

Abrupt Onset of Crescentic IgA Nephropathy Superimposed on Glycogen Storage Disease Type Ia: A 15-Year Longitudinal Pediatric Case Report

Xu Zhang

Huazhong University of Science & Technology

Fengjie Yang

Huazhong University of Science & Technology

Yaping Liu

Huazhong University of Science & Technology

Yu Zhang

Huazhong University of Science & Technology

Jianhua Zhou

jhzhou99@qq.com

Huazhong University of Science & Technology

Case Report

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Abstract

Background

Renal involvement is a primary determinant of long-term morbidity in glycogen storage disease type Ia (GSD-Ia). It classically presents as non-immune-mediated metabolic nephropathy that slowly advances from asymptomatic glomerular hyperfiltration to focal segmental glomerulosclerosis. The concurrence of an immune-complex glomerulopathy is exceptionally rare. We report the first pediatric case of GSD-Ia complicated by biopsy-proven crescentic IgA nephropathy followed longitudinally over 15 years, shedding light on the diagnostic vigilance and therapeutic adaptations required for superimposed glomerulonephritis.

Case presentation:

A 15-year-old male with genetically confirmed GSD-Ia had a history of early glomerular hyperfiltration, recurrent nephrolithiasis, and low-grade proteinuria since age 4, remaining clinically stable for over six years on dietary management and angiotensin-converting enzyme inhibitors. At 11 years of age, despite well-controlled metabolic parameters, he abruptly developed nephrotic-range proteinuria (urinary protein-to-creatinine ratio: 7207.5 mg/g Cr; 24-hour urine protein: 4483.8 mg) and hematuria. Given this sharp deviation from typical metabolic nephropathy, a percutaneous renal biopsy was performed. Histopathology revealed chronic tubulointerstitial injury superimposed with crescentic IgA nephropathy featuring cellular and fibrocellular crescents in 7 of 25 glomeruli, strong mesangial IgA deposition, and confluent electron-dense deposits. Induction therapy with oral glucocorticoids and mycophenolate mofetil markedly reduced proteinuria. Due to residual proteinuria, treatment was transitioned to low-dose glucocorticoids combined with tacrolimus, which successfully achieved clinical remission. All immunosuppressants were discontinued by early 2026. At the 15-year follow-up, the patient maintained durable clinical remission with preserved renal function (serum creatinine: 31 μ mol/L; urinary protein-to-creatinine ratio: 1051.3 mg/g Cr).

Conclusions

In patients with GSD-Ia, an abrupt onset of nephrotic-range proteinuria strongly warrants suspicion of superimposed glomerulonephritis rather than intrinsic metabolic nephropathy alone. Prompt renal biopsy is essential to establish an accurate diagnosis. Combining tight metabolic control with targeted calcineurin inhibitor-based immunosuppressive therapy represents an effective dual-track strategy to induce remission and preserve long-term renal function in this complex scenario.

Introduction

Glycogen storage disease type I (GSD-I) is an inborn error of carbohydrate metabolism that is primarily classified into two subtypes: GSD-Ia, caused by mutations in the catalytic subunit gene of glucose-6-phosphatase (*G6PC*), and GSD-Ib, resulting from mutations in the microsomal glucose-6-phosphate translocase gene (*SLC37A4*)[1]. As an autosomal recessive disorder, GSD-Ia is associated with more than 100 documented *G6PC* pathogenic variants, among which c.648G>T (p.L216L) and c.248G>A (p.R83H) predominate in Asian populations[2]. These genetic defects lead to a profound catalytic deficiency of endoplasmic reticulum-anchored glucose-6-phosphatase- α (G6Pase- α) across gluconeogenic organs: primarily the liver, kidneys, and intestinal mucosa. Consequently, patients present with hepatomegaly, fasting hypoglycemia, hyperlactatemia, hyperlipidemia, hyperuricemia, growth failure, and progressive renal impairment[3]. Although modern dietary regimens utilizing uncooked cornstarch (UCCS) combined with nocturnal continuous feeding have substantially mitigated life-threatening hypoglycemia, progressive nephropathy has emerged as a major cause of long-term morbidity and mortality with advancing age[4-7].

Renal involvement in GSD-I was first described by Stein and Zollinger in 1967, yet it was not until the 1990s that chronic kidney disease (CKD) was recognized as a consistent and formidable long-term complication[8, 9]. Renal manifestations in GSD-I encompass persistent proteinuria, proximal and distal renal tubular acidosis, nephrocalcinosis/nephrolithiasis, and ultimately renal failure[1]. The classic trajectory of GSD-Ia-associated glomerulopathy progresses through four distinct stages: (1) asymptomatic glomerular hyperfiltration in early childhood; (2) persistent microalbuminuria (typically emerging during adolescence or young adulthood, though occasionally in infants with suboptimal metabolic control); (3) progression to overt proteinuria; and (4) irreversible decline in glomerular filtration rate (GFR), leading to end-stage renal disease (ESRD)[4, 10, 11].

