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Nephrotic syndrome with sunitinib-associated focal segmental glomerulosclerosis in a patient with renal carcinoma: partial reversibility after dose adjustment. Case Report.

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Received: March 23, 2025.
Accepted: August 1, 2025.
Published: August 8, 2025.
Edited by Dr. Franklin Mora Bravo.

How to cite:
Quinchuela J, Arias A, Araujo P, Mafla C, Landeta P, Remache V, Rincón H. Nephrotic syndrome with sunitinib-associated focal segmental glomerulosclerosis in a patient with renal carcinoma: partial reversibility after dose adjustment. Case report. REV SEN 2025; 13(2):149-155.

DOI: http://doi.org/10.56867/118
Sociedad Ecuatoriana de Nefrología, Diálisis y Trasplantes.

ISSN-L: 2953-6448

Abstract

Introduction: Vascular endothelial growth factor (VEGF) is produced by podocytes and helps maintain the endothelial structure and the glomerular filtration barrier. Inhibition of VEGF, used in cancer treatment with sunitinib, can cause kidney side effects. These include high blood pressure, proteinuria, and sometimes structural damage such as focal segmental glomerulosclerosis.

Case report: A 78-year-old woman with a history of high blood pressure, asthma, hypothyroidism, and deep vein thrombosis. In November 2022, an active bone lesion was detected in the left femur. The biopsy confirmed metastatic tubular clear cell adenocarcinoma, consistent with a primary renal tumor. A right radical nephrectomy was performed, and palliative treatment with Sunitinib was initiated, later adjusted to a schedule of 2 weeks on treatment and 1 week off due to toxicity. The patient also received cervical radiotherapy and placement of a prosthesis in the left femur. During oncological follow-up, progressive edema and anasarca were observed. Renal biopsy reported lesions with focal and segmental glomerulosclerosis.

Treatment: Treatment was started with valsartan 80 mg QD, intravenous furosemide, and subsequently rotated to indapamide, statin, and sodium glucose cotransporter inhibitor type 2 with dapaglifozin 10 mg once daily. The dose of sunitinib was decreased to 50% (25 mg once daily).

Evolution: A favorable evolution of the clinical picture was evidenced with progressive improvement of peripheral edema, decreased proteinuria, and azotemia.

Conclusions: In this case of glomerulopathy induced by VEGF inhibitors, the use of ARBs II and SGLT2 inhibitors may contribute to preserving renal function and promoting the continuity of cancer treatment.

Keywords:

Focal segmental glomerulosclerosis, Sunitinib, Nephrotic syndrome, Case report.

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Vascular endothelial growth factor (VEGF) functions to maintain glomerular endothelium homeostasis and podocyte survival, preserving the integrity of the renal filtration barrier. Under physiological conditions, VEGF is produced locally by podocytes and acts in a paracrine manner on the endothelial cells of glomerular capillaries, contributing to the structural and functional maintenance of the renal filtration unit.

The pharmacological inhibition of VEGF, which is commonly used to treat solid tumors like renal cell carcinoma, has shown significant clinical success. Sunitinib is a multikinase inhibitor that blocks VEGFR, PDGFR, and c-Kit receptors and is used in advanced stages of disease. Its use has been linked to various kidney problems, including high blood pressure, proteinuria, and occasionally, structural glomerulopathies such as focal segmental glomerulosclerosis (FSGS).

In recent years, more cases of renal injury caused by VEGF inhibitors have been reported, both with systemic and local use. The clinical signs range from mild proteinuria to full nephrotic syndrome with worsening kidney function. In many of these patients, renal biopsy shows a pattern consistent with FSGS, indicating direct podocyte damage due to disruption of the VEGF-VEGFR axis [1]. We present the case below.

Clinical case

Clinical history

A 78-year-old woman with a history of high blood pressure, asthma, hypothyroidism, and deep vein thrombosis. In November 2022, an active bone lesion was detected in the left femur. Biopsy confirmed clear cell metastatic tubular adenocarcinoma, consistent with a primary renal tumor. She underwent right radical nephrectomy, and palliative treatment with sunitinib was initiated, with a schedule of 2 weeks of treatment followed by 1 week of recovery due to toxicity. The patient also received cervical radiotherapy and placement of a megaendoprosthesis in the left femur. During follow-up, progressive edema and anasarca were observed.

