Kidney Medicine

Subcutaneous Daratumumab in Recurrent Posttransplant Focal Segmental Glomerulosclerosis: A Report of 2 Cases

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Recurrent primary focal segmental glomerulosclerosis (FSGS) after kidney transplantation requires prolonged treatment, often with unsatisfactory results. We report 2 cases of FSGS recurrence that achieved remission with subcutaneous daratumumab and propose novel mechanisms of its action that demonstrate efficacy in this disease. The first patient was a 51-year-old woman who experienced early FSGS recurrence 1 month after transplantation. With regular biweekly plasma exchange, her daily proteinuria was 1-1.5 g, and the estimated glomerular filtration rate was 43 mL/min/1.73 m^2. Although 2 doses of rituximab depleted CD19/20 B lymphocytes, they were ineffective in reducing proteinuria, leading to the reintroduction of plasma exchange. Based on histological persistence of FSGS at the 1-year surveillance biopsy, subcutaneous daratumumab treatment was initiated, which led to a rapid decrease in proteinuria and disease remission. The second patient was a 25-year-old woman with a second relapse of FSGS 7 years after transplantation, which was immune adsorption dependent as rituximab was ineffective in inducing remission. A kidney biopsy performed 2 years later showed persistence of FSGS as well as chronic active antibody-mediated rejection. Daratumumab treatment was initiated using the chronic active antibody-mediated rejection treatment protocol. With this treatment, daily proteinuria decreased from 6 g to 0.3-0.5 g, and immune adsorption was discontinued. In conclusion, daratumumab shows promise in controlling recurrent FSGS in selected kidney transplant recipients with potential mechanisms beyond plasma and natural killer cells.

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Kidney Med. 8(9):101473. Published online July 15, 2026.

doi: 10.1016/j.xkme.2026.101473

INTRODUCTION

Primary focal segmental glomerulosclerosis (FSGS) has a high posttransplant recurrence rate[1,2] that is associated with an increased risk of graft loss.[1,3,4] Despite early initiation of plasma exchange (PEX) or immune adsorption (IA) often in combination with rituximab, complete remission is achieved in about 40% of cases, with treatment often poorly tolerated and burdensome.[5] Newer agents such as the B cell–depleting obinutuzumab and the plasma cell–targeting daratumumab have shown promise in small case series, mostly in combined infusion treatment.[6]

In this study, we present 2 cases of FSGS recurrence that were successfully treated with subcutaneous daratumumab, resulting in complete remission and withdrawal of PEX/IA.

A REPORT OF 2 CASES

Case 1

The first patient was a 52-year-old White woman who presented with nephrotic syndrome at the age of 37. The initial kidney biopsy (KB) revealed minimal change disease, and a year later, FSGS, perihilar variant, was diagnosed. Unfortunately, despite treatment, her kidney function slowly deteriorated, and she underwent a deceased-donor kidney transplant (KT) 13 years later. The patient was anuric before KT. One month after KT, nephrotic-range proteinuria was detected during routine outpatient follow-up, and KB revealed FSGS recurrence with 70% fusion of podocyte foot processes. PEX was initiated, along with pulse steroids. Perindopril 4 mg daily was started. After partial remission was achieved, the frequency of PEX was reduced to biweekly treatment. A native arteriovenous fistula was constructed in her left forearm to provide vascular access. PEX and methylprednisolone were poorly tolerated and resulted in only partial remission of the disease, with daily proteinuria of 1-2 g. Eight months after FSGS recurrence, 2 doses of rituximab were administered with no effect, which led to the reintroduction of biweekly PEX. At that time, dapagliflozin was initiated, and the dose of perindopril was increased to 4 mg twice daily. Based on the results of the 1-year surveillance KB, which showed histological persistence of FSGS (Fig 1) and poorly tolerated maintenance treatment, we opted for an experimental treatment with daratumumab, an anti-CD38 monoclonal antibody previously reported as successful.[6,7] We decided to try daratumumab alone in the subcutaneous form and a fixed dose of 1,800 mg. The treatment protocol that was used is described in detail in Item S1. The first dose of daratumumab was well tolerated and resulted in a rapid decrease in proteinuria from 1.5 g/d to 0.3-0.5 g/d, as well as discontinuation of PEX. Another dose of daratumumab 1,800 mg subcutaneously was given almost 3 months later owing to persistent low-grade proteinuria (0.3-0.5 g/d), which led to a further decrease in daily proteinuria to 0.16-0.2 g. No prophylactic therapy was initiated, and no clinically relevant opportunistic infections were detected. Maintenance immunosuppression was not modified. One month after