To date, histopathological data from available renal biopsy reports in GSD-I demonstrate consistent features: light microscopy reveals glomerulomegaly, irregular thickening of the glomerular basement membrane, tubular atrophy, cystic dilatation, and vacuolar degeneration with glycogen and lipid accumulation in tubular epithelial cells and the interstitium, accompanied by interstitial fibrosis. Immunofluorescence typically demonstrates non-specific entrapment of IgM and C3 within sclerotic areas, while electron microscopy exhibits pronounced mesangial matrix expansion. Among biopsied cases, focal segmental glomerulosclerosis (FSGS) accounts for approximately 44% (8/18 cases), with occasional reports of tubulointerstitial nephritis[9, 12-18].

Herein, we report an exceptional pediatric case of GSD-Ia complicated by IgA nephropathy (IgAN). The longitudinal clinical course encapsulates the full spectrum of renal progression from early metabolic disturbance, hyperfiltration, and microalbuminuria to an unexpected, abrupt acceleration into nephrotic-range proteinuria. Renal biopsy confirmed chronic tubulointerstitial nephropathy superimposed with crescentic IgAN. This case sheds new light on the clinical phenotypic overlap, diagnostic challenges, and therapeutic management of GSD-Ia with concurrent glomerulonephritis.

Case Presentation

1. Patient Demographics and Initial Presentation (Age 6 Months to 4 Years)

A 15-year-old male, the second child of non-consanguineous parents born at term via Cesarean delivery, presented with developmental delay and mild cognitive impairment with poor academic performance. There was no family history of inherited metabolic disorders, renal diseases, or premature cardiovascular diseases. At 6 months of age, he was brought to our medical center due to irritability and progressive abdominal distension lasting 10 days. Laboratory workup revealed marked fasting hypoglycemia (1.9 mmol/L), hyperlactatemia (12.07 mmol/L), hyperuricemia (623.3 μ mol/L), and elevated transaminases (ALT 211 U/L, AST 294 U/L). A percutaneous liver biopsy demonstrated diffuse hepatocellular ballooning, vacuolar degeneration, and strong Periodic-acid-Schiff (PAS) positivity. Transmission electron microscopy revealed a classic "honeycomb" appearance with severe steatosis and abundant intracytoplasmic lipid droplet accumulation. Genetic testing identified compound heterozygous variants in the *G6PC* gene: a maternal missense variant, c.241G>A (p.G81R), and a paternal canonical splice-site variant, c.648G>T (p.L216L), confirming the diagnosis of GSD-Ia. Dietary therapy with UCCS was instituted; however, due to suboptimal dietary compliance, hepatomegaly persisted, and metabolic control remained erratic.

2. Early Clinical Course and GSD-Related Nephropathy (Age 4 to 10 Years)

Beginning at age 4, routine urinalysis intermittently detected persistent mild proteinuria and microscopic hematuria. Abdominal ultrasonography demonstrated marked hepatomegaly (6.5 cm below the right costal margin along the midclavicular line; maximum oblique diameter of the right lobe:11.3cm). Renal ultrasound revealed enlarged kidneys with heightened parenchymal echogenicity (left kidney: 9.3x4.8 cm; right kidney: 9.6x4.4 cm), accompanied by mild separation of the right pelvicalyceal system (anteroposterior diameter: 0.9 cm) and multiple nephrolithiasis (largest:1.1x0.7cm). Presuming early GSD-associated hyperfiltration-mediated metabolic nephropathy, treatment with an angiotensin-converting enzyme inhibitor (ACEI) was initiated alongside hypouricemic and lipid-lowering agents and intensified dietary management. During the subsequent 6 years of outpatient follow-up, proteinuria fluctuated between 1+ and 2+, with a urinary protein-to-creatinine ratio (UPCR) consistently below 500 mg/g Cr, and fasting blood glucose levels stabilized between 3.38 and 4.17 mmol/L.

3. Acute Deterioration, Diagnostic Evaluation, and Renal Biopsy (Age 11 Years)

At 11 years of age, the patient experienced an unexpected and acute disease acceleration characterized by the onset of nephrotic-range proteinuria (UPCR: 7207.5 mg/g Cr; 24-hour urinary protein: 4483.8 mg/24h) and persistent hematuria (occult blood 2+) (Figure 1). Creatinine clearance reached 167 mL/min/1.73m², consistent with sustained glomerular hyperfiltration. Renal ultrasonography showed a left kidney of 8.8x4.5 cm and a right kidney of 9.3x4.2 cm with mildly increased parenchymal echogenicity, non-dilated collecting systems, multiple right renal cysts (largest: 1.1x1.0cm), and recurrent microlithiasis (largest: 0.6x0.5cm) (Figure 2). Notably, GSD-related metabolic parameters remained clinically stable compared to baseline (fasting blood glucose: 4.39 mmol/L; serum lactate: 2.1

mmol/L; serum uric acid: 339 μ mol/L; triglycerides: 3.75 mmol/L; serum creatinine: 25 μ mol/L). (Table 1: Key laboratory parameters of renal function and metabolism at biopsy)

