Almomany O, Albashtawi Y, Rawashdeh Z, Abdulsahib F, Alnemrawy M, Shadid S. Early Rituximab-Based Immunosuppression for Recurrent FSGS Post-Kidney Transplant: Implications for Perioperative Management. *Academic Anesthesia*. Published online October 7, 2025. doi:10.62186/VDDC4260

CASE REPORTS

Early Rituximab-Based Immunosuppression for Recurrent FSGS Post-Kidney Transplant: Implications for Perioperative Management

Omar Almomany, M.D., Ph.D.[1], Yahia Albashtawi, M.D.[2], Zaina Rawashdeh[3], Fatima Abdulsahib, M.D.[3], Maram Alnemrawy[3], Sama Shadid[4]

[1] Director of Kidney Transplant Program, Department of Nephrology, Middle East Kidney and Transplant Center, Jordan, [2] Department of Nephrology, Abdali Hospital, [3] Department of Medicine, University of Jordan, [4] Department of Pharmacy, Jordan University of Science and Technology

Keywords: focal segmental glomerulosclerosis, hypoalbuminemia, immunosuppression, kidney transplant, nephrotic syndrome, podocyte injury, proteinuria, rituximab, perioperative management

https://doi.org/10.62186/VDDC4260

Academic Anesthesia

Recurrent focal segmental glomerulosclerosis (FSGS) after kidney transplantation is a rare but serious complication that can rapidly compromise graft function. A 35-year-old male with end-stage renal disease (ESRD) secondary to primary FSGS underwent deceased-donor kidney transplantation. Two weeks post-transplant, he developed nephrotic-range proteinuria, hypoalbuminemia, generalized edema, and new-onset hypertension. Renal biopsy confirmed recurrent FSGS, showing diffuse podocyte effacement and segmental glomerular sclerosis. The patient was treated with a tailored immunosuppressive regimen including low-dose tacrolimus, mycophenolate mofetil, and rituximab. Management included close monitoring and titration of immunosuppressive therapy according to response and tolerability. No major complications were noted during treatment. This case highlights the importance of early recognition, biopsy confirmation of recurrent FSGS, and the potential benefits of targeted therapies such as rituximab in improving outcomes in high-risk transplant recipients.

Introduction

Focal segmental glomerulosclerosis (FSGS) is a major cause of nephrotic syndrome in adults and a major contributor to end-stage renal disease (ESRD) worldwide.[1] Kidney transplantation is the definitive treatment for ESRD; however, recurrent FSGS occurs in 30–40% of patients with primary disease and is strongly linked to early graft loss.[2,3] The pathogenesis is thought to involve circulating permeability factors such as soluble urokinase-type plasminogen activator receptor (suPAR), anti-CD40 antibodies, and cardiotrophin-like cytokine factor-1 (CLCF-1), which injure podocytes, resulting in proteinuria and progressive glomerular scarring.[4,5]

Recurrent FSGS poses a significant therapeutic challenge as conventional immunosuppressants, including corticosteroids and calcineurin inhibitors, often fail to prevent relapse or adequately reduce proteinuria.[6] Emerging evidence suggests that B-cell–targeted therapy, particularly rituximab, can stabilize podocytes and improve outcomes in recurrent FSGS, though most data are derived from case series and small cohort studies.[7,8] Early detection of recurrence through laboratory monitoring and timely renal biopsy is

Table 1. Key Laboratory Parameters Monitoring Proteinuria, Renal Function, and Immunosuppressive Therapy Response in a Patient with Recurrent FSGS Post-Kidney Transplant.

Parameter	Post-Transplant Day 14	Reference Range	Clinical Significance
Serum Creatinine	1.5 mg/dL	0.8–1.3 mg/dL	Mild elevation
eGFR	52 mL/min/1.73 m²	>90	Mild impairment
Urine Protein-to-Creatinine Ratio	6.8 g/g	<0.2 g/g	Nephrotic-range proteinuria
Serum Albumin	2.3 g/dL	3.5–5.0 g/dL	Hypoalbuminemia
Cholesterol	310 mg/dL	<200 mg/dL	Hyperlipidemia
Blood Pressure	140/90 mmHg	<130/80	Mild hypertension

eGFR was calculated using the CKD-EPI 2021 equation.

critical to preserve graft function.[9] This case demonstrates successful reversal of recurrent FSGS with an early, intensified immunosuppression protocol and highlights the importance of prompt recognition, biopsy, and individualized therapy to prevent graft loss.