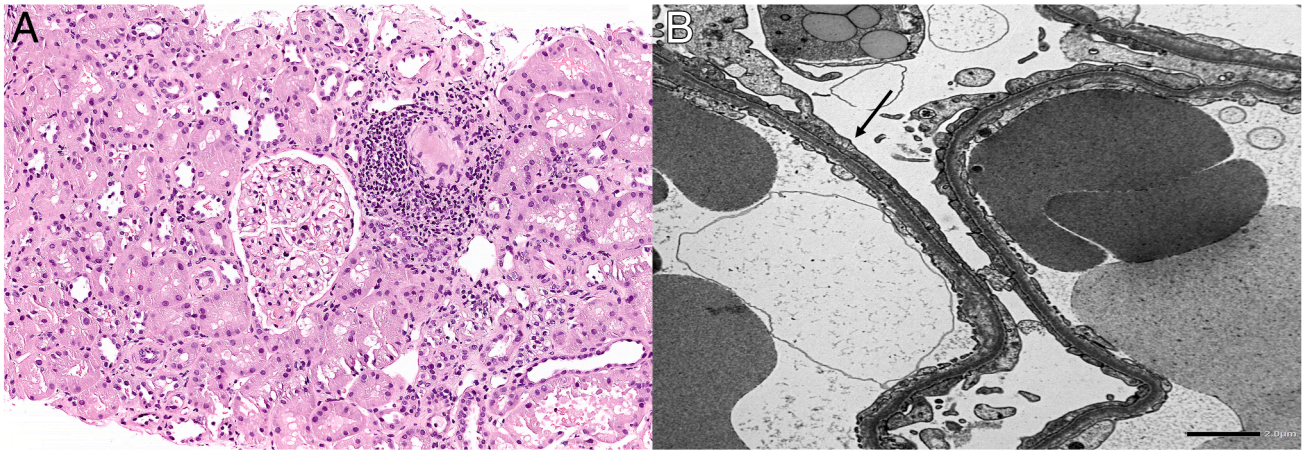

Figure 1. Light microscopy (hematoxylin and eosin, ×20) showing only focal, nonspecific chronic changes involving all parts of the nephron. (A) Viable glomeruli that are histologically unremarkable. (B) Electron microscopy of the viable glomeruli confirming ultrastructural signs of persistent podocytopathy (diffuse, ∼70% foot process effacement of reactively altered podocytes, indicated by the arrow).

the second dose of daratumumab and 5 months after PEX was withdrawn, the disease remained in full remission (daily proteinuria below 0.3 g), and we decided to gradually withdraw steroids owing to poor tolerance, particularly weight gain and hypertension. Nine months after PEX was withdrawn and 6 months after the second dose of daratumumab, the patient is in good overall health with stable kidney function and daily proteinuria averaging below 0.3 g. The timeline of treatment and changes in daily proteinuria are shown in Fig 2. Before and during treatment, we measured lymphocytic populations in the peripheral blood with results presented in Item S1.