- **Table 1 about here.**

Given the abrupt manifestation of nephrotic-range proteinuria, which deviated significantly from the typical indolent trajectory of metabolic nephropathy in GSD-Ia, an ultrasound-guided percutaneous renal biopsy was performed. Light microscopy of 25 retrieved glomeruli revealed global glomerulosclerosis in 1 glomerulus, fibrocellular crescents in 7 glomeruli (2 of which exhibited segmental sclerosis), and periglomerular fibrosis in 14 glomeruli. Glomerulomegaly, focal capillary lumen collapse, patchy endothelial cell proliferation, and mild-to-moderate segmental mesangial cell proliferation were also present. Tubulointerstitial assessment revealed focal tubular atrophy and necrosis accompanied by patchy interstitial fibrosis and infiltration of mononuclear and foam cells. Immunofluorescence microscopy demonstrated prominent, chunky mesangial deposits of IgA (4+) and IgM (1+), while IgG, C3, and C1q were negative; light chain staining showed strong lambda predilection (3+). Electron microscopy demonstrated mesangial cell proliferation, expanded matrix, and dense, confluent, paramesangial electron-dense deposits. The histopathological findings confirmed chronic tubulointerstitial nephropathy superimposed with crescentic IgA nephropathy (Oxford MEST-C classification: M0 E0 S1 T1 C2; WHO classification: grade IV) (Figure 3).

4. Immunosuppressive Management, Remission, and Long-Term Outcome (Age 11 to 15 Years)

Following histological confirmation, induction therapy was promptly initiated with oral prednisone combined with mycophenolate mofetil (MMF). After 6 months, the UPCR declined to 2574.6 mg/g Cr, and prednisone was successfully tapered and discontinued. However, following 1 year of MMF maintenance, the UPCR plateaued at approximately 1500 mg/g Cr without significant further improvement. The regimen was subsequently adjusted to low-dose oral glucocorticoids combined with tacrolimus (TAC); 1 mg twice daily, targeting a trough concentration of 4–6 ng/mL). Approximately 4 months later, the UPCR declined substantially to 363.2 mg/g Cr. Over the subsequent 1-year period of step-down weaning, the UPCR was generally maintained between 400–1000 mg/g Cr, transiently peaking at 1348.3 mg/g Cr during acute episodes of pancreatitis and enteritis. All immunosuppressive therapies were completely withdrawn by early 2026. (Figure 1,4).

At the latest follow-up in July 2026 (age 15 years), the patient demonstrated sustained clinical remission with stable renal function: serum creatinine remained at 31 μ mol/L and UPCR was stable at 1051.3 mg/g Cr (Figure 1,4). Follow-up ultrasonography demonstrated left and right kidney dimensions of 11.1x5.3 cm and 11.2x5.3 cm, respectively, with mild cortical hyper-echogenicity and stable right nephrolithiasis (largest: 1.7x1.0 cm) (Figure 2). Under continuous UCCS therapy, allopurinol, and lipid-lowering agents, metabolic parameters remained controlled: fasting blood glucose 4.4–4.9 mmol/L, serum uric acid 469 μ mol/L, total cholesterol 7.79 mmol/L, and triglycerides 8.46 mmol/L. Hepatic ultrasound revealed persistent hepatomegaly (3.7 cm below the costal margin; maximum oblique diameter: 13.4 cm) with

heterogeneous echotexture and a 0.6x0.4 cm gallbladder polypoid lesion, without hepatic adenomas or biliary tract dilatation (Figure 2).

Discussion and Conclusions

To our knowledge, this report represents the first documented pediatric case of GSD-Ia complicated by biopsy-proven crescentic IgAN, supported by a comprehensive 15-year longitudinal follow-up that delineates the entire trajectory of renal involvement.

In GSD-Ia, the loss of catalytic activity of G6Pase- α , predominantly expressed in proximal tubular epithelial cells, triggers intracellular glycogen accumulation, cellular energetic exhaustion, and tubular dysfunction. The pathophysiology of GSD-Ia-related nephropathy exhibits remarkable hemodynamic similarities to early diabetic kidney disease [8, 10, 19]. Impairment of tubuloglomerular feedback (TGF) combined with cellular metabolic perturbation induces early glomerular hyperfiltration and elevated capillary intraglomerular hydraulic pressure [10, 19]. This mechanical shear stress, compounded by local activation of the renin-angiotensin-aldosterone system (RAAS), stimulates transforming growth factor-beta (TGF- β) upregulation, culminating in progressive mesangial matrix deposition [5, 19]. Structurally, pure GSD-Ia nephropathy is an entirely non-immune-mediated metabolic disorder [8, 10]. Histopathologically, it initially manifests as glomerulomegaly, inexorably advancing to FSGS, global sclerosis, tubular atrophy, and interstitial fibrosis, accompanied by extensive neutral lipid accumulation in tubular cells and the interstitium. Immunofluorescence in isolated GSD-Ia nephropathy demonstrates only non-specific, focal trapping of IgM and C3 within sclerotic scars, devoid of true immune-complex deposition [8, 20].

