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Background

- IgAN is the most common primary glomerulonephritis worldwide¹
- IgAN is also the most common form of nephropathy associated with anticoagulant related nephropathy (ARN)²
- ARN is currently defined as AKI without an obvious etiology in the setting of INR > 3.0, SCr ≥ 0.3 mg/dL increase from baseline with or without hematuria in a patient taking an anticoagulant³
- Apixaban (Eliquis), is a direct factor Xa inhibitor and the most common DOAC prescribed in the United States and the United Kingdom⁴

Case Narrative

- A 70-year-old man with atrial fibrillation on apixaban, non-small cell lung cancer status post wedge resection, chemotherapy held due to concern for pneumonitis, and nontuberculous mycobacterial pulmonary infection, without prior kidney disease, presented for routine GI follow-up after upper endoscopy without acute symptoms. Outpatient laboratory testing demonstrated an acute rise in serum creatinine from baseline. The patient also reported incomplete bladder emptying and nocturia. Prior CT urography suggested cystitis or possible bladder outlet obstruction, prompting admission for evaluation of acute kidney injury in December 2024.

1st Admission (5 Days)

- Lab serology** demonstrated mild anemia, preserved PLT, elevated free light chain
- Coagulation studies** normal INR 1.04, PT 12.1, aPTT 34.1
- Clinical findings:** persistent gross hematuria, hypotension, bradycardia, hemoptysis (pulm. M. abscessus infection), mild lacticemia w/o shock
- Serological, autoimmune and infectious studies were **unremarkable**
- 24 UA:** proteinuria, pyuria, gross hematuria with stable leukocytes and with sterile urine culture
- Renal Ultrasound:** no hydronephrosis, no post-void retention, small non-obstructing stone
- Management:** Initial 5 mg BID apixaban routine held concomitant w/ hematuria, p/t treated with fluids to no significant effect. Patient remained stable and was discharged after 5 days.

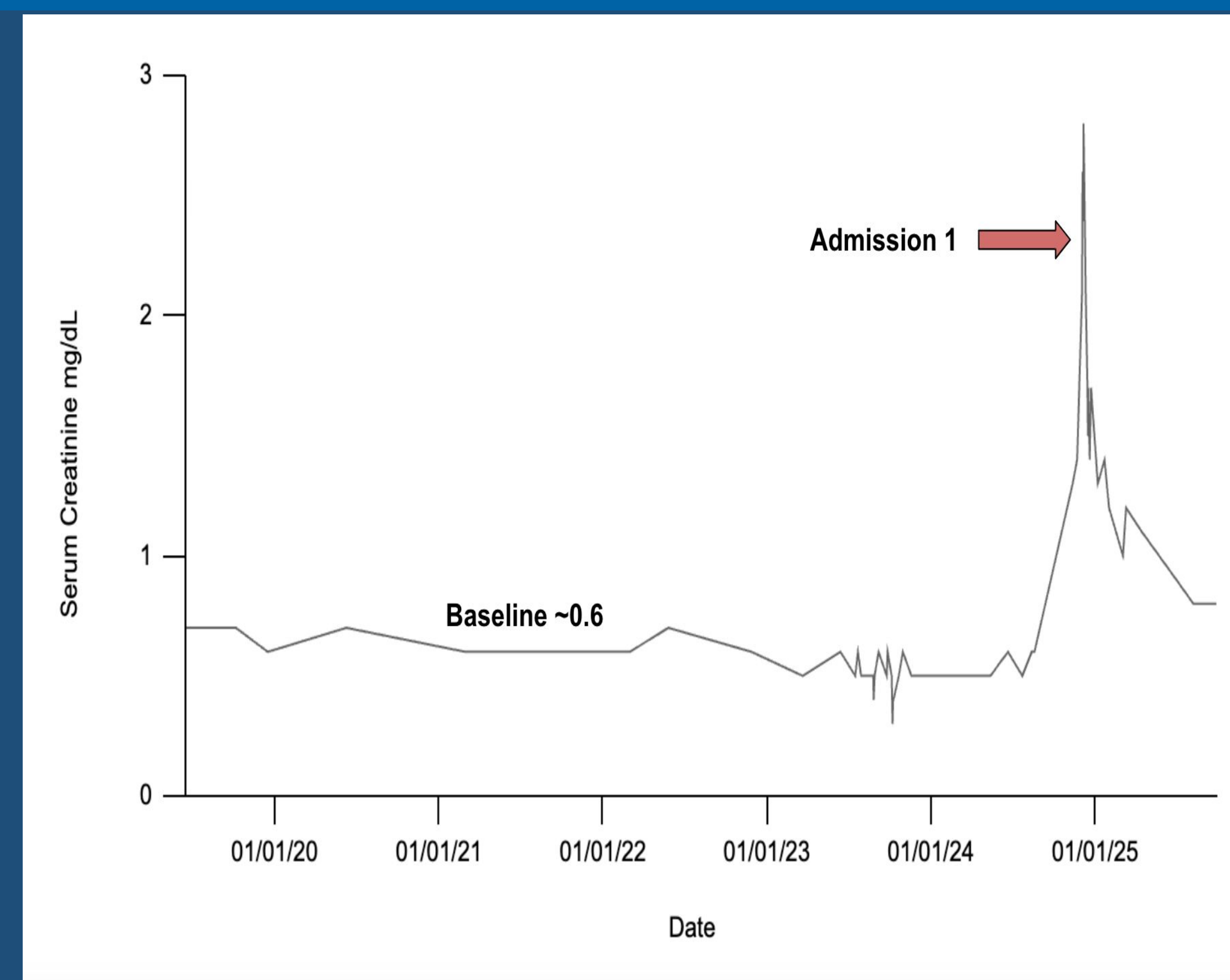
2nd Admission (5 Days)