Case 2

The second patient was a previously reported 25-year-old woman who carried single heterozygous *NPHS1* (p.N188I; AAC>ATC) and *NPHS2* (p.R229Q; CGA>CAA) genetic variants.[8] She had been treated with hemodialysis and was anuric before KT. Eleven days posttransplant, early FSGS recurrence required the introduction of PEX that was performed through a jugular central venous catheter that led to the formation of right atrial thrombus requiring surgical removal. After several unsuccessful attempts, a right forearm arteriovenous fistula was successfully constructed, ensuring vascular access for PEX. Four years after KT, full disease remission was achieved. Seven years after KT, FSGS relapsed with no signs of rejection on KB. The patient was retreated with pulse steroids and reintroduction of the intensive PEX regimen (2-3 weekly sessions) followed by 2 fixed doses of rituximab 1,000 mg. The treatment was unsuccessful, and IA was started 8 years after transplantation. Biweekly IA induced a partial remission with daily proteinuria ranging from 2-2.5 g. Unfortunately, recurrent thromboses led to the failure of arteriovenous fistula. Given the history of atrial thrombus after the insertion of jugular central venous catheter, IA was subsequently performed through a temporary central venous catheter inserted in the femoral vein before every IA procedure. With limited vascular access options and low proteinuria (0.3-0.5 g/d), the frequency of IA was reduced to every 4 and later to every 8 weeks. Nine years after KT and 3 years after FSGS recurrence, an increase in daily proteinuria to 1g was detected on routine outpatient follow-up. Antiproteinuric agents were not initiated because of low blood pressure (100-110/60 mm Hg). Donor-derived cell-free DNA (dd-cfDNA) was increased at 4%, and de novo donor-specific antibodies (DSA) anti-A11, -B56, -Cw1, -Cw12, and -DR1 were present in the patient's serum with a low mean fluorescence intensity (180-340). A KB confirmed chronic active antibody-mediated rejection (cABMR) with segmental fusion of podocyte foot processes (30%). IA was discontinued, and daratumumab was started following our center's experimental protocol for cABMR used at the time. Before daratumumab treatment was initiated, proteinuria increased to 6.4 g/d and later gradually decreased. A rebiopsy after 6 months of treatment showed no signs of active rejection in conventional and molecular biopsy (Molecular Microscope Diagnostic System [MMDx]) together with low levels of proteinuria (0.2 g/d) and low dd-cfDNA (0.3%). The change in dd-cfDNA is shown in Fig S1. The change in DSA with daratumumab treatment are presented in Table S2 and the trend in peripheral lymphocyte count measured by flow cytometry in Table S3. The patient recently received another fixed dose of daratumumab owing to a mild increase in dd-cfDNA to 0.6% 9 months after initial treatment and is under close supervision at the transplant clinic. Detailed description of both cases is presented in Table S1.

DISCUSSION

Our 2 cases show that daratumumab is an effective treatment option in selected individuals with recurrent FSGS and can lead to full remission with no relevant side effects.

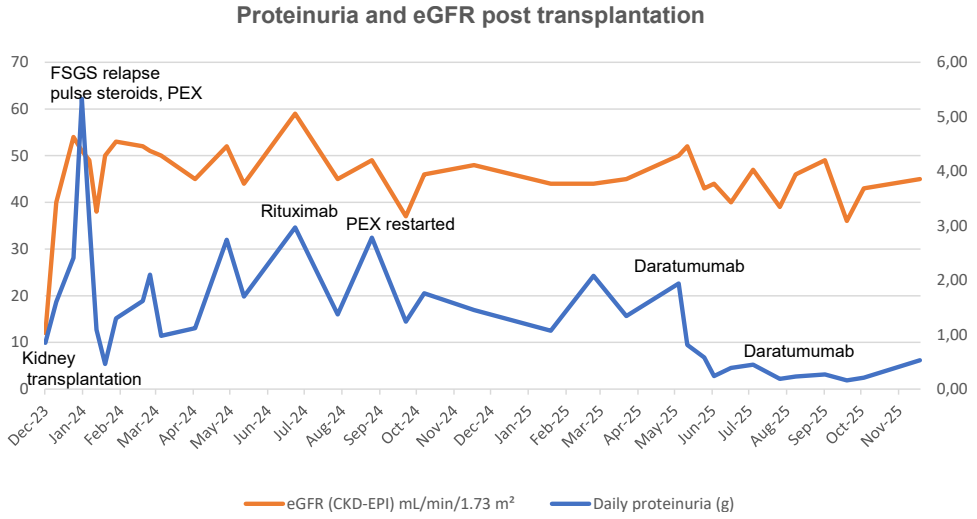

Figure 2. The timeline of treatment and the change in proteinuria in case 1. Abbreviations: eGFR CKD-EPI, estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration; FSGS, focal segmental glomerulosclerosis; PEX, plasma exchange.

