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Urinary Frequency and Polydipsia Mimicking Diabetes Mellitus: Obesity-Related Secondary Focal Segmental Glomerulosclerosis with Concurrent Overactive Bladder — A Case Report

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Abstract

Background

Focal segmental glomerulosclerosis (FSGS) is a histopathological pattern of podocyte injury with primary, secondary, and genetic forms that differ in treatment and prognosis. Correct classification is important because secondary (adaptive) forms, including obesity-related glomerulopathy, do not respond to immunosuppression. Obesity-related secondary FSGS may produce heavy proteinuria yet preserved serum albumin, and chronic urinary frequency may reflect lower-urinary-tract rather than metabolic disease.

Case presentation

A 23-year-old man with class II obesity presented with a two-year history of urinary frequency, polydipsia and intermittent hand paraesthesia, a picture initially suggestive of diabetes mellitus. Evaluation showed nephrotic-range proteinuria, mildly reduced estimated glomerular filtration rate (eGFR), preserved serum albumin, dyslipidaemia and hyperuricaemia, without diabetes mellitus, urinary obstruction or serological evidence of systemic autoimmune disease. Kidney biopsy showed segmental sclerosis with perihilar and arteriolar hyalinosis, intracapillary foam cells, capsular adhesions, and only focal mesangial (IgA/IgM) staining, consistent with a secondary (adaptive) pattern of FSGS. He was managed without immunosuppression, using an angiotensin-receptor blocker, a statin (later combined with ezetimibe), urate-lowering therapy, empagliflozin, and weight-directed tirzepatide. Renal function and metabolic parameters fluctuated, and proteinuria did not achieve durable remission over follow-up. Empagliflozin-induced glycosuria transiently worsened and obscured the urinary symptoms; on directed re-evaluation, the chronic frequency was attributed to overactive bladder, and low-dose oxybutynin produced marked symptomatic improvement.

Conclusions

This case illustrates the coexistence of obesity-related secondary FSGS and overactive bladder in a young adult whose presentation mimicked diabetes mellitus. Distinguishing true polyuria from urinary frequency, and recognising adaptive FSGS are essential to avoid misdiagnosis and unnecessary immunosuppression.

Background

Focal segmental glomerulosclerosis (FSGS) is a histopathological pattern of podocyte injury rather than a single disease. Contemporary frameworks classify it both aetiologically, into primary (immune-mediated), secondary (adaptive, viral or drug-associated), and genetic forms, and morphologically, using the Columbia classification, which recognises the collapsing, tip, cellular, perihilar and not-otherwise-specified variants.[1,3,7] FSGS is among the leading glomerular causes of nephrotic-range proteinuria and progression to kidney failure.[1] The separation of primary from secondary disease is clinically decisive:

adaptive and genetic forms generally do not respond to immunosuppression and are managed by treating the underlying haemodynamic and metabolic drivers.[1,6,7] Obesity-related glomerulopathy is an increasingly recognised secondary (adaptive) form that typically presents with slowly progressive, often non-nephrotic-range proteinuria and glomerulomegaly, frequently without the hypoalbuminaemia and oedema of primary disease.[4,5]

A second, independent diagnostic problem in young adults is the interpretation of chronic urinary symptoms. Polyuria and polydipsia classically raise the possibility of diabetes mellitus, diabetes insipidus or primary polydipsia, whereas urinary frequency with urgency may instead reflect lower-urinary-tract dysfunction such as overactive bladder.[11,12] We report a young man in whom these two processes coexisted, and in whom careful clinicopathological correlation both established a secondary FSGS and reattributed his long-standing “polyuria” to urinary frequency.

Case presentation

History

A 23-year-old Pakistani male presented with a two-year history of frequent urination and excessive thirst, together with intermittent tingling (paraesthesia) of both hands. The urinary symptoms had begun insidiously two years earlier. He described frequent daytime voiding that he was unable to quantify, with nocturia once or twice nightly. At presentation, he denied dysuria, urinary urgency, hesitancy, a weak stream, or other obstructive symptoms, and reported no visible haematuria, frothy urine, or change in urine colour. Driven by persistent thirst, he drank approximately 4–5 L of water daily; fluids relieved the thirst only transiently. He had not undertaken a formal fluid-restriction trial, and the symptoms had persisted without remission.

The hand paraesthesia was purely sensory, without numbness, weakness, incoordination, or functional impairment; it was unrelated to posture or sleep position but was provoked by physical or mental fatigue, particularly after prolonged clinical or academic work. A systems review was otherwise unremarkable: he denied peripheral, facial, or generalised oedema, recent weight change, polyphagia, and symptoms of thyroid dysfunction, and reported no hypertension, headache, visual disturbance, chest pain, dyspnoea, fever, or inflammatory symptoms.