Natural history cohorts indicate that glomerular hyperfiltration can serve as the sole initial renal manifestation in young GSD-I patients, with creatinine clearance reaching up to 248 mL/min/1.73m² [12, 21]. In the European GSD-I cohort, microalbuminuria and/or overt proteinuria developed in virtually all patients older than 25 years, with median onset ages of 13 and 16 years, respectively [10]. Elevated serum lactate, triglycerides, and uric acid correlate strongly with premature microalbuminuria, underscoring that strict metabolic control retards renal progression [11, 22]. In our patient, glomerular hyperfiltration was present at baseline, followed by the appearance of persistent microalbuminuria at age 4. Under dietary and antiproteinuric support, microalbuminuria remained stable for over six years, aligning precisely with the classic indolent course of GSD-Ia. However, the abrupt explosion of nephrotic-range proteinuria (UPCR: 7207.5 mg/g Cr) at age 11, occurring in the absence of acute metabolic decompensation—deviated drastically from this expected paradigm, prompting a renal biopsy that unveiled crescentic IgAN.

Histopathologically, beyond the characteristic GSD-Ia-related tubulointerstitial and metabolic lesions, the diagnosis of superimposed IgAN in our patient was unequivocally established by the presence of prominent cellular/fibrocellular crescents, fuchsinophilic mesangial deposits on Masson trichrome staining, intense mesangial IgA deposition on immunofluorescence, and dense electron-dense deposits

confirmed via transmission electron microscopy (TEM). To date, an extensive literature review identified only a single reported case of a 25-year-old adult GSD patient exhibiting mesangial IgA positivity on immunofluorescence[17]. However, that previous case lacked ultrastructural verification by TEM, leaving the precise nature of the IgA deposition unconfirmed. Consequently, our case represents the first pediatric report of GSD-Ia with biopsy-proven IgAN corroborated by comprehensive light microscopy, immunofluorescence, and ultrastructural electron microscopy, thereby providing the most definitive morphological evidence of this overlap to date.

This unusual presentation raises a fundamental pathophysiological question: does this represent an incidental coincidence, or is there an underlying mechanistic synergy? Given that GSD-Ia is an ultra-rare monogenic inborn error of metabolism, whereas IgAN is the most prevalent primary glomerulonephritis worldwide (particularly in Asian pediatric populations)[23, 24], the coexistence of these distinct entities may well be an incidental overlap. Nonetheless, GSD-Ia-associated metabolic pathology may generate a permissive microenvironment for secondary IgA mesangial deposition. The liver serves as the principal scavenger of polymeric IgA and circulating IgA-containing immune complexes via the asialoglycoprotein receptor (ASGPR) and the reticuloendothelial Kupffer system; chronic severe steatosis, glycogen overloading, and architectural hepatic distortion in GSD-Ia may significantly compromise this physiological clearance kinetics, precipitating the systemic accumulation and subsequent mesangial entrapment of IgA complexes[25, 26]. Furthermore, G6Pase- α is physiologically expressed in intestinal enterocytes, and local metabolic failure may disrupt mucosal barrier integrity, permitting aberrant exposure to luminal antigens, hyperactivating mucosal immunity, and augmenting galactose-deficient IgA synthesis. Remarkably, our patient's renal tissue exhibited strong IgA positivity with negative IgA1 staining, reinforcing the hypothesis of an atypical secondary variant likely exacerbated by impaired hepatic catabolism[25, 26].

Following the histological confirmation of IgAN, oral glucocorticoid therapy combined with MMF was promptly initiated alongside pre-existing ACEI and metabolic supportive care [27]. After two years of MMF maintenance, the patient still exhibited low-grade residual proteinuria. Considering that tacrolimus has increasingly emerged as an effective therapeutic agent for refractory nephrotic syndrome[28-30], and recent evidence has demonstrated its capacity to rapidly and efficiently induce proteinuria remission in refractory IgAN [31, 32], the therapeutic regimen was switched to low-dose oral glucocorticoid combined with tacrolimus. This adjusted regimen enabled the successful, complete withdrawal of both corticosteroids and tacrolimus by early 2026, achieving durable clinical remission. Mechanistically, MMF is a potent, lymphocyte-selective immunosuppressive agent that suppresses B-cell antibody production more effectively than conventional immunosuppressants[33]. Tang et al. demonstrated that MMF therapy yields transient and partial proteinuria remission in the short term while conferring long-term renoprotection in Chinese patients with IgAN [27]. MMF functions through the selective, non-competitive inhibition of inosine monophosphate dehydrogenase (IMPDH), depleting intracellular dGTP pools required for DNA synthesis and thereby arresting lymphocyte proliferation[33]. However, patients with GSD-Ia inherently suffer from altered purine degradation and accelerated nucleotide turnover; furthermore, MMF lacks a direct cytoprotective effect on glomerular podocytes.

In contrast, tacrolimus, a potent calcineurin inhibitor (CNI), not only suppresses T-cell gene transcription and dampens the immune cascade to reduce proteinuria, but also exerts well-documented, non-immunological podocyte-protective effects. Animal studies have established that the calcineurin inhibitor cyclosporine stabilizes the podocyte actin cytoskeleton, thereby facilitating proteinuria reduction[34]. Similarly, Zhang et al. demonstrated that tacrolimus directly preserves the podocyte cytoskeleton via calcineurin pathway inhibition[32]. In refractory IgAN, intraglomerular calcineurin expression is characteristically upregulated, whereas synaptopodin (a crucial actin-associated protein) is downregulated and displays segmental loss; this vulnerability is compounded in GSD-Ia, where intrinsic metabolic derangements severely impair podocyte viability. Therefore, the unique capacity of tacrolimus to stabilize the podocyte cytoskeleton by preventing synaptopodin degradation represents a vital non-immune mechanism that pure antiproliferative agents like MMF lack, providing a compelling pharmacological explanation for its superiority in eliminating residual proteinuria in this patient.