Diagnostic workshop

Proteinuria was documented in the nephrotic range (8,747.6 mg/24 h) with preserved urinary volume (950 mL/24 h), along with hypoalbuminemia (2.55 g/dL), dyslipidemia, and progressive deterioration of renal function (GFR CKD-EPI <30 mL/min/1.73 m²), leading to the diagnosis of complete nephrotic syndrome and a high suspicion of nephropathy secondary to sunitinib. Table 1 shows the evolution of the nitrogenous parameters in detail, showing a progressive increase in serum urea and creatinine levels, with maximum values of 68.7 mg/dL and 2.33 mg/dL, respectively. This trend is consistent with a deterioration in acute or subacute renal function, possibly associated with glomerular involvement.

Immunological tests were negative for related autoimmune or infectious diseases (ANA, ANCA, HBsAg, anti-HCV, HIV, and VDRL), supporting a toxic and secondary cause of glomerular involvement.

On March 12, 2025, a percutaneous renal biopsy was performed, revealing a renal parenchyma composed of the cortex, medulla, and corticomedullary junction. Thirteen glomeruli were identified in the optical analysis: one with global sclerosis and four with segmental sclerosis, some of which were associated with the vascular pole. All glomeruli showed widening of the mesangial matrix and evidence of hyalinosis. Tubular atrophy was less than 5%, and focal interstitial fibrosis was also less than 5%, accompanied by lymphocytic inflammatory infiltration and pigmented casts. The arterioles exhibited hyalinization of their walls without evidence of amyloid deposits (Congo Red negative).

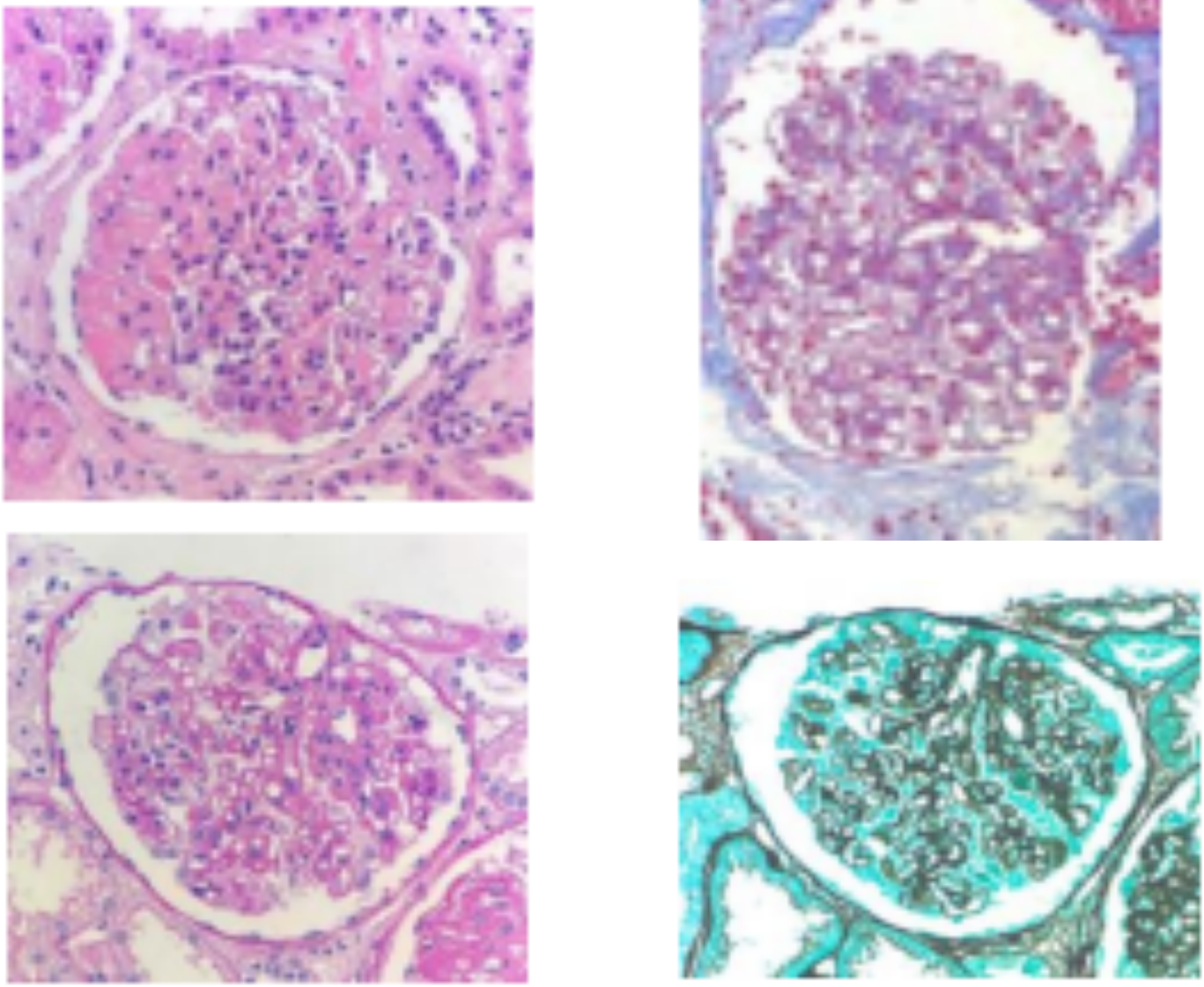
In the direct immunofluorescence study, negative results were observed for IgG, IgA, C3, C1q, kappa, and lambda light chains; IgM entrapment was seen only in nodular areas. These findings confirmed the histological diagnosis of focal segmental glomerulosclerosis (FSGS) with a low chronicity index (score of 1), which is consistent with a secondary form induced by drugs (Figure 1).

