QUIZ 26-01-2026--MGRS

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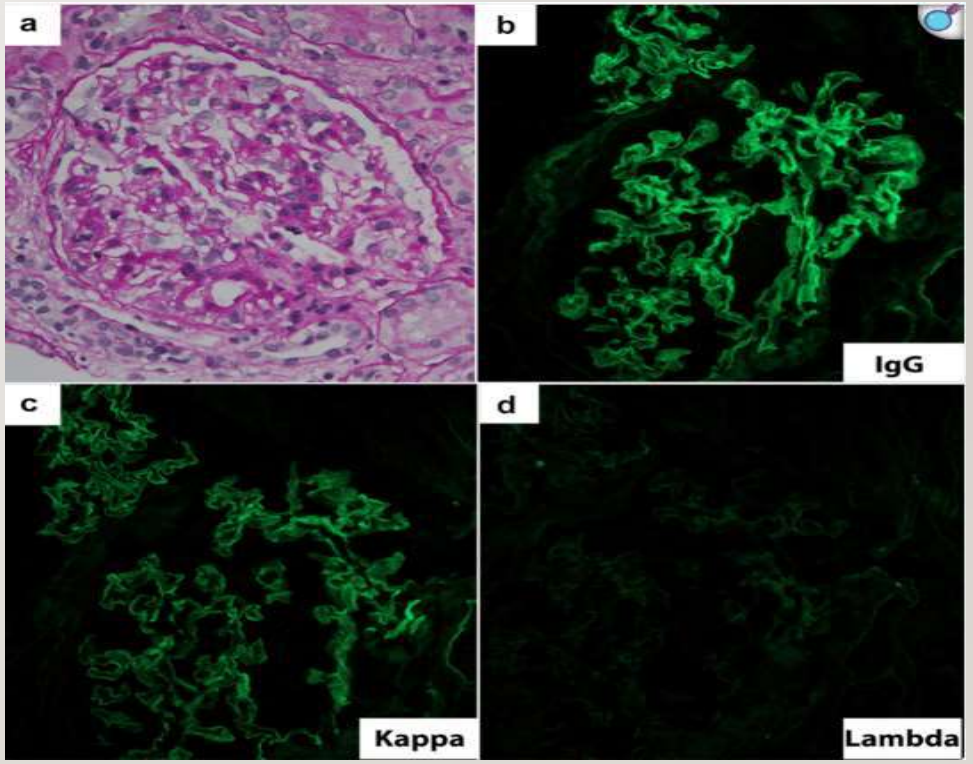
QUESTION 1

- A 55-year-old woman with long-standing rheumatoid arthritis on etanercept presents with worsening renal function and gross hematuria. Kidney biopsy shows no proliferative GN. IF pictures given below



WHICH OF THE FOLLOWING IS INCORRECT

- A. The cornerstone of therapy is clone-directed treatment
- B. Supportive care with RAAS blockade and blood-pressure control is essential but is insufficient
- C. Hematologic evaluation with serum and urine immunofixation, serum free light chains, and bone marrow examination is indicated even if no monoclonal spike is initially detected.
- D. All patients with MIDD linear IgG require urgent plasmapheresis as first-line therapy to rapidly clear deposited monoclonal IgG and prevent progression to ESRD.

ANSWER --All patients with MIDD linear igG require urgent plasmapheresis as first-line therapy to rapidly clear deposited monoclonal igg and prevent progression to ESRD.

- Some glomerulonephritides show linear anti-GBM–type IF but are not classic anti-GBM disease → termed atypical anti-GBM disease.
- These cases are usually clinically less aggressive than classic anti-GBM GN.
- Serum anti-GBM antibodies are negative by standard ELISA in most patients.Kidney biopsy typically lacks crescentic, necrotizing, or florid proliferative lesions.
- In many cases, the anti-GBM antibodies are monoclonal (light-chain restricted).

- **A.** The cornerstone of therapy is **clone-directed treatment** (e.g., bortezomib- or rituximab-based regimens), even if bone marrow shows only a small or indolent plasma/B-cell clone.
- **B.** Supportive care with RAAS blockade and blood-pressure control is essential but is **insufficient as sole therapy** in most patients with progressive renal dysfunction.
- **C.** Hematologic evaluation with serum and urine immunofixation, serum free light chains, and bone marrow examination is indicated even if no monoclonal spike is initially detected.
- **D.** All patients with MIDD/MGRS require **urgent plasmapheresis** as first-line therapy to rapidly clear deposited monoclonal IgG and prevent progression to ESRD.

