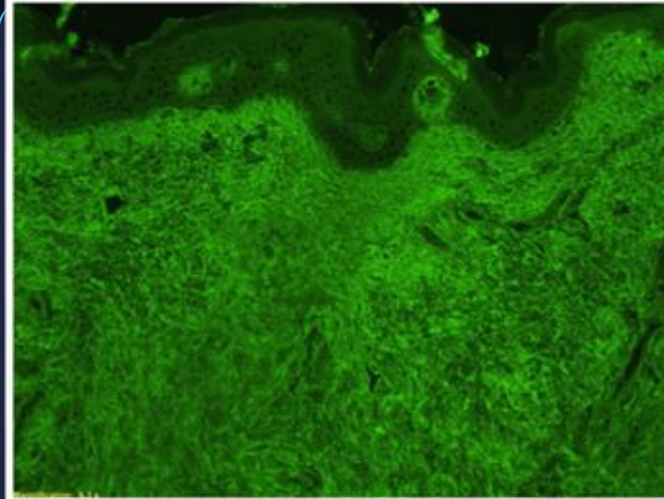
Targeted Screening: Specifically assesses for **systemic AL amyloidosis** driven by the clonal lambda free light chains.

Diagnostic Procedure

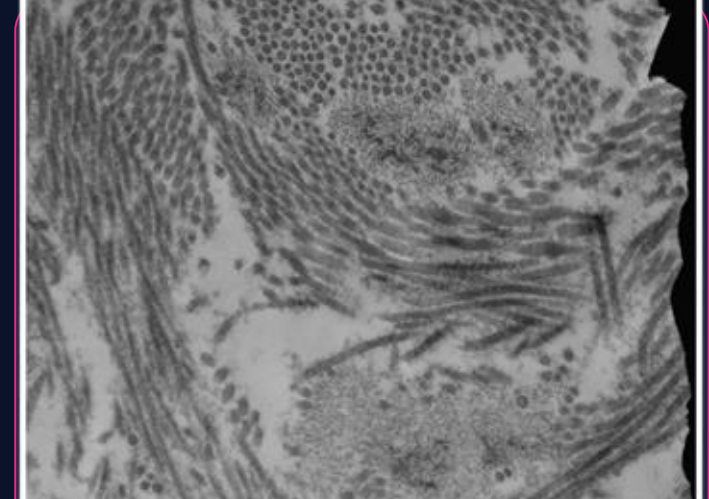
Fat Pad Biopsy



IF IgG Staining +++



IF Lambda Staining +++

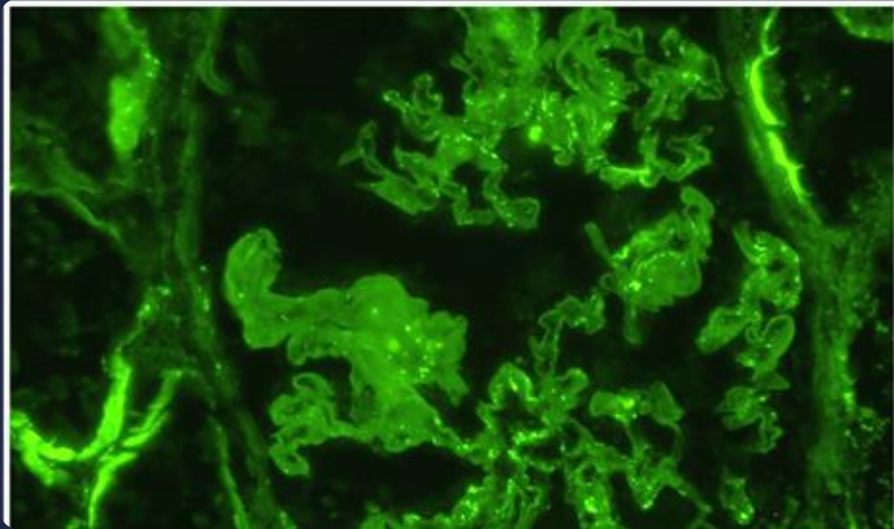


Electron Microscopy

Ill defined aggregates in papillary dermis.
Congo red negative (

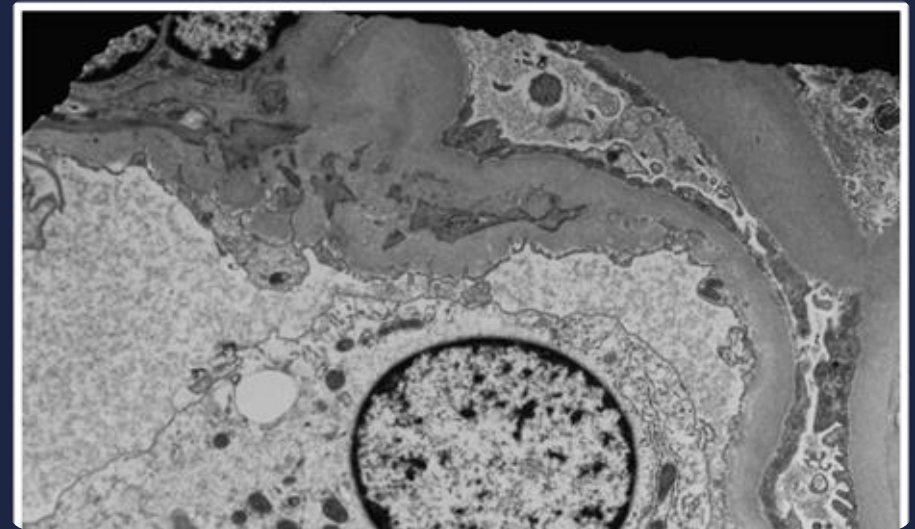
Diagnostic Procedure

Kidney Biopsy



Immunofluorescence (IF)