Past medical, drug, social, and family history

He had been obese since adolescence, predating the urinary symptoms, without recent rapid weight gain. He had allergic rhinitis with recurrent upper-respiratory symptoms and a history of nephrolithiasis since early adolescence (two to three episodes, none requiring intervention). He used non-steroidal anti-inflammatory drugs (NSAIDs) occasionally during periods of heavy workload but denied long-term medications, corticosteroids, anabolic steroids, bodybuilding, or herbal supplements. His diet was high

in fast food and sugary drinks, with low physical activity. He did not smoke, use alcohol, or use recreational drugs.

The family history was notable for type 2 diabetes mellitus in both parents (his father was also hypertensive, his mother hypothyroid), diabetic nephropathy progressing to kidney failure in his paternal grandfather, and chronic hepatitis C–related cirrhosis in his paternal grandmother. There was no family history of primary glomerular disease, nephrotic syndrome, or dialysis-dependent kidney failure.

Examination and anthropometry

On examination, he was normotensive and without oedema. Height was 182.9 cm and weight 121 kg, giving a body mass index (BMI) of 36.2 kg/m² (World Health Organization obesity class II).

Investigations

Urinalysis showed clear, yellow urine (specific gravity 1.015; pH 5.0) with 4+ protein and 2+ blood. Glucose, ketones, bilirubin, nitrites, and leukocyte esterase were negative, and urobilinogen was normal. Microscopy showed 2 red cells per high-power field, occasional leukocytes, and a few bacteria, with no casts or crystals; urine culture was sterile. A 24-hour collection confirmed nephrotic-range proteinuria at 4320 mg/24 h. The spot urine protein-to-creatinine ratio (UPCR) was 1.76 mg/mg.

Serum creatinine was 1.4 mg/dL, corresponding to an estimated GFR of approximately 72 mL/min/1.73 m² by the 2021 CKD-EPI creatinine equation (CKD category G2); blood urea was normal. Despite heavy proteinuria, serum albumin was preserved at 4.6 g/dL, with total protein 8.4 g/dL, globulin 3.8 g/dL, and an albumin-to-globulin ratio of 1.2. Serum uric acid was elevated at 9.6 mg/dL. The lipid profile showed total cholesterol 256 mg/dL, triglycerides 267 mg/dL, LDL cholesterol 172 mg/dL, HDL cholesterol 37 mg/dL, and VLDL 53 mg/dL. HbA1c was 5.1% with no hyperglycaemia. Electrolytes were normal with a borderline-low bicarbonate of 22.8 mmol/L; calcium and 25-hydroxy-vitamin D were normal.

Erythrocyte sedimentation rate was 34 mm/h and C-reactive protein 6.9 mg/L. Antinuclear antibody was positive at low titre (fine speckled, 2+), but anti-mitochondrial, anti–smooth-muscle and an extended extractable-nuclear-antigen panel were negative, as were anti-neutrophil cytoplasmic antibodies. Serum complement was normal. Anti-streptolysin-O titre was marginally raised at 209 IU/mL (reference <200).

Serologies for HIV, hepatitis B, and C were negative. Haemoglobin electrophoresis, performed to exclude the sickle cell trait, a recognised cause of impaired urinary concentration, nocturia, and increased thirst, was normal. Serum vitamin B12 and thyroid-stimulating hormone were normal. Liver function tests showed a normal bilirubin and alkaline phosphatase (90 U/L), with mild elevations of alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transferase, a pattern in keeping with concomitant obesity-related (metabolic dysfunction–associated) hepatic steatosis.

The immunological, Serological and Inflammatory markers are summarised in Table 1.

Table 1. Immunologic, serologic and inflammatory work-up.

Test	Result	Reference/interpretation	Date
ESR	**34 mm/h**	*0–15 mm/h*	29 Sep 2025
CRP	**6.90 mg/L**	*<10 mg/L*	29 Sep 2025
ANA (immunofluorescence)	**Positive — fine speckled (+2)**	*Negative*	17 Sep 2025
AMA	**Negative**	*Negative*	17 Sep 2025
ASMA	**Negative**	*Negative*	17 Sep 2025
Anti-dsDNA (IF)	**Negative**	*Negative*	19 Sep 2025
ENA panel (immunoblot [1]	**All 16 antigens negative**	*Nucleosomes, histones, SmD1, PCNA, ribosomal-P, Ro60, Ro52, La, CENP-B, Scl-70, U1-snRNP, Sm/RNP, Jo-1, PM-Scl, Mi-2, Ku*	26 Oct 2025
ANCA (IF)	**p-ANCA negative; c-ANCA weak positive [2]**	*Negative*	29 Sep 2025
ANCA (quantitative)	**p-ANCA 1.19 U/mL; c-ANCA <0.3 U/mL**	*Negative <9.6 / <1.7 U/mL*	4 Oct 2025
Complement C3	**1.76 g/L**	*0.9–1.8 g/L*	19 Sep 2025
Complement C4	**0.27 g/L**	*0.1–0.4 g/L*	19 Sep 2025
ASO titre	**208.6 IU/mL**	*<200 IU/mL*	19 Sep 2025
HIV / HBsAg / anti-HCV	**Negative**	*Negative*	19 Sep 2025
Haemoglobin electrophoresis	**Normal**	*Normal*	19 Sep 2025