Case Presentation

A 35-year-old male with end-stage renal disease (ESRD) secondary to biopsy-confirmed primary focal segmental glomerulosclerosis (FSGS) underwent a deceased-donor kidney transplant. His medical history included steroid-responsive nephrotic syndrome during adolescence, which slowly progressed to ESRD over the course of 10 years. He had not experienced any complications from immunosuppressive treatment in the past. For induction, he was given intravenous methylprednisolone and basiliximab, and his maintenance regimen consisted of tacrolimus (with a target trough of 8–10 ng/mL) and mycophenolate mofetil (1 g/day). The immediate postoperative course went smoothly, with the graft showing prompt function, urine output reached 3.2 L/day, and his serum creatinine dropped from 8.5 mg/dL before the transplant to 1.1 mg/dL by the fifth postoperative day.

On postoperative day 14, the patient developed generalized edema, most noticeable as periorbital puffiness, along with a weight gain of 3.5 kg and mild exertional dyspnea. His blood pressure was 140/92 mmHg, heart rate 88 bpm, respiratory rate 18/min, and temperature 36.8°C. Laboratory studies showed nephrotic-range proteinuria, with a urine protein-to-creatinine ratio of 6.8 g/g, accompanied by hypoalbuminemia (2.3 g/dL) and hypercholesterolemia (total cholesterol 310 mg/dL). Despite these findings, the transplanted kidney function remained stable, and his serum creatinine remained steady at 1.5 mg/dL. Urinalysis revealed heavy proteinuria (4+), but there was no blood in the urine and the sediments were otherwise unremarkable (Table 1).A comprehensive serologic evaluation for secondary causes of FSGS, including viral hepatitis, HIV, antinuclear antibodies, complement levels, and serum protein electrophoresis, was negative.

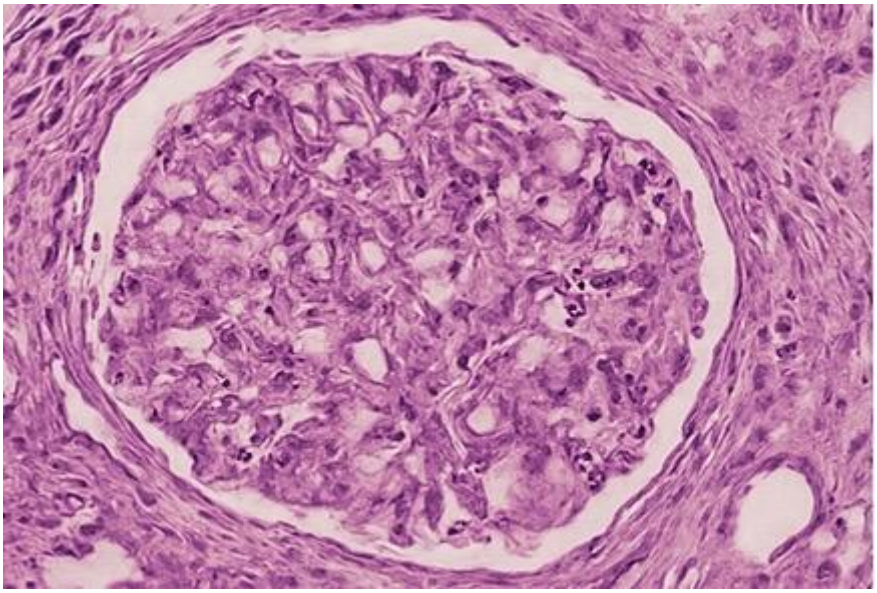

Figure 1. Histopathological features of recurrent focal segmental glomerulosclerosis in a renal allograft biopsy showing segmental glomerular sclerosis and mesangial expansion (periodic acid-Schiff stain; original magnification ×400).

To clarify the cause of his proteinuria, a percutaneous biopsy of the renal allograft was performed on postoperative day 14. The biopsy revealed segmental sclerosis affecting 3 of the 12 glomeruli, with associated moderate mesangial expansion. On electron microscopy, there was diffuse effacement of the podocyte foot processes, findings characteristic of recurrent FSGS (Figure 1). Importantly, there were no features to suggest acute cellular or antibody-mediated rejection, thrombotic microangiopathy, or calcineurin inhibitor toxicity. Immunofluorescence staining was negative for immune complex deposition.