Daratumumab is a fully human monoclonal antibody that targets CD38, a transmembrane glycoprotein highly expressed on plasma cells[9] as well as other cell types.[10,11] CD38 is an important molecule in immune regulation and signaling, with its expression induced under inflammatory conditions. Recently, the role of CD38 in immune-mediated diseases has become increasingly recognized.[11]

In the field of KT, anti-CD38 therapies have been successfully used to treat cABMR in both donor-specific antibody–positive and donor-specific antibody–negative cases, which is consistent with their action on plasma as well as natural killer cells.[12]

Anti-CD38 therapies have also been studied in immunoglobulin A nephropathy and membranous nephropathy. In both diseases, a very rapid response to treatment was observed, which could not be attributed solely to the reduction of plasma or natural killer cells. It can be inferred that anti-CD38 therapy has an additional effect on other cell types expressing CD38 that contribute to glomerular damage. For example, CD38 receptors are expressed on the surface of macrophages, in which they promote podocyte injury and apoptosis.[13] In recurrent FSGS, macrophages secrete soluble permeability factors, such as calcium/calmodulin-dependent serine/threonine kinase that contribute to podocyte damage.[14] In addition, it had been shown that podocyte injury can be promoted through chemokine CCL2-dependent macrophage infiltration and activation.[15] Last, CD38 is not only a surface glycoprotein but also a multifunctional enzyme that reduces the tissue NAD+ level and increases NF-κB signal transduction promoting the expression of proinflammatory genes.[16] It had been previously recognized that antibodies targeting anti-CD38 will also affect macrophage function.[16] Therefore, we speculate that the efficacy of daratumumab in our 2 cases was attributed to a decrease in the number of pathogenic macrophages contributing to podocyte injury. It was this targeted action of daratumumab that led us to opt for this treatment alone and not another B cell–depleting agent, because prior rituximab treatment was ineffective in both our patients. We believe CD38+ macrophages may serve as an inflammatory marker of disease activity and could potentially guide treatment decisions in patients with recurrent FSGS.

In our 2 cases, daratumumab was used subcutaneously, in a fixed dose (1,800 mg) as proposed by the Columbia study[17] and recently by a Singapore group in the treatment of cABMR.[18] Daratumumab, administered subcutaneously, is shown to have fewer infusion-related reactions with equal efficacy and easier preparation, with no absolute requirement for a vascular access.[18] In our 2 cases, no infusion-related reactions occurred, and the treatment was well tolerated.

In case 2, although the patient carried single heterozygous *NPHS1* (p.N188I; AAC>ATC) and *NPHS2* (p.R229Q; CGA>CAA) genetic variants, current evidence does not support a pathogenic role for this combination in the absence of additional mutations[19,20] and does not confirm genetic FSGS. The patient suffered from FSGS recurrence 3 years before daratumumab was initiated, which was managed with PEX and later IA. The diagnosis of recurrent FSGS at that time was made histologically with no histological evidence of rejection. Although treatment was successful in inducing a partial remission of FSGS, it required a vascular access that was difficult to maintain owing to recurrent thrombosis of arteriovenous fistula and previous thrombus in the right atrium after central venous catheter insertion. When KB performed owing to an increase in proteinuria and increased dd-cfDNA showed signs of cABMR, we opted for the treatment with daratumumab that has shown previous additional potential in the treatment of recurrent FSGS and required no vascular