[1] Performed by immunoblot assay; anti-extractable nuclear antigen antibodies were not detected.

[2] c-ANCA was weakly positive on indirect immunofluorescence but was not confirmed on the quantitative assay (c-ANCA <0.3 U/mL); in the absence of clinical vasculitis, this was considered non-significant.

Trans-abdominal ultrasound showed a normal prostate with an intact capsule, a pre-void bladder volume of 245 mL and a post-void residual of 17 mL, excluding bladder-outlet obstruction. Renal ultrasound showed normal-sized kidneys with preserved corticomedullary differentiation, no calculus, mass or hydronephrosis, and a normal bladder. U/S Bladder Pre vs Post void is shown in Figure 1

The longitudinal laboratory and anthropometric data are summarised in Table 2.

Table 2. Longitudinal laboratory and anthropometric data.

Parameter (reference range)	18 Jul 2025	17–22 Sep 2025	7 Oct 2025	16 Oct 2025
Renal function				
Serum creatinine *(0.9–1.3 mg/dL)*	—	1.4	1.1	—
Blood urea *(12–41 mg/dL)*	—	27.82	—	—
Electrolytes & acid–base				
Sodium *(136–146 mmol/L)*	—	140	141	—
Potassium *(3.5–5.1 mmol/L)*	—	3.7	3.9	—
Chloride *(98–107 mmol/L)*	—	106	104	—
Bicarbonate *(23–29 mmol/L)*	—	22.8	27.6	—
Calcium *(8.6–10.2 mg/dL)*	—	9.90	—	—
Serum proteins & metabolic				
Total protein *(6.4–8.3 g/dL)*	—	8.40	—	—
Albumin *(3.5–5.2 g/dL)*	—	4.60	—	—
Globulin *(1.8–3.6 g/dL)*	—	3.8	—	—
A/G ratio *(>1)*	—	1.2	—	—
Uric acid *(3.5–7.2 mg/dL)*	—	9.6	—	—
Total cholesterol *(<200 mg/dL)*	—	256	—	—
Triglycerides *(<150 mg/dL)*	—	267	—	—
LDL cholesterol	—	172	—	—
HDL cholesterol *(≥40 mg/dL)*	—	37	—	—
VLDL *(<30 mg/dL)*	—	53	—	—
HbA1c *(<5.7 %)*	—	5.14	—	—
Vitamins & endocrine				
Vitamin D (25-OH) *(≥30 ng/mL)*	9.6	30.6	—	—
Vitamin B12 *(206–678 pg/mL)*	347	—	—	—
TSH *(0.4–4.2 µIU/mL)*	3.304	—	—	—
Urinalysis (dipstick & microscopy)				
Specific gravity *(1.005–1.025)*	—	1.015	—	1.032

Parameter (reference range)	18 Jul 2025	17–22 Sep 2025	7 Oct 2025	16 Oct 2025
Protein (dipstick) *(negative)*	—	4+ (5 g/L)	—	4+ (5 g/L)
Glucose (dipstick) *(negative)*	—	Negative	—	4+ (56 mmol/L)
Blood/Hb (dipstick) *(negative)*	—	2+ (25/µL)	—	2+ (25/µL)
Bilirubin (dipstick) *(negative)*	—	Negative	—	Negative
RBCs (microscopy) *(0–2/HPF)*	—	2/HPF	—	Occasional
Quantitative proteinuria				
Spot urine protein *(<15 mg/dL)*	—	86.30	—	—
Spot urine creatinine *(28–217 mg/dL)*	—	48.9	—	—
Spot UPCR *(<0.2 adult)*	—	1.76	—	—
24-h urine protein *(0–150 mg/24h)*	—	4320 *	—	—
Liver function tests				
Total bilirubin *(0.2–1.2 mg/dL)*	0.68			
Direct bilirubin *(0–0.3 mg/dL)*	0.23			
Indirect bilirubin *(0.25–0.9 mg/dL)*	0.45			
ALT (SGPT) *(<45 U/L)*	**50**			
AST (SGOT) *(<35 U/L)*	**37**			
Alkaline phosphatase *(53–128 U/L)*	90			
Gamma-GT (GGT) *(<55 U/L)*	**104**			

Values are as reported by the testing laboratories (DOW Diagnostic/DUHS and Aga Khan University Hospital). Em dash (—) = not measured at that time point.