- Within the week, new-onset HTN, persistent hematuria, and sustained elevated SCr brought patient back on suspicion of rapid progressive glomerulonephritis
- Renal biopsy** (M0 E1 S1 T0 C1) w/ unusually proportioned crescents.
 - Pattern of injury
 - focal endocapillary proliferative and focal sclerosing glomerulonephritis with single rare segmental cellular crescent (<5%)
 - focal segmental glomerular scars (~7%)
 - focal global glomerulosclerosis (~10%)
 - no IFTA
 - focally severe arteriosclerosis
 - tubular red blood cell casts
 - Immunofluorescence
 - diffuse segmental to global glomerular mesangial C3 (3+) and IgA (3+)
- Management:** s/p biopsy apixaban was held for 2 weeks and patient was started on sparsentan. Repeat UA analyzed and found microscopic hematuria.
 - Renal function improved w/ return to baseline SCr with long-term f/u

Lab Summary

Serology - Autoimmune Labs - 24hr UA – 1st Admission	
SCr	2.1 mg/dL
Kappa, free light chain	98.91 mg/L
Lambda, free light chain	73.72 mg/L
Anti-DS-DNA	negative
ANCA	Not detected
ANA	negative
Cardiolipin Antibody, IgG	negative
Cardiolipin Antibody, IgM	negative
C3, blood	126
C4, blood	33
PLA2R, immunofluorescence	negative
THSD7A, Immunofluorescence	Lab error, test not performed
Cryoglobulin Qualitative	negative
Lacticemia	2.2 mmol/L (mild excess LA)
eGFR (MDRD)	33 (mL/min/1.73 m ²)
PLT	338 xe9/L
HGB	11 g/dL
	1.04 (no DOAC expect 0.8 - 1.1) ** hx elevated INR 2x ~ 1 yr prior to admit
INR	