At the same time, the patient presented progressive pancytopenia, as detailed previously in Table 2, where hemoglobin (from 10.1 to 8.1 g/dL), leukocytes (from 3,460 to 2,480 cells/µL), and platelets (from 57,000 to 42,000 cells/µL) significantly decreased.

Treatment

Supportive treatment commenced with a type 2 angiotensin receptor blocker, specifically 80 mg of valsartan once daily, along with a loop diuretic, intravenous furosemide. It was then switched to indapamide, a statin, and a type 2 sodium-glucose cotransporter inhibitor, dapagliflozin, 10 mg once daily. In conjunction with the oncology service, the sunitinib dose was reduced to 25 mg once daily, which is 50%, since there was no other chemotherapy option and treatment suspension was ruled out due to the patient's characteristics.

Figure 1. Kidney biopsy.



Evolution

The positive progression of the clinical condition was shown by steady improvements in peripheral edema and reductions in proteinuria and nitrogen oxide levels after sunitinib was discontinued.

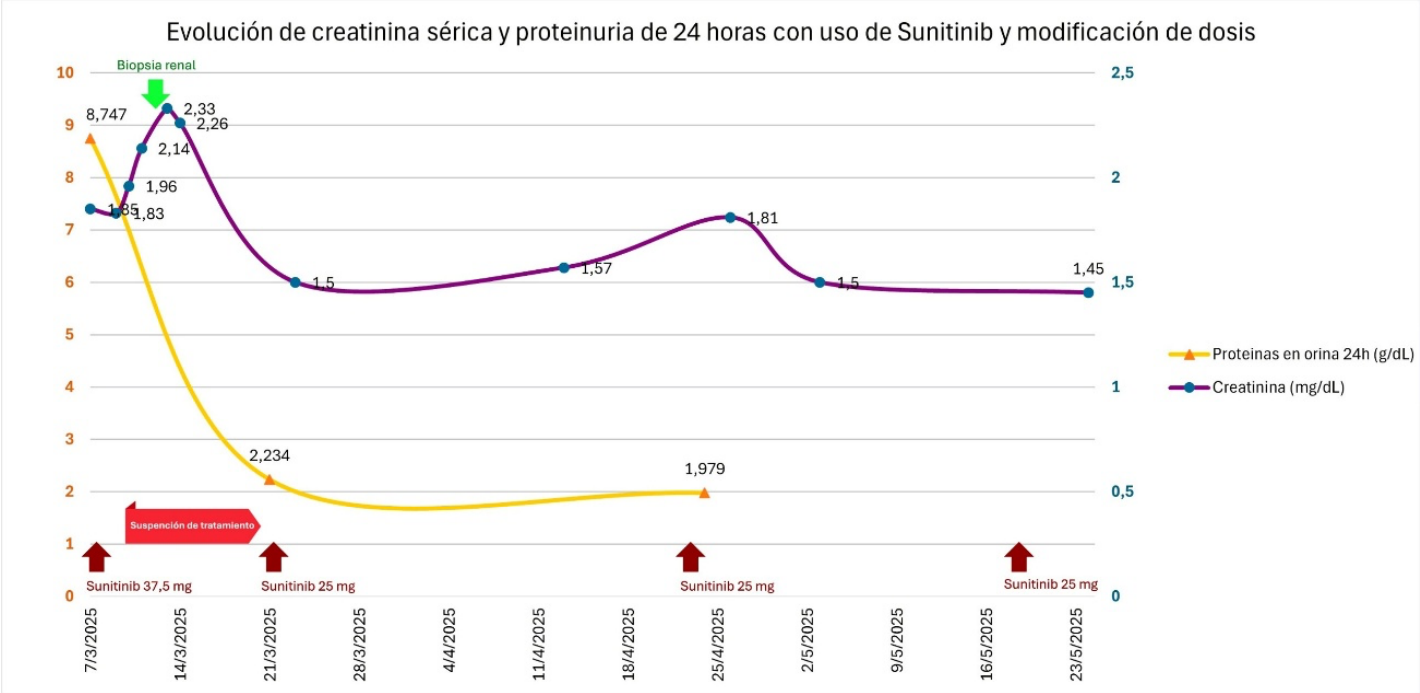
Table 1. Evolution of nitrogenous parameters (March 5 to 12, 2025).