** 24-hour urine collection obtained 22 Sep 2025 and lipid profile/uric acid 18 Sep 2025; remaining baseline values 17 Sep 2025.*

‡ Weight and BMI are from clinical records (not laboratory reports); only the baseline measurement was available in the documents provided.

Dipstick glucose from 16 Oct 2025 onward reflects empagliflozin-induced glycosuria (HbA1c normal).

The laboratory did not print a numeric eGFR; it uses the CKD-EPI-Pakistan equation (Ahmed et al., JCPSP 2017).

Kidney biopsy

An ultrasound-guided kidney biopsy yielded two cores of predominantly cortical tissue. Of 37 glomeruli, 5 were globally sclerosed, and 6 showed segmental scarring with intracapillary foam cells; 4 had adhesions to Bowman's capsule, 4 showed segmental hyalinosis, and 3 showed arteriolar hyalinosis. One glomerulus showed segmental tuft collapse with overlying podocyte hyperplasia, and one showed mildly increased mesangial cellularity; the remainder showed only minor changes. There was mild tubular atrophy with occasional hyaline and red-cell casts, mild patchy interstitial inflammation, and minimal focal scarring. Small arteries showed hyalinosis. Immunohistochemistry for C4d was negative. Immunofluorescence showed only a focal granular mesangial trace for IgA and IgM, with IgG, C3, and C1q negative. Electron microscopy was not available. The predominant pattern, segmental sclerosis with perihilar and arteriolar hyalinosis, capsular adhesions and foam cells, with only trace immune deposits, corresponds to the perihilar variant in the Columbia scheme and, in this clinical context, to a secondary (adaptive) FSGS.[3,4]

Treatment and follow-up

Because the findings indicated secondary (adaptive) FSGS, immunosuppression was withheld.[1,6,7] He was started on losartan 25 mg once daily, febuxostat 40 mg once daily, empagliflozin 10 mg once daily, rosuvastatin 10 mg once daily, and subcutaneous tirzepatide 2.5 mg once weekly (used off-label for weight reduction in this non-diabetic patient), up-titrated to 5 and 7.5 every four weeks subsequently.

At three months, creatinine had fallen to 1.0 mg/dL (eGFR ≈108 mL/min/1.73 m²) and urea to 23.5 mg/dL, but proteinuria persisted (UPCR 2.00 mg/mg; dipstick 3+). New 3+ glycosuria with a normal HbA1c (5.4%) reflected the expected pharmacological effect of empagliflozin. Serum albumin remained 4.8 g/dL. Dyslipidaemia had improved substantially (total cholesterol 180, LDL 117, HDL 42 mg/dL; triglycerides 191 mg/dL), and uric acid had normalised to 4.2 mg/dL. Weight was 117 kg (BMI 34.98 kg/m², class I). Losartan was increased to 50 mg daily and tirzepatide to 7.5 mg weekly.

One month later, creatinine was 1.1 mg/dL (eGFR ≈97) with stable electrolytes, and proteinuria had fallen (UPCR 1.19 mg/mg; dipstick 2+). Glycosuria persisted (3+) without ketonuria, haematuria or active sediment. Uric acid was 3.5 mg/dL. Weight was 115 kg (BMI 34.4, class I). Febuxostat was changed to alternate-day dosing, and tirzepatide was increased to 10 mg weekly.

At a further three-month visit, the patient was concerned that his frequency to urinate and polydipsia had increased, which he attributed to empagliflozin. Proteinuria had risen again (UPCR 1.71 mg/mg; dipstick 3+), with 1+ glycosuria, but no bilirubin, red cells, casts, or evidence of infection. Glycaemic control

remained normal (fasting glucose 78 mg/dL; HbA1c 5.1%), the lipid profile was controlled (total cholesterol 187, LDL 117, HDL 44 mg/dL; triglycerides 165 mg/dL), serum albumin was 4.9 g/dL and calcium, phosphate and uric acid were normal. Haemoglobin was 16.3 g/dL with normocytic indices. Weight was 105 kg (BMI 31.4, class I), a cumulative reduction of 16 kg. Creatinine was 1.3 mg/dL (eGFR ≈79).