Intense C3 glomerular staining



Electron Microscopy (EM)

Ultrastructural analysis confirming subendothelial dense deposits in the basement membrane.

CLINICAL STUDY SUMMARY

Early C3G Recurrence After Kidney Transplantation

But this is not de novo

89%

High Recurrence Rate

C3G recurred in **16/18 patients** (89%) at a median of just **33 days** post-transplant.

Subclinical

Mild Initial Presentation

1/3 were caught in protocol screenings.

Favorable

Short-Term Outcomes

all allografts remained functioning at the end of the median 37-month follow-up

CLINICAL STUDY SUMMARY

De Novo C3G Post-Transplant

~15

Extremely Rare Cases

Unlike recurrent disease, **de novo C3G** developing after kidney transplantation is an exceptionally rare clinical phenomenon.

Only approximately **15 cases** have been documented in scientific literature globally, presenting unique diagnostic challenges.

CLINICAL SIGNIFICANCE & PATHOLOGY

Key Distinctions from Recurrent C3G

Pathological Novelty: Occurs in patients with no prior history of C3 glomerulopathy in their native kidneys, suggesting an acquired post-transplant trigger.

Immunological Triggers: Frequently associated with alternative pathway dysregulation driven by infections or MGUS/PTLD. 1 Case of de novo C3G attributed to CFH mutation with C3 Nephritic factor

Diagnostic Protocol: Requires careful differentiation from transplant glomerulopathy and MGRS via advanced immunofluorescence and electron microscopy. Requires careful hematological and complement workup.

CLINICAL COHORT ANALYSIS

Monoclonal Ig-Associated C3 Glomerulopathy

Prevalence & Age-Specific Frequency

65.1%

In Patients Aged ≥50 Years

In a cohort of 95 C3G patients, monoclonal immunoglobulins (MIg) were detected in **37.9% overall** (36/95 cases)

The prevalence increases dramatically with age.

Treatment & Kidney Outcomes

70%

Renal Response to Targeted Therapy

MIg-targeted therapy achieved a hematologic response in 62.5% of treated patients, which correlated strongly with **70% renal response rate**

Conversely, **100% of patients with no hematologic response failed** to show any kidney improvement.

Ravindran A, Fervenza FC, Smith RJH, Sethi S. C3 Glomerulopathy-associated with a Monoclonal Ig is a distinct subtype. *Kidney Int.* 2018;94(1):178-186. doi:10.1016/j.kint.2018.01.037. [cite: 3]

Subsequent Diagnostics & Interventions

Diagnostic Panel Results

- Atypical HUS/C3G Functional Panel: **Negative, C3NEF Negative**
- Atypical HUS/C3G Genetic Panel: **No pathogenic mutations** detected
- Serial PET/CT Surveillance: **No FDG uptake** observed
- M Protein & FLC Ratio: **Extremely stable** overall (no clone-directed therapy received)

Intervention & Baseline Metrics

Therapy Initiated at Initial Visit (10/4/2024):

Lisinopril + Jardiance

Clinical Parameters:

- Protein/Creatinine Ratio (Pr/Cr): **0.4 mg/mg**
- Albumin/Creatinine Ratio (UACR): **491 mg/mg**
- **UA without RBC**
- Serum Creatinine (Cr): **~1.6 s**
- eGFR: **45-50 mL/min/1.73m²**

Key Questions for the Experts

01. Case Reflections

What are your reflections on this highly unusual case of post-transplant de novo C3G?

02. Future Diagnostics

What other diagnostic studies or labs would you recommend at this juncture?

03. Pathological Discordance

What are your thoughts regarding the clinical discordance between the cutaneous heavy/light chain deposition and the biopsy-confirmed renal C3GN?

04. Intervention vs. Care

What therapeutic interventions would you recommend immediately, or would you continue with active surveillance?

05. Disease Heterogeneity

What are your final thoughts on the highly heterogeneous presentation of C3G?

ACKNOWLEDGEMENTS

Special Thanks & Collaborations

01 / PATHOLOGY

**Professor Helmut
Rennke**

02 / ONCOLOGY

Dr. Yuxin Liu
and Dana-Farber
Myeloma

03 / RESEARCH TEAM

**Heme-Renal
Focus Group**
(Chowdhury Lab)

04 / DISCUSSION

Audience Q&A