BIOPSY-PROVEN IgA NEPHROPATHY PRESENTING WITH PERSISTENT PROTEINURIA AND MICROSCOPIC HEMATURIA FOLLOWING A FEBRILE ILLNESS IN A YOUNG ADULT MALE

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INTRODUCTION

IgA nephropathy (Berger disease) is the most common primary glomerular disease worldwide and an important cause of chronic kidney disease in young adults.

It is characterized by mesangial deposition of IgA-containing immune complexes, causing glomerular inflammation and progressive renal injury. Presentation ranges from isolated microscopic hematuria to nephrotic-range proteinuria and renal dysfunction.

The Oxford Classification (MEST-C score) is an important histopathological tool for predicting prognosis and guiding management.

CASE PRESENTATION

A 28-year-old previously healthy man was evaluated after developing acute kidney injury during a febrile illness about six weeks earlier. Serum creatinine at presentation was 2.64 mg/dL.

At nephrology follow-up, fever had completely resolved. He denied facial puffiness, edema, dyspnea, gross hematuria, oliguria, rash, arthralgia or constitutional symptoms, and took no regular medications.

Repeat testing showed improving renal function (creatinine 1.64 mg/dL), but significant proteinuria (UPCR 3.9 g/g, later 3.0 g/g) and persistent microscopic hematuria remained.

The differential diagnosis included post-infectious glomerulonephritis and IgA nephropathy. Because of persistent proteinuria and hematuria despite renal recovery, a native kidney biopsy was performed.

LABORATORY INVESTIGATIONS

TABLE 1. LABORATORY FINDINGS

Parameter	*Result*
Serum creatinine	2.64 → 1.64 mg/dL
UPCR	3.9 → 3.0 g/g
Urine microalbumin	853.6 mg/L
Albumin/creatinine ratio	1012.6 mg/g
Urine protein / blood	++ / ++
Urine RBC (per HPF)	5–10
Urine WBC (per HPF)	0–5
WBC count	10.86 × 10^9/L
Hemoglobin	14.3 g/dL
PT / INR	9.9 s / 0.9

WORK-UP FOR SECONDARY CAUSES

TABLE 2. SECONDARY CAUSES WORK-UP

Test	*Result*
Hepatitis B / Hepatitis C	Negative
HIV	Negative
ANA	Positive (1:80)
c-ANCA / p-ANCA	Negative
Anti-PLA2R antibody	Negative
Anti-streptolysin O	Negative

Renal ultrasonography: bilateral increased renal cortical echogenicity, consistent with medical renal disease.

RENAL BIOPSY FINDINGS

18 glomeruli sampled; 4 (22%) globally sclerosed.

Light microscopy

- Mesangial hypercellularity in >50% of glomeruli with mesangial matrix expansion
- Segmental glomerulosclerosis in five glomeruli
- Podocyte hyperplasia with adhesion of tuft to Bowman's capsule
- No endocapillary hypercellularity, crescents, or GBM duplication/spikes

Tubulointerstitium and vessels

- Moderate chronic lymphocytic interstitial inflammation
- Interstitial fibrosis and tubular atrophy: ~30–35% of cortex
- Mild arteriosclerosis and arteriolar hyalinosis

Immunofluorescence

- Moderate granular mesangial IgA; mild mesangial C3
- Moderate mesangial kappa and lambda
- IgG, IgM and C1q negative

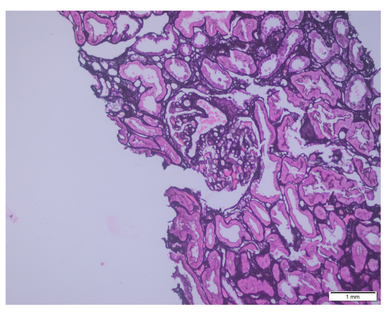


Fig 1: Kidney biopsy, Jones methenamine silver (JMS) stain (scale bar = 1 mm).

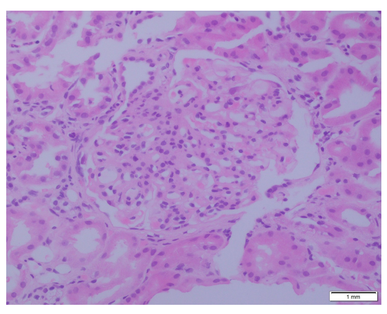


Fig 2: Kidney biopsy, hematoxylin and eosin (H&E) stain (scale bar = 1 mm).