Because the metabolic and renal parameters that might explain an osmotic polyuria had normalised or were attributable to empagliflozin, the urinary complaints were re-evaluated. On directed questioning, the patient now recalled urinary urgency at relatively low bladder volumes (around the 245 mL pre-void volume recorded on the initial ultrasound), a feature he had not reported at presentation. A clinical diagnosis of overactive bladder was made; a urodynamic study was advised to confirm it, but the patient declined. Oxybutynin 2.5 mg at night was added, rosuvastatin was changed to rosuvastatin/ezetimibe 10/10 mg, and tirzepatide was continued. At one month, the urinary frequency had improved markedly, while the other parameters were unchanged.

Table 3: Longitudinal Laboratory Monitoring of Clinical and Renal Parameters (January–May 2026)

Parameter	Reference Range	Jan 14, 2026	Feb 14, 2026	May 11, 2026
Hematology & Inflammatory Markers				
Hemoglobin (g/dL)	13.0 - 17.0	16	-	16.3
RBC Count (1012/L)	4.5 - 5.5	6.1	-	6.2
HCT (%)	40 - 50	46	-	49
MCV (fL)	80 - 100	76	-	79
MCH (pg)	27 - 32	26	-	26
MCHC (g/dL)	31.5 - 34.5	35	-	33
WBC Count (109/L)	4.0 - 10.0	10.7	-	-
Platelets (109/L)	150 - 400	340	-	-
ESR (mm/Hr)	0 - 15	45	-	-
Renal Function & Electrolytes				
Serum Creatinine (mg/dL)	0.9 - 1.3	-	-	1.3
Uric Acid (mg/dL)	4.2 - 8.0	-	-	4.5
Sodium (mEq/L)	136 - 146	-	141	-
Potassium (mEq/L)	3.5 - 5.1	-	4.3	-
Chloride (mEq/L)	98 - 107	-	104	-
Bicarbonate (mEq/L)	23 - 29	-	23.5	-
Glycemic Control				
Fasting Glucose (mg/dL)	< 100	-	-	78
HbA1c (%)	< 5.7	5.44	-	-
Liver / Serum Proteins				
Total Proteins (g/dL)	6.4 - 8.3	8.6	-	-
Albumin (g/dL)	3.5 - 5.2	4.8	-	-
Globulins (g/dL)	1.8 - 3.6	3.8	-	-
A/G Ratio	> 1.0	1.3	-	-
Lipid Profile				
Total Cholesterol (mg/dL)	< 200	-	-	187

Triglycerides (mg/dL)	< 150	-	-	165
HDL Cholesterol (mg/dL)	> 40	-	-	44
LDL Cholesterol (mg/dL)	< 100	-	-	117
VLDL Cholesterol (mg/dL)	≤ 30	-	-	33
Non-HDL Cholesterol (mg/dL)	< 130	-	-	143
Urinalysis (Spot / Routine)				
UPCR	< 0.2	2	1.19	1.71
Urine Protein (Spot) (mg/dL)	< 15	471.8	84.1	655.9
Urine Creatinine (Spot) (mg/dL)	28 - 217	235.5	70.5	382.9
Urine Protein (Dipstick)	Negative	≥3.0 g/L (+3)	1.0 g/L (+2)	-
Urine Glucose (Dipstick)	Negative	28 mmol/L (+3)	28 mmol/L (+3)	-
Urine Specific Gravity	1.005 - 1.025	≥ 1.030	1.02	-
Urine pH	5.0 - 8.0	5.5	6	-
Pus Cells (HPF)	0 - 4	1 - 2	0 - 1	-

Discussion

This case presented two parallel diagnostic problems: heavy proteinuria in a young man with obesity, and long-standing urinary frequency with polydipsia that initially suggested a metabolic disorder. The biopsy and clinical phenotype favour an obesity-related, secondary (adaptive) FSGS over primary disease. Obesity-related glomerulopathy characteristically produces heavy, sometimes nephrotic-range proteinuria without the full nephrotic syndrome, and the absence of oedema and hypoalbuminaemia is a useful pointer away from a primary podocytopathy.[4,5] The preserved serum albumin, absence of oedema, obesity since adolescence, dyslipidaemia, hyperuricaemia, and a biopsy showing perihilar and arteriolar hyalinosis, foam cells, capsular adhesions and only trace immune staining are all consistent with an adaptive lesion arising from obesity-related hyperfiltration rather than an immune-mediated process.[3,4] In keeping with KDIGO guidance, genetic testing was not pursued, as a secondary cause was evident and there was no family history of nephrotic syndrome.[7]

Obesity-related glomerulopathy is understood as an initially adaptive response that becomes maladaptive: increased body mass drives glomerular hyperfiltration and hypertrophy and imposes podocyte stress, and as injury accumulates, focal and segmental sclerosis develops.[4,5] This matters therapeutically, because secondary and genetic forms, unlike primary FSGS, do not respond to immunosuppression and instead require correction of the haemodynamic and metabolic drivers.[1,6,7]