Given early biopsy-confirmed recurrence, the patient was started on low-dose tacrolimus (target trough 4–6 ng/mL), continued mycophenolate mofetil (1 g/day), and received rituximab (375 mg/m^2 weekly for 2 doses). Supportive therapy included ramipril 5 mg once daily (an angiotensin-converting enzyme inhibitor), along with dietary salt and protein restriction and loop diuretics for edema control. Laboratory monitoring was performed weekly for the first month and then monthly.

Within four weeks, proteinuria decreased to 4.2 g/g, serum albumin rose to 2.9 g/dL, and serum creatinine remained stable at 1.4 mg/dL. At three months, proteinuria further declined to 2.1 g/g with normalization of serum albumin (3.4 g/dL). By 12 months, proteinuria was 0.9 g/g, serum albumin 3.8 g/dL, and creatinine 1.2 mg/dL. No infectious complications, hematologic abnormalities, or adverse events related to rituximab or tacrolimus were observed (Table 2).

Table 2. Follow-Up Profile of Kidney Function and Proteinuria from Early Post-Transplant to 12 Months in a Patient with Recurrent (FSGS).

Parameter	Day 14	Week 4	Week 12	Month 12	Reference Range
Creatinine (mg/dL)	1.5	1.4	1.2	1.2	0.8–1.3
Urine Protein-to-Creatinine Ratio (g/g)	6.8	4.2	2.1	0.9	<0.2
Serum Albumin (g/dL)	2.3	2.9	3.4	3.8	3.5–5.0
eGFR (mL/min/1.73 m²)	~52	~56	~68	~68	>90

eGFR was calculated using CKD-EPI 2021 equation.

Discussion

Recurrent FSGS is an uncommon but clinically significant complication following renal transplantation. It occurs in approximately one-third of patients with primary FSGS, and typically presents within the initial post-operative weeks.[10] Early recurrence is linked to circulating permeability factors, such as suPAR, anti-CD40 antibodies, and CLCF-1, which enhance podocyte motility and disrupt slit-diaphragm integrity, leading to foot process effacement and segmental sclerosis.[11,12] These mechanisms result in podocyte injury, resulting in nephrotic-range proteinuria and progressive glomerular sclerosis.[11] Although circulating permeability factors were not directly measured in our patient, the clinical course and biopsy findings strongly suggest permeability factor–driven pathogenesis. In our patient, onset at day 14 post-transplant is consistent with previously reported timelines, which highlights the importance of early recognition. Laboratory markers, including proteinuria and hypoalbuminemia, were critical for early detection, and renal biopsy provided definitive confirmation, aligning with the current recommendations for prompt tissue diagnosis.[12]

Conventional immunosuppressive strategies, including corticosteroids and calcineurin inhibitors, are often ineffective at preventing recurrent FSGS.[13] B-cell-targeted therapy with rituximab has emerged as a potential adjuvant, stabilizing podocytes, reducing proteinuria, and improving graft survival.[14] In our patient, the combination of rituximab, low-dose tacrolimus, and mycophenolate mofetil led to a progressive improvement of proteinuria, normalization of serum albumin over a 12-month follow-up, and minimization of nephrotoxicity while maintaining immunosuppressive efficacy, thereby demonstrating the impact of early, targeted therapy.

Strengths of this case include detailed clinical and laboratory monitoring, early biopsy confirmation, structured immunosuppressive adjustment, and longitudinal follow-up documenting stable graft function. Limitations include the single-patient design, follow-up limited to 12 months, and the absence of direct measurement of circulating permeability factors, which would have offered additional mechanistic insight. Nevertheless, this case supports the growing evidence on early, targeted immunosuppressive regimens for recurrent FSGS post-transplant.

Conclusion

Recurrence of focal segmental glomerulosclerosis post-kidney transplant is uncommon but carries a high risk of graft dysfunction. Early recognition through laboratory monitoring and biopsy, combined with tailored immunosuppressive therapy including rituximab, low-dose tacrolimus, and mycophenolate mofetil, can lead to remission of proteinuria, normalization of hypoalbuminemia, and stabilization of renal function. This case highlights the need for physicians to remain vigilant for possible FSGS recurrence post-kidney transplantation, as well as the importance of individualized management and emerging therapeutic strategies to optimize outcomes in post-transplant FSGS.