DIAGNOSIS

Primary IgA nephropathy (Berger disease)

TABLE 3. OXFORD CLASSIFICATION: M1 E0 S1 T1 C0

Score	*Finding*
M1	Mesangial hypercellularity
E0	No endocapillary hypercellularity
S1	Segmental glomerulosclerosis
T1	Moderate IF/TA (30–35%)
C0	No crescents

MANAGEMENT

After histological confirmation the patient was started on:

- Prednisolone 60 mg once daily
- Empagliflozin 10 mg once daily
- Losartan 25 mg once daily (dose escalation planned)
- Omeprazole 20 mg once daily
- Calcium and vitamin D (bone protection)
- Co-trimoxazole three times weekly (PJP prophylaxis)

Advice: sodium restriction, avoidance of nephrotoxins, and close nephrology follow-up (renal function, proteinuria, electrolytes, BP, glucose, steroid adverse effects).

FOLLOW-UP AND OUTCOME

Renal function remained stable, with creatinine improving from 2.64 to 1.64 mg/dL. Albuminuria was tracked serially.

Fig 3: Serum creatinine (mg/dL)

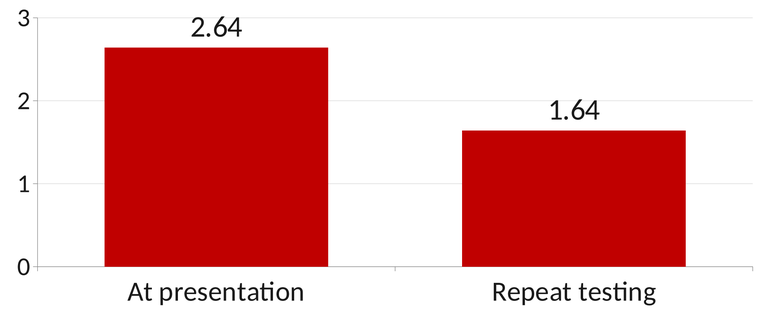
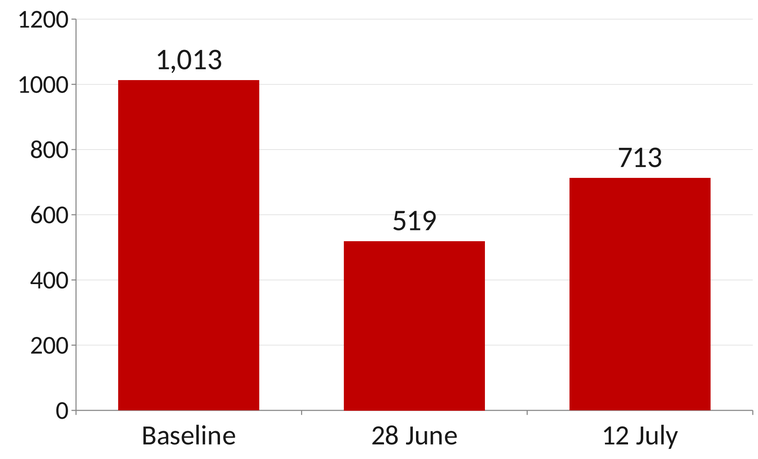


TABLE 4. ALBUMINURIA DURING FOLLOW-UP

Date	*Microalbumin (mg/L)*	*ACR (mg/g)*
Baseline	853.6	1012.6
28 June	532.4	518.9
12 July	824.4	712.6

Fig 4: Albumin-to-creatinine ratio (mg/g)



ACR fell ~49% from baseline within two weeks, then partially rose by 12 July, though still below baseline. Prednisolone and supportive therapy continue with close follow-up.

DISCUSSION

IgA nephropathy is the most common primary glomerulonephritis with a worldwide incidence of 2.5 per 100,000. Its pathophysiology is described as a 4 hit model, starting with excessive production of galactose deficient IgA1 primarily in gut mucosa influenced by genetics and cytokines including B cell activation factor (BAFF) and a proliferation induced ligand (APRIL). Second hit involves production of autoantibodies galactose deficient IgA1 followed by immune complex formation (hit 3) and lastly deposition of immune complexes in the glomerulus. Complement activation plays a prominent role in mesangial injury and glomerular inflammation.

Oxford classification of IgA nephropathy includes 4 variables that correlate most strongly with patient outcomes. The introduction of IgA nephropathy risk prediction tool further refines risk stratification by integrating histological findings and clinical factors to predict renal outcomes at the time of biopsy and up to 7 years.

The treatment of IgAN targets reduction of proteinuria with RAAS blockade, SGLT2i and dual endothelin and angiotensin receptor antagonist, sparsentan. Immunosuppressive therapy includes systemic steroids and targeted release formulation (TRF) budesonide. Mycophenolate mofetil has shown promising results as steroid sparing agent. Future treatment options include complement inhibitors, anti B cell therapies and anti plasma cell therapies.

CONCLUSION

Biopsy established primary IgA nephropathy in a young man with persistent proteinuria and hematuria after a febrile illness, excluded alternative causes, and gave prognostic information (Oxford M1E0S1T1C0).

Early biopsy, histological risk stratification and close follow-up guide management and long-term renal outcome.

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