In conclusion, this 15-year longitudinal study provides the first comprehensive clinicopathological characterization of GSD-Ia complicated by IgAN. Clinicians should maintain a high index of suspicion for superimposed glomerulonephritis in GSD-Ia patients who develop atypical nephrotic-range proteinuria. Early histological verification via renal biopsy and the timely implementation of a dual-track strategy, combining strict metabolic regulation with targeted calcineurin inhibitor-based immunosuppression, are crucial for salvaging long-term renal outcomes in such complex clinical scenarios.

Abbreviations

GSD-I	Glycogen storage disease type I
G6PC	Gene of glucose-6-phosphatase
G6Pase- α	Glucose-6-phosphatase- α
CKD	Chronic kidney disease
GFR	Glomerular filtration rate
ESKD	End-stage renal disease
FSGS	Focal segmental glomerulosclerosis
IgAN	IgA nephropathy
PAS	Periodic-acid-Schiff
ACEI	Angiotensin-converting enzyme inhibitor
UPCR	Urinary protein-to-creatinine ratio
MMF	Mycophenolate mofetil
TAC	Tacrolimus
TGF	Tubuloglomerular feedback
RAAS	Renin-angiotensin-aldosterone system
TGF- β	Transforming growth factor-beta
TEM	Transmission electron microscopy
ASGPR	Asialoglycoprotein receptor
IMPDH	Inosine monophosphate dehydrogenase
CNI	Calcineurin inhibitor

Declarations

Ethics approval and consent to participate

This paper followed the Helsinki Declaration. The study was approved by the Medical Ethics Committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology. Written informed consent was obtained from the patient's parents for the publication of this case report and any accompanying images.

Consent for publication

We have obtained written informed consent from the parents of the patient for the publication of clinical details and clinical images.

Availability of data and materials

The data generated and analyzed in this case are presented within the article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

XZ and FY summarized and interpreted the patient's data and were the main contributors to the writing of the manuscript. YL provided the clinical data and changes in the patient's condition during the course of his treatment. JZ and YZ was responsible for supervision, as well as review and editing of the manuscript. All the authors read and approved the final manuscript.

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Table

Table 1. Key laboratory parameters of renal function and metabolism at biopsy.

Laboratory test	laboratory values	Unit	Reference Ranges
Complete blood count			
RBC	4.47 x10 ¹²	/L	4.5-5.9
WBC	8.16 x10 ⁹	/L	4.1-11.0
Hb	124	g/L	129-172
PLT	554 x10 ⁹	/L	150.0-407.0
Clinical biochemistry			
LA	4.54	mmol/L	0.50-2.20
PA	163.3	mmol/L	20-100
TC	4.7	mmol/L	<1.70
HDL-C	1.19	mmol/L	1.04-1.55
LDL-C	3.62	mmol/L	<3.37
TP	61.2	g/L	66-87
Alb	37.1	g/L	40-55
AST	19	U/L	9-50
ALT	25	U/L	15-40
LDH	206	U/L	120-250
BUN	4.3	mmol/L	1.7-8.3
Cr	27	μmol/L	59-104
Na	137.5	mmol/L	136-145
K	4.03	mmol/L	3.5-5.1
Cl	102.0	mmol/L	99-110
Ca	2.30	mmol/L	2.1-2.55
Cys-C	1.01	mg/L	0.63-1.25
α ₁ -MG	5.20	mg/L	0-5
NGAL	135.0	ng/mL	0-100
Immune-related			
C3	1.48	g/L	0.65-1.39

C4	0.26	g/L	0.16-0.38
IgG	4.6	g/L	7.0-15.6
IgA	0.66	g/L	0.58-3.21
IgM	0.93	g/L	0.49-2.61
Urinalysis			
Occult blood	2+		Negative
URBCs	15.6	/μl	Negative
UPCR	7207.54	μg/mg Cr	0-150
UWBC	92.9	/μl	Negative
β2-MG	<0.1	mg/L	<0.2
24-UP	4483.8	mg/24h	<140

WBC, white blood cells; RBC, red blood cells; Hb, hemoglobin; PLT, platelets; LA, lactic acid; PA, pyruvic acid; TC, total cholesterol; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; TP, total protein; Alb, albumin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen; Cr, creatinine; Na, sodium; K, potassium; Cl, chloride; Ca, calcium; Cys-C, cystatin C; α₁-MG, alpha-1-microglobulin; NGAL, neutrophil gelatinase-associated lipocalin; C3, complement component 3; C4, complement component 4; IgG, immunoglobulin G; IgA, immunoglobulin A; IgM, immunoglobulin M; PR3-ANCA, proteinase 3 anti-neutrophil cytoplasmic antibody; MPO-ANCA, myeloperoxidase anti-neutrophil cytoplasmic antibody; UPCR, urine protein-to-creatinine ratio; β2-MG, beta-2 microglobulin; 24-UP, 24-hour urine protein.