Withholding immunosuppression was therefore appropriate. The management priorities were renin–angiotensin system blockade, proteinuria reduction and, above all, sustained weight loss, which has shown the most consistent antiproteinuric effect in obesity-related glomerulopathy.[4,5]

Two histological features warrant caution. First, a single glomerulus showed segmental tuft collapse with podocyte hyperplasia. Although isolated and set against an otherwise perihilar, adaptive pattern, a collapsing lesion is not typical of obesity-related FSGS and, when prominent, should prompt consideration of viral (including HIV), APOL1-associated or drug-induced collapsing glomerulopathy.[3] In this patient, HIV, hepatitis B and hepatitis C serologies were negative, making a virus-associated lesion unlikely; APOL1 genotyping was not performed. The isolated collapsing feature was therefore interpreted as incidental within a predominantly adaptive lesion. Second, the urinalysis showed microscopic haematuria, and the biopsy contained red-cell casts, findings more usually associated with an active or proliferative glomerular process than with a bland adaptive lesion. A concurrent low-grade mesangial process (for example, IgA nephropathy) cannot be excluded on the trace mesangial IgA alone, although normal complement and the absence of significant mesangial hypercellularity argue against an active immune-complex glomerulonephritis. Interpretation is further limited by the absence of electron microscopy, which is the principal tool for grading podocyte foot-process effacement and thereby for distinguishing primary (typically diffuse effacement) from secondary (typically segmental) FSGS.[1]

The case also illustrates that a preserved serum albumin should not provide false reassurance. In adaptive, hyperfiltration-related FSGS, massive proteinuria can occur without hypoalbuminaemia or other features of the nephrotic syndrome.[4] In a biopsy series of patients with nephrotic-range proteinuria, the proportion with FSGS rose as serum albumin increased, and renal survival remained poor even among those with serum albumin above 35 g/L.[8] The discrepancy in this patient between the 24-hour protein (4.3 g) and the spot UPCR (1.76 mg/mg) is also instructive: in a large, muscular individual, high urinary creatinine excretion causes the UPCR to underestimate daily protein loss, so the timed collection is the more reliable measure.

Beyond RAS blockade and weight loss, the patient received empagliflozin and weight-directed tirzepatide. Sodium–glucose cotransporter-2 inhibition now has an established role in proteinuric chronic kidney disease, irrespective of diabetes, having reduced kidney-disease progression in both diabetic and non-diabetic participants in the DAPA-CKD and EMPA-KIDNEY trials, and it also lowers serum uric acid.[9,10] In a patient whose dominant complaint was urinary, however, empagliflozin carried a foreseeable trade-off: the resulting glycosuria and osmotic diuresis transiently worsened his urinary symptoms and, by providing a ready explanation for them, delayed recognition of the true cause. Tirzepatide, used off-label for weight reduction, achieved a 16 kg fall in weight; yet, consistent with the often slow and incomplete response of secondary FSGS, proteinuria fluctuated and did not reach durable remission, and serum creatinine, after an early fall, returned close to baseline. The outcome is therefore best described as metabolic improvement with an active, only partially controlled glomerular lesion rather than as remission.

The urinary symptoms required separate reasoning. Despite presenting with “polyuria” and polydipsia, the patient never had biochemical evidence of diabetes mellitus, and the work-up did not include the measurements, paired serum and urine osmolality, a formal water-deprivation (or copeptin-based) test, and a frequency–volume chart, needed to distinguish diabetes insipidus, primary polydipsia, and true polyuria from urinary frequency.[11] Several features nonetheless argued against pathological water diuresis: a 24-hour urine volume of 3000 mL is at or below the conventional polyuria threshold (and well below a weight-based threshold of roughly 50 mL/kg/day for this patient), the urine was not inappropriately dilute (specific gravity 1.015), the symptoms long predated any osmotic stimulus, and haemoglobin electrophoresis excluded sickle cell trait as a cause of a renal concentrating defect. Although a formal water-deprivation test was not performed, the patient repeatedly tolerated the prolonged dry fasting of Ramadan (approximately 17–18 hours without any fluid) without difficulty, an informal but clinically telling observation, since significant diabetes insipidus or true polyuria would not be expected to be tolerated in this way. The clinical picture instead fits overactive bladder, defined by urinary urgency, usually with frequency and nocturia, in the absence of infection or other obvious pathology.[12]

Overactive bladder is a symptom syndrome rather than an ultrasonographic or urodynamic diagnosis; urgency is its defining element, and many patients have no demonstrable detrusor overactivity.[12] Two caveats apply: the patient explicitly denied urgency at presentation and recalled it only on later, directed questioning, raising the possibility of recall bias; and the diagnosis rests on symptoms and the therapeutic response rather than on a voiding diary or urodynamics. The marked improvement on a low dose of the antimuscarinic oxybutynin is consistent with standard overactive-bladder management, in which antimuscarinics remain a mainstay.[12,13] The persistent polydipsia is not fully explained by overactive bladder and may represent habitual or primary polydipsia; notably, antimuscarinic-induced dry mouth could, if anything, aggravate thirst, so the symptomatic benefit observed related principally to urinary frequency.