Ethical Considerations

Written informed consent was obtained from the patient for publication of this case report and accompanying images. IRB approval was not required for this single-patient case report, as per institutional policy. All procedures were conducted in accordance with the Declaration of Helsinki.

Submitted: October 03, 2025 EDT. Accepted: October 05, 2025 EDT. Published: October 07, 2025 EDT.

REFERENCES

1. Sethi S, Fervenza FC, Zand L, et al. Focal segmental glomerulosclerosis: clinical and kidney biopsy correlations. *Clinical Kidney Journal*. doi:10.1093/ckj/sfu100

2. Raina R, Jothi S, Haffner D, et al. Post-transplant recurrence of focal segmental glomerulosclerosis: consensus statements. *Kidney Int*. 2024;105(3):405-463. doi:10.1016/j.kint.2023.10.017

3. Boonpheng B, Hansrivijit P, Thongprayoon C, et al. Rituximab or plasmapheresis for prevention of recurrent focal segmental glomerulosclerosis after kidney transplantation: a systematic review and meta-analysis. *World J Nephrol*. 2021;10(3):45-55. doi:10.5500/wjt.v11.i7.303

4. Harshman LA, Bartosh S, Engen RM. Focal segmental glomerulosclerosis: Risk for recurrence and interventions to optimize outcomes following recurrence. *Pediatr Transplant*. 2022;26(6):e14307. doi:10.1111/petr.14307

5. Rheault MN, Gadegbeku CA, Kopp JB, et al. A randomized controlled trial of preemptive rituximab to prevent recurrent focal segmental glomerulosclerosis post-kidney transplant (PRI-VENT FSGS): protocol and study design. *Front Nephrol*. 2023;3:1181076. doi:10.3389/fneph.2023.1181076

6. Plonsky-Toder M, Pollack S, Tibi R, et al. Management and long-term outcome of recurrent focal segmental glomerulosclerosis after kidney transplantation. *Sci Rep*. 2024;14(1):1234. doi:10.1038/s41598-024-74184-z

7. Gharaei S, Gharaei J, Ragy O, et al. Use of rituximab and plasma exchange in treatment and prevention of recurrent focal segmental glomerulosclerosis after kidney transplantation. *Clin Kidney J*. 2025;18(3):345-352. doi:10.1093/ckj/sfaf058

8. Angeletti A, Bin S, Magnasco A, et al. Efficacy of combined rituximab and daratumumab in treatment-resistant recurrent focal segmental glomerulosclerosis after kidney transplantation. *Am J Transplant*. 2024;24(5):1234-1240. doi:10.1016/j.ajt.2023.12.010

9. Sabarinath S, Prasad N. Recurrent Focal Segmental Glomerulosclerosis after Kidney Transplantation: Challenges and Evolving Strategies. *Indian Journal of Transplantation*. 2025;19(1):1-2. doi:10.4103/ijot.ijot_32_25

10. Pollack S, Plonsky-Toder M, Tibi R, et al. Subcutaneous ofatumumab in recurrent focal segmental glomerulosclerosis after kidney transplantation: a pilot study. *Clin Kidney J*. 2025;18(4):567-573. doi:10.1093/ckj/sfaf083

11. Bai J, Zhang T, Wang Y, et al. Incidence and risk factors for recurrent focal segmental glomerulosclerosis after kidney transplantation: a multicenter study. *J Nephrol*. 2023;36(2):345-352. doi:10.1080/0886022x.2023.2201341

12. Hou S, Yang B, Chen Q, et al. Potential biomarkers of recurrent focal segmental glomerulosclerosis after kidney transplantation: a review. *BMC Nephrol*. 2024;25(1):45. doi:10.1186/s12882-024-03695-8

13. Lanaret C, Anglicheau D, Audard V, et al. Rituximab for recurrence of primary focal segmental glomerulosclerosis after kidney transplantation: a case series. *Am J Transplant*. 2022;22(5):1234-1240. doi:10.1111/ajt.16504

14. Wang L, Yu L, Wang Y, et al. Rituximab treatment of adults with primary focal segmental glomerulosclerosis: a retrospective study. *Sci Rep*. 2023;13(1):6740. doi:10.1038/s41598-023-33678-y