access. Because daratumumab targets the pathophysiological mechanisms of both cABMR and FSGS, it can be a valuable single therapeutic option for patients with a history of both diseases. In addition, even in a patient with known FSGS and suspected recurrence after KT, an increase in proteinuria should prompt additional tests, including KB, to rule out pathologies other than FSGS. Rebiopsy should not be delayed owing to known FSGS recurrence, as this may prevent the patient from receiving prompt and adequate treatment. The importance of a biopsy to confirm FSGS recurrence has recently been emphasized by a commentary on the role of bleselumab in preventing recurrent FSGS.[21] Bleselumab, a humanized monoclonal CD40 antibody, not only failed to show a significant benefit in preventing FSGS recurrence but also has shown potential to increase the risk of rejection when replacing mycophenolate mofetil.[22] It seems that standard maintenance immunosuppression should not be modified or minimized in patients who receive additional treatment for recurrent FSGS, as this may increase the risk of rejection. In case 2, the dose of mycophenolic acid was lowered when she started treatment of FSGS recurrence 3 years prior, potentially contributing to the development of cABMR.

In conclusion, our report demonstrates that subcutaneous daratumumab is an effective and safe treatment option for patients with recurrent FSGS and concomitant cABMR. Treatment decisions should be based on histological findings detected on KB and not only on the level of proteinuria. The dosing interval of daratumumab should be individualized, considering daily proteinuria, potential side effects of increased immunosuppression, and possibly rebiopsy results. We need novel biomarkers to better predict successful treatment outcomes of recurrent FSGS with daratumumab.

SUPPLEMENTARY MATERIALS

Supplementary File (PDF)

Figure S1: The Relative Percentage Change in Donor-Derived Cell-Free DNA in Case 2.

Item S1: Supplementary Appendix.

Table S1: The Trend in Peripheral Lymphocyte Count Measured by Flow Cytometry in Case 1.

Table S2: The Change in DSA (Luminex/One Lambda-LabScreen Single Antigen Assay) With Daratumumab Treatment in Case 2.

Table S3: The Trend in Peripheral Lymphocyte Count Measured by Flow Cytometry in Case 2.

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Support: The funding of this article was supported by the Slovenian Research and Innovation Agency under grant P3-0323.

Financial Disclosure: The authors declare that they have no relevant financial interests.

Acknowledgments: The authors would like to thank the Institute of Microbiology and Immunology at the Faculty of Medicine, University of Ljubljana, for the analysis of lymphocytic populations.

Patient Protections: The authors declare that they have obtained informed consent from the patients reported in this article for publication of the information about them that appears within this Case Report.

Peer Review: Received January 12, 2026. Evaluated by 1 external peer reviewer, with direct editorial input from an Associate Editor and the Editor-in-Chief. Accepted in revised form May 01, 2026.