Figures

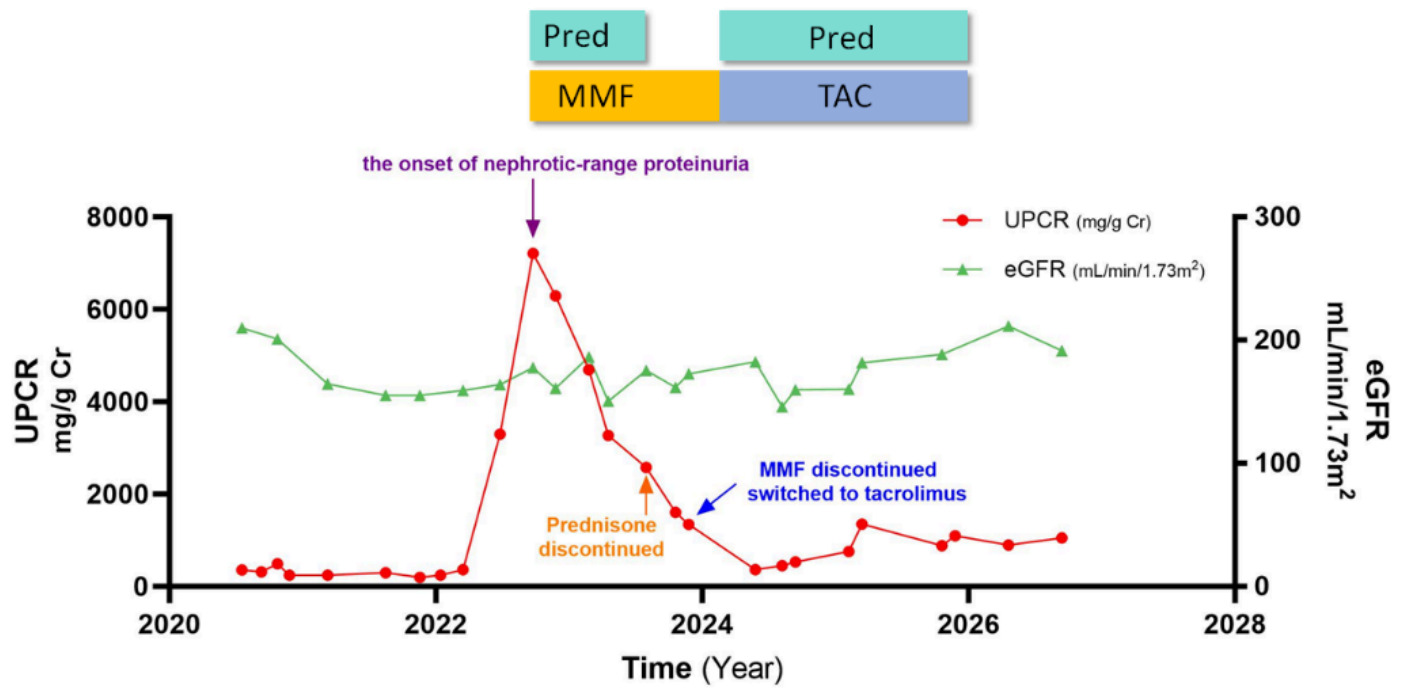


Figure 1

Longitudinal trajectory of urine protein-to-creatinine ratio and renal function over the period 2022-2026.

Left Y-axis: UPCR (mg/g Cr); Right Y-axis: estimated glomerular filtration rate (eGFR, mL/min/1.73 m²); MMF: mycophenolate mofetil; Pred: prednisone; TAC: tacrolimus;