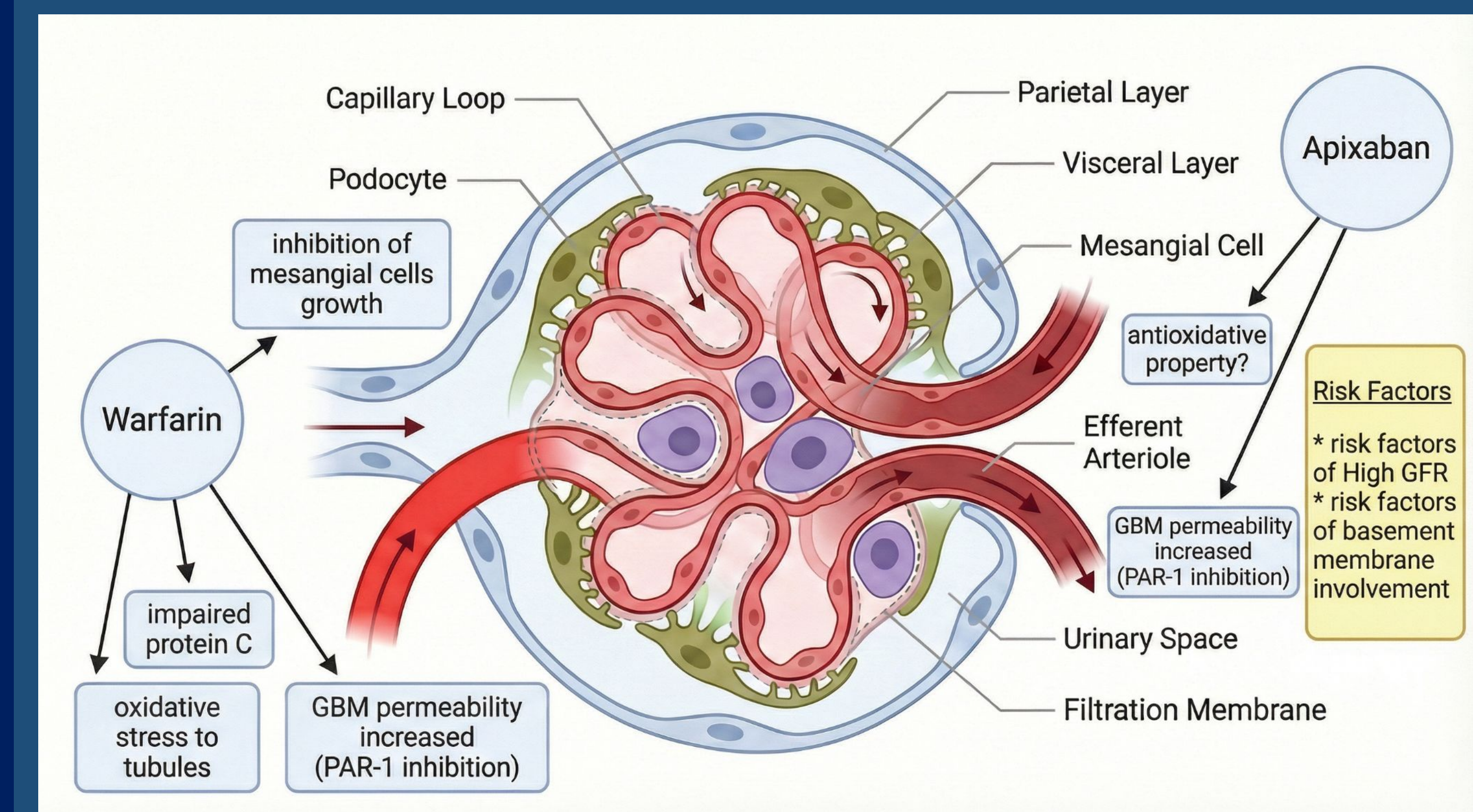
Serum Creatinine Over Time



Lab Summary cont.

Serology - 24hr UA – 2nd Admission	
SCr	1.7 mg/dL
BUN	39 mg/L
eGFR (MDRD)	43 mg/L
PLT	365 billion/L
HGB	10.1 g/dL
Urine Cr	48.2 mg/dL
Urine Protein	54 mg/dL
Microalb	149 mg/L

Mechanism and Epidemiology



Mechanism of ARN

- excessive glomerular proliferation
- glomerular hypertension causing hematuria
- heme molecules that result in oxidative stress and activation of inflammatory cascade in the tubules*

Epidemiology

- Little to no epidemiological data is available for ARN
- A 2023 systematic review⁵ of DOACs causing ARN identified only 20 total events across all DOACs with only 1 by apixaban. Since then, 2 case reports have been published showed apixaban worsening preexisting CKD or AKI with glomerulopathies other than IgAN.

Conclusions

- With consideration for ANCA serology and unique proportion of tubular red blood cell casts to rare cellular crescents, although these findings are plausible in IgAN alone, they resemble those findings in cases of ARN.
- Safety data from patients randomized to **apixaban** in ARISTOTLE⁶ trial showed worsening GFR of >20% in 16,869 patients (2,3) (with exclusionary criteria of serum creatinine clearance 25 mL/min). More data is needed to qualify CKD as the foremost risk factor for ARN.
- To the best of our knowledge, this is the 3rd known case of apixaban ARN and the 1st case with apixaban at the genesis new AKI without previous renal injury later identified as IgAN.

Acknowledgements

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