REFERENCES

1. Uffing A, Perez-Saez MJ, Mazzali M, et al. Recurrence of FSGS after kidney transplantation in adults. *Clin J Am Soc Nephrol*. 2020;15(2):247-256.
2. Chadban SJ, Ahn C, Axelrod DA, et al. KDIGO clinical practice guideline on the evaluation and management of candidates for kidney transplantation. *Transplantation*. 2020;104(4S1)(suppl 1):S11-S103.
3. Francis A, Trnka P, McTaggart SJ. Long-term outcome of kidney transplantation in recipients with focal segmental glomerulosclerosis. *Clin J Am Soc Nephrol*. 2016;11(11):2041-2046.
4. Kim DK, Huh H, Kim Y, et al. Recurrent and de novo focal segmental glomerulosclerosis after kidney transplantation: comparison of clinical features and transplant outcomes. *Transplant Proc*. 2024;56(8):1752-1756.
5. Hansrivijit P, Ghahramani N. Combined rituximab and plasmapheresis or plasma exchange for focal segmental glomerulosclerosis in adult kidney transplant recipients: a meta-analysis. *Int Urol Nephrol*. 2020;52(7):1377-1387.
6. Randone P, Sanna E, Dolla C, et al. Rescue with obinutuzumab and daratumumab as combined B cell/plasma cell targeting approach in severe posttransplant focal segmental glomerulosclerosis recurrence. *Am J Transplant*. 2024;24(10):1896-1900.
7. Angeletti A, Bin S, Magnasco A, Bruschi M, Cravedi P, Ghiggeri GM. Efficacy of combined rituximab and daratumumab treatment in posttransplant recurrent focal segmental glomerulosclerosis. *Am J Transplant*. 2024;24(4):688-692.
8. Battelino N, Arnol M, Kandus A, Ponikvar R, Novljan G. Post-transplant recurrence of focal segmental glomerulosclerosis in a child with heterozygous mutations in NPHS1 and NPHS2. *Ther Apher Dial*. 2016;20(3):312-317.
9. Sanchez L, Wang Y, Siegel DS, Wang ML. Daratumumab: a first-in-class CD38 monoclonal antibody for the treatment of multiple myeloma. *J Hematol Oncol*. 2016;9(1):51.
10. Roccatello D, Fenoglio R, Sciascia S, et al. CD38 and anti-CD38 monoclonal antibodies in AL amyloidosis: targeting plasma cells and beyond. *Int J Mol Sci*. 2020;21(11):4129.
11. Ye X, Zhang J, Song M, et al. Evolving understandings for the roles of CD38 protein in autoimmunity and autoimmune disease. *Clin Exp Immunol*. 2026;220(1):uxag014.

12. Mayer KA, Schrezenmeier E, Diebold M, et al. A randomized phase 2 trial of felzartamab in antibody-mediated rejection. *N Engl J Med*. 2024;391(2):122-132.
13. Li HD, You YK, Shao BY, et al. Roles and crosstalks of macrophages in diabetic nephropathy. *Front Immunol*. 2022;13:1015142.
14. Zhang X, Herr F, Vernochet A, Lorenzo HK, Beaudreuil S, Durrbach A. CASK, the soluble glomerular permeability factor, is secreted by macrophages in patients with recurrent focal and segmental glomerulo-sclerosis. *Front Immunol*. 2020;11:875.
15. Ren J, Xu Y, Lu X, et al. Twist1 in podocytes ameliorates podocyte injury and proteinuria by limiting CCL2-dependent macrophage infiltration. *JCI Insight*. 2021;6(15):e148109.
16. Li W, Li Y, Jin X, et al. CD38: a significant regulator of macrophage function. *Front Oncol*. 2022;12:775649.
17. Mateos MV, Nahi H, Legiec W, et al. Subcutaneous versus intravenous daratumumab in patients with relapsed or refractory multiple myeloma (COLUMBA): a multicentre, open-label, non-inferiority, randomised, phase 3 trial. *Lancet Haematol*. 2020;7(5):e370-e380.
18. Lye WC, Loh HL. Anti-CD38 daratumumab treatment of chronic active antibody-mediated kidney allograft rejection. *Kidney Int Rep*. 2025;10(10):3506-3515.
19. Gibson J, Gilbert RD, Bunyan DJ, Angus EM, Fowler DJ, Ennis S. Exome analysis resolves differential diagnosis of familial kidney disease and uncovers a potential confounding variant. *Genet Res (Camb)*. 2013;95(6):165-173.
20. Rood IM, Deegens JKJ, Lugtenberg D, Bongers E, Wetzels JFM. Nephrotic syndrome with mutations in NPHS2: the role of R229Q and implications for genetic counseling. *Am J Kidney Dis*. 2019;73(3):400-403.
21. Mahgoub M, Zand L. Recurrent FSGS post-kidney transplantations: where do we stand? *Transplantation*. 2026;110(1):e21-e22.
22. Shoji J, Goggins WC, Wellen JR, et al. Efficacy and safety of bleselumab in preventing the recurrence of primary focal segmental glomerulosclerosis in kidney transplant recipients: a phase 2a, randomized, multicenter study. *Transplantation*. 2024;108(8):1782-1792.