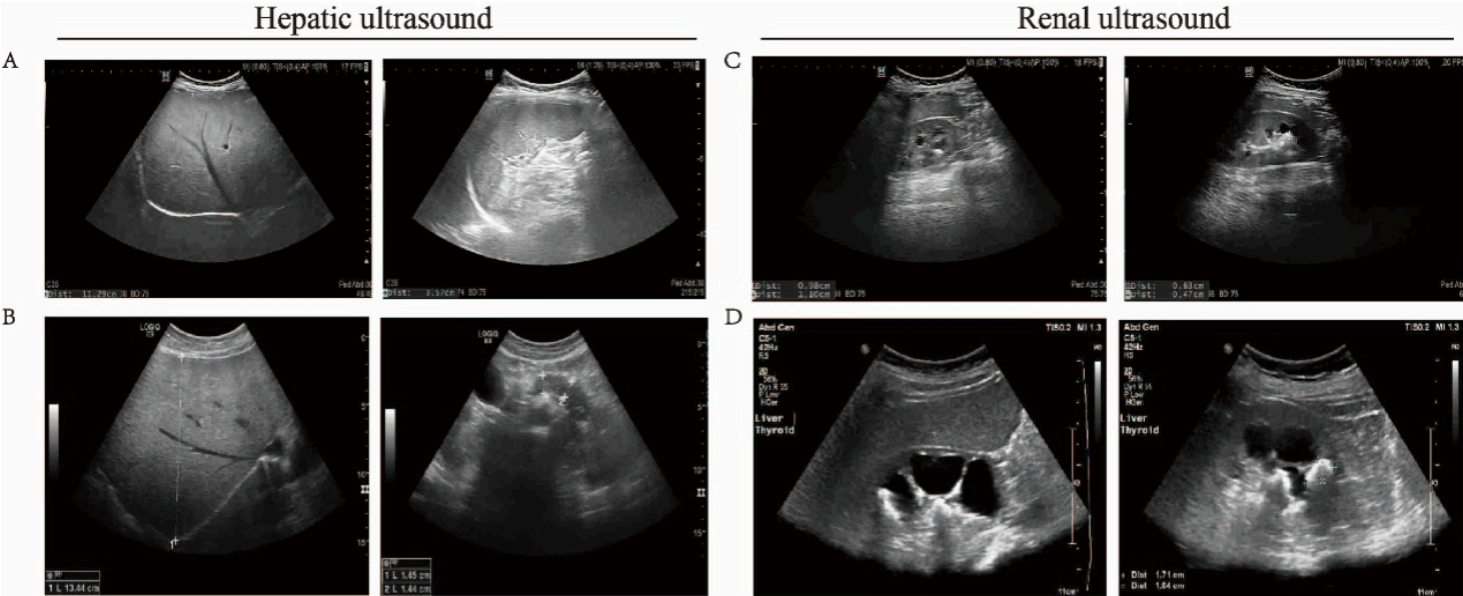


Figure 2

Liver and renal ultrasonography.

Liver (A) and renal (C) ultrasonography at the onset of nephrotic-range proteinuria (July 2022); liver (B) and renal (D) ultrasonography at the last follow-up (July 2026).

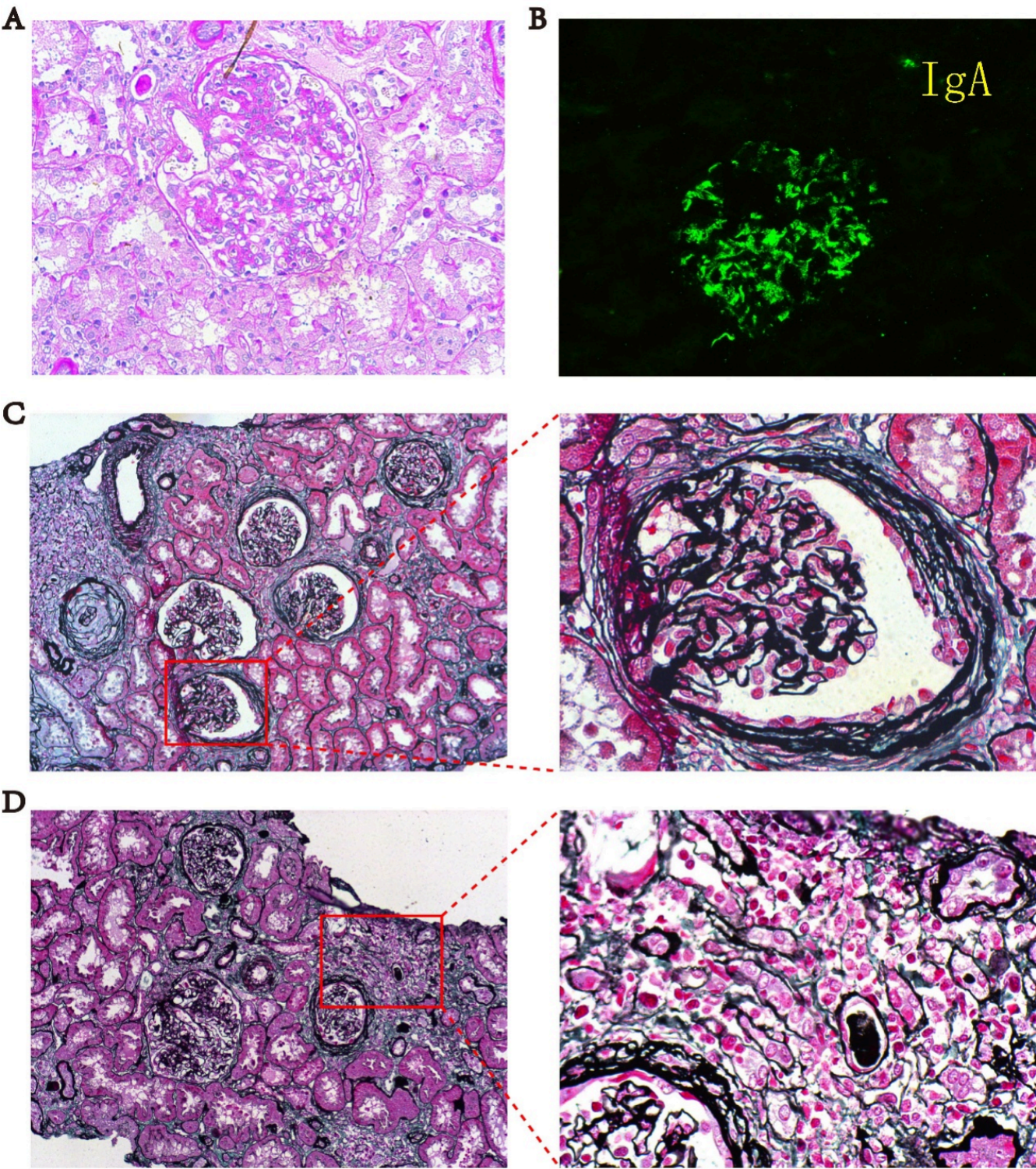


Figure 3

Renal pathological changes in the patient.