Two further findings deserve brief comment. The intermittent, fatigue-provoked hand paraesthesia was purely sensory and non-progressive, with normal serum calcium, potassium, vitamin B12 and thyroid function and no other identified cause; it remained unexplained but benign and is presumed unrelated to the renal and urological diagnoses. The mild elevation of hepatic transaminases and gamma-glutamyl transferase, with normal bilirubin, was consistent with obesity-related (metabolic dysfunction–associated) hepatic steatosis, part of the same metabolic phenotype driving the glomerular lesion, and would also be expected to benefit from weight reduction.

Taken together, the case shows how readily chronic urinary frequency can be misread as polyuria from systemic disease. In a young adult with obesity, diagnostic anchoring is especially hazardous: obesity offers a plausible explanation for renal disease, while thirst and frequent voiding pull attention towards diabetes. Here, biopsy clarified the renal diagnosis and prevented unnecessary immunosuppression, while bladder-directed therapy addressed the urinary symptoms. The combination is unusual enough to be worth reporting, chiefly as a reminder to separate true polyuria from urinary frequency, and to let

histology, timed urine quantification, and bladder assessment each answer the question it is best suited to answer.

Limitations

This report has limitations. Electron microscopy was not available, limiting formal sub-classification of the FSGS lesion and assessment of foot-process effacement. The work-up of polyuria and polydipsia did not include serum and urine osmolality, a formal water-deprivation or copeptin test, or a frequency–volume chart, so true polyuria and primary polydipsia were not formally excluded, although the patient's uneventful tolerance of prolonged Ramadan fasting argues strongly against significant diabetes insipidus. The diagnosis of overactive bladder was clinical: the recommended urodynamic study was declined, and the diagnosis rested partly on retrospectively recalled urgency. APOL1 genotyping and a metabolic stone work-up were not performed. Finally, follow-up was relatively short, and the persistence of proteinuria indicates an ongoing process that requires continued monitoring.

Conclusion

This case illustrates two concurrent and easily conflated problems, obesity-related secondary FSGS and overactive bladder, in a young man whose presentation mimicked diabetes mellitus. FSGS is a pattern of podocyte injury with distinct primary, secondary, and genetic forms, and correct classification is essential because secondary disease does not respond to immunosuppression but requires treatment of the underlying driver. The combination of obesity, nephrotic-range proteinuria, preserved serum albumin, and the biopsy appearances supported an adaptive, secondary process, and immunosuppression was appropriately withheld in favour of renin–angiotensin blockade, SGLT2 inhibition, and weight reduction. The chronic urinary frequency, long mistaken for polyuria, was ultimately attributed to an overactive bladder and responded to antimuscarinic therapy. Clinicians evaluating polyuria and polydipsia should pair a metabolic assessment with quantification of urine output and an assessment of lower-urinary-tract function, and should remember that a preserved serum albumin does not exclude clinically important glomerular disease.

Abbreviations

ANA, antinuclear antibody; ANCA, anti-neutrophil cytoplasmic antibody; BMI, body-mass index; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; ENA, extractable nuclear antigen; ESR, erythrocyte sedimentation rate; FSGS, focal segmental glomerulosclerosis; HDL/LDL, high-/low-density lipoprotein; NSAID, non-steroidal anti-inflammatory drug; OAB, overactive bladder; RAS, renin–angiotensin system; SGLT2, sodium–glucose cotransporter-2; UPCR, urine protein-to-creatinine ratio.

Declarations

Ethics approval and consent to participate: Not applicable. Institutional Review Board (IRB) approval is typically waived for individual case reports involving a single patient; however, rigorous ethical standards were maintained. The patient involved in this case report is the first author of this manuscript, thereby ensuring complete autonomy, transparency, and compliance with ethical principles.

Consent for publication: Written informed consent for publication of this clinical case report and the accompanying ultrasound images was obtained from the patient. Because the patient is also the first author of this manuscript, authorship and consent are fully aligned. A copy of the signed, formal consent documentation is available for review by the Editor-in-Chief upon request.