LITERATURE REVIEW

Author	Monotypic	Age	Gender	Pretreatment creatinine	Immunofluorescence	Treatment	Post treatment creatinine	Outcome	
								Patient	Kidney
Troxell and Houghton[4]	Yes/1 case	68	Male	1.2 mg/dl	IgG3-lambda monotypic	PLX/IVIG/steroids/rituximab	1.0 mg/dl	Alive	Persistent kidney dysfunction
Nasr *et al.*[3]	Yes/10 cases	51	Male	1.2 mg/dl	Lin GBM IgG (3+) and lambda (3+)	Tacrolimus	1.3 mg/dl	Alive	Persistent kidney dysfunction
		77	Male	1.6 mg/dl	Lin GBM and focal TBM for IgG (3+) and lambda (3+)	Prednisone	ESRD	Expired	ESRD
		57	Male	3.5 mg/dl	Lin GBM and focal TBM IgG (2+) and lambda (2+)	None	2.8 mg/dl	Alive	Persistent kidney dysfunction
		49	Female	1.0 mg/dl	Lin GBM and focal TBM IgG (3+) and lambda (3+)	None	0.9 mg/dl	Alive	Persistent kidney dysfunction
		59	Female	1.9 mg/dl	Lin GBM IgG (3+) and lambda (3+)	Pred/CYC	2.0 mg/dl	Alive	Persistent kidney dysfunction
		19	Male	1.7 mg/dl	Lin GBM IgG (3+) and kappa (3+)	Pred/MMF/Bort/CYC/rituximab/tacrolimus	ESRD	Alive	ESRD
		61	Male	2.6 mg/dl	Lin GBM IgG (3+) and lambda (3+)	Prednisone	1.8 mg/dl	Alive	Persistent kidney dysfunction
		69	Female	0.9 mg/dl	Lin GBM IgM (3+) and kappa (1+)	Dexa/Bort	0.7 mg/dl	Alive	Persistent kidney dysfunction
		64	Male	1.1 mg/dl	Lin GBM IgM (3+) and kappa (2+)	N/A	N/A	N/A	N/A
		63	Male	2.6 mg/dl	Lin GBM IgA (2+), lambda (3+)	N/A	N/A	N/A	N/A
Olivier *et al.*[5]	yes	53	Female	2.4 mg/dl	IgG1-kappa monotypic	PLX/steroids/CYC	1.3 mg/dl	Alive	Kidney function returned to baseline
Coley *et al.*[6]	yes	53	Male	3.0 mg/dl	IgG1-kappa monotypic	IV steroids/CYC, followed by MFA	1.9 mg/dl	Alive	Persistent kidney dysfunction
Bonilla *et al.*	Yes	55	Female	1.44 mg/dl	IgG1-kappa monotypic	Pred/rituximab	1.16 mg/dl	Alive	Kidney function returned to baseline

WINNER

- Dr. Kumaresh
- Final year DNB
- GMKMCH salem

QUESTION 2

- *A 61-year-old man presents with proteinuria, microscopic hematuria, and progressive renal dysfunction.*
- **Kidney biopsy shows:**
- **Light microscopy (LM):** Membranoproliferative pattern with mesangial expansion and capillary-wall double contours
- **Routine immunofluorescence (frozen sections):** Bright C3 staining; negative IgG, IgA, IgM, kappa, lambda
- **Electron microscopy (EM):** Mesangial and subendothelial electron-dense deposits
- Serum C3 is low.
  Serum and urine immunofixation are negative for a monoclonal protein.

WHICH IS THE **MOST APPROPRIATE NEXT STEP**?

A. Treat with high-dose corticosteroids for immune-complex MPGN

B. Diagnose primary C3 glomerulonephritis and start eculizumab

C. Perform paraffin immunofluorescence after protease digestion

D. Reassure the patient; manage conservatively with RAAS blockade alone

ANSWER -- Perform paraffin immunofluorescence after protease digestion.

- A subset of cases that look like "pure" C3 GN on routine IF actually harbor **masked monoclonal immunoglobulin deposits**.
- These are invisible on frozen IF but become detectable on **paraffin IF after protease digestion**.
- Missing these deposits leads to misclassification of **MGRS-related C3 GN** as primary C3 GN.
- This step is essential before labeling the disease as primary C3 GN and committing to complement-based therapy.

- **Paraffin IF with Pronase Digestion — Technique & Rationale**
- Routine frozen IF may miss **masked immunoglobulin deposits** due to antigen conformational changes.
- Paraffin-embedded tissue is treated with **pronase (protease)** to digest cross-linked proteins and expose hidden antigenic epitopes.
- Less sensitive than immunofluorescence on frozen tissue for detecting certain antigens, particularly C3 and IgG in specific disease entities
- Requires optimization of the pronase digestion protocol to achieve reliable results
- May not be as effective in detecting IgG in membranous glomerulopathy and anti-GBM disease, with only 50% and 20% detection rates respectively compared to frozen tissue immunofluorescence

- **B. Primary C3 GN → start eculizumab**
- MGRS-related C3 GN can look identical on routine IF.
- Complement inhibition is inappropriate if the driver is monoclonal Ig.
- **C. Immune-complex MPGN → steroids**
- Immune-complex MPGN should show polyclonal Ig on IF.
- C3-only staining excludes this diagnosis.
- **D. RAAS blockade alone**
- Progressive GN with active sediment is not a conservative disease.

WINNER

- Dr Saravana Balaji
- DM nephrology resident-3rd year
- Madras Medical College