- A** Hematoxylin and eosin (HE) staining (200×): Showing mild glomerulomegaly with segmental mesangial hypercellularity and matrix expansion, accompanied by prominent vacuolar degeneration in adjacent tubular epithelial cells.
- B** Immunofluorescence staining for IgA (200×): Demonstrating intense, chunky, and confluent deposition of IgA (++++), predominantly restricted to the glomerular mesangium.
- C** Periodic acid–silver methenamine (PASM) staining (left: 100×; right: magnified boxed area, 400×): Displaying a prominent fibrocellular crescent compressing the glomerular capillary tuft and leading to capillary lumen collapse, accompanied by periglomerular fibrosis.
- D** PASM staining (left: 100×; right: magnified boxed area, 400×): Illustrating chronic tubulointerstitial changes, including patchy tubular atrophy, interstitial fibrosis, dense clusters of mononuclear inflammatory cell infiltration, and foam cell accumulation.

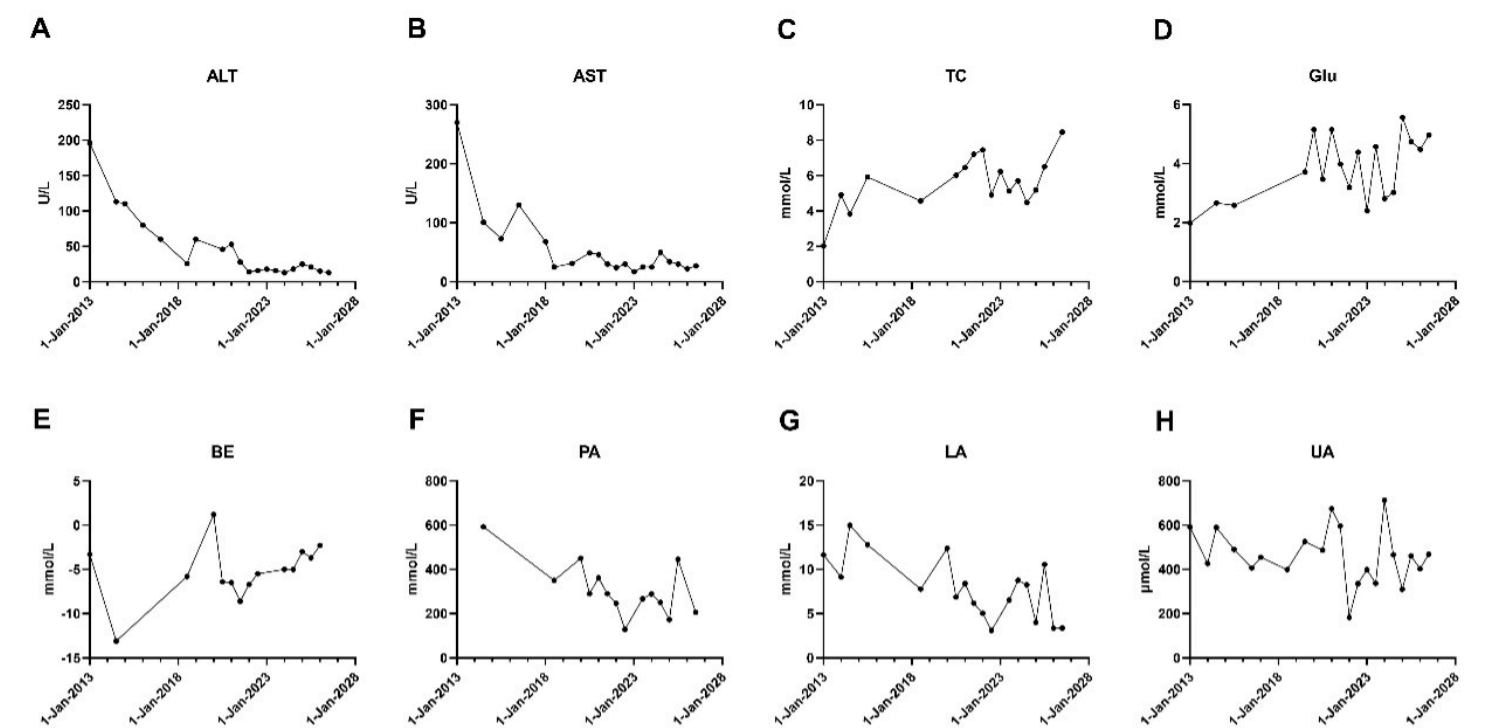


Figure 4

Longitudinal changes in hepatic enzymes, lipid profiles and metabolic biomarkers over the follow-up period.

A. Alanine aminotransferase (ALT, U/L);

B. Aspartate aminotransferase (AST, U/L);

C. Serum cholesterol (mmol/L);

D. Glucose (Glu, mmol/L);

E. Base excess (BE, mmol/L);

F. Pyruvic acid (PA, mmol/L);

G. Lactic acid (LA, mmol/L);

H. Uric acid (UA, μ mol/L).