Availability of data and materials: The data that support the findings of this case report are thoroughly documented within the manuscript itself (including all longitudinal laboratory investigations presented in Table 1, Table 2, and Table 3, and the ultrasound findings in Figure 1). Any additional underlying clinical records are restricted from public deposition to maintain patient privacy, but can be made available from the corresponding author upon reasonable academic request.

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Authors' contributions

Muhammad Saad Bin Arshad Arain: Manuscript writing (Case presentation)

Dr. Farah Anum Jameel: Consultant in case and manuscript review

Zahra Ali Haque: Manuscript review

Haider Imran: Manuscript review

Dania Hussain: Manuscript writing (Introduction)

Anas Nasir: Manuscript writing (Discussion)

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Figures

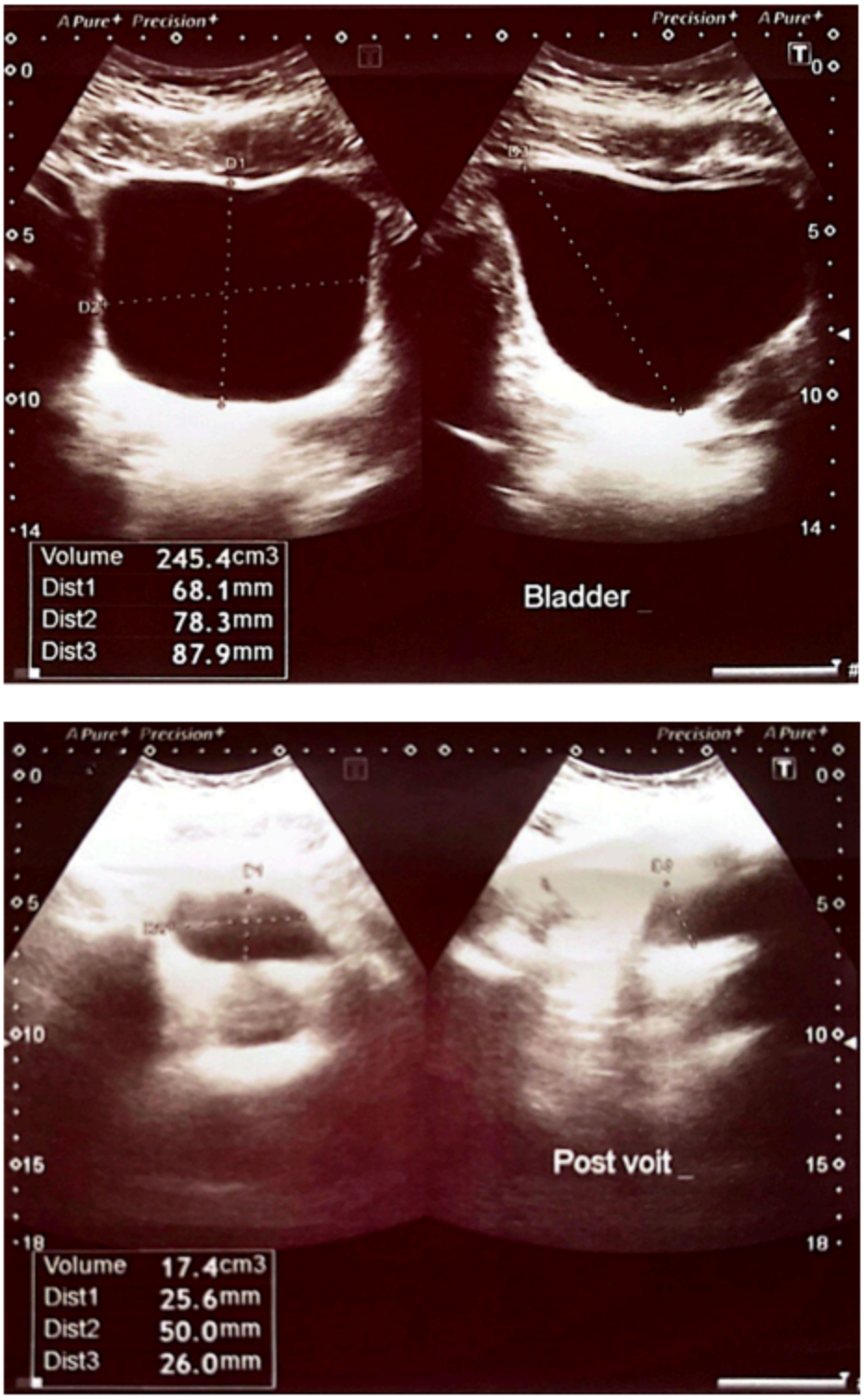


Figure 1

(a-b): Ultrasound bladder showing 245.4 mL pre-void and 17.4mL post void urine volume.