Parameter	5/3/2025	7/3/2025	8/3/2025	9/3/2025	11/3/2025	12/3/2025
Urea (mg/dL)	54,0	55,1	57,2	61,5	68,7	57,9
Creatinine (mg/dL)	1,85	1,83	1,96	2,14	2,33	2,26
BUN (mg/dL)	29,9	25,7	26,7	28,7	32,1	31,4

Table 2. Evolution of hematic biometry parameters (March 5 to 12, 2025).

Parameter	5/3/2025	7/3/2025	8/3/2025	9/3/2025	10/3/2025	11/3/2025	12/3/2025
Hemoglobin (g/dL)	10,1	9,6	9,2	8,9	10,2	8,3	8,1
Platelets (cel/µL)	57.000	42.000	51.000	58.000	59.000	176.000	173.000
Leukocytes (cel/µL)	3.460	1.860	1.830	2.340	2.780	2.920	2.480
Neutrophils (cel/µL)	2.360	1.300	820	910	1.660	1.780	1.160

Figure 2. Changes in serum creatinine levels and 24-hour proteinuria in a patient treated with sunitinib (March - May 2025).



Discussion

Inhibitors of vascular endothelial growth factor (VEGF), such as sunitinib, have revolutionized the treatment of several solid tumors. However, their renal toxicity profile necessitates strict clinical monitoring, as they can cause glomerular lesions like focal segmental glomerulosclerosis (FSGS). Although this is a rare adverse event, it may be reversible if detected early and the treatment plan is adjusted [2-4].

In the case presented here, the patient developed complete nephrotic syndrome, which was confirmed by renal biopsy, such as FSGS, with no findings of underlying autoimmune or infectious disease. The clinical context and timing support a causal link with sunitinib treatment. Notably, dose adjustments of the drug, along with nephrological support, allowed partial stabilization of renal function, preventing the need to definitively discontinue oncological treatment. These findings align with previous reports [1], showing that stopping or adjusting the dose of VEGF inhibitors can reverse glomerular injury. Therefore, the importance of regularly monitoring proteinuria and renal function in patients on antiangiogenic therapies is emphasized.

The graph and tables provide a clear view of how renal parameters changed between March 7 and May 24, 2025. Serum creatinine levels initially rose from 1.83 mg/dL (03/09/2025) to a peak of 2.33 mg/dL (03/17/2025), indicating impaired kidney function shortly after starting treatment. A gradual improvement followed, with levels

decreasing to 1.5 mg/dL (03/23/2025) and remaining stable at 1.45 mg/dL through the end of the follow-up. This pattern aligns temporarily with the dose adjustment of sunitinib.

Meanwhile, 24-hour urine proteinuria dropped significantly from 8.747 g/dL (03/07/2025) to 2,234 g/dL (03/23/2025), and finally to 1.979 g/dL (04/22/2025). This sustained decline suggests improved glomerular health, likely due to reduced renal toxicity following treatment adjustment. From a clinical perspective, these findings align with what has been documented in the literature. VEGF inhibitor-induced FSGS, although rare, is an increasingly recognized complication. Similar cases have been reported with partial or complete reversibility after adjustment of antiangiogenic therapy [3], and it has been reported that renal toxicity induced by these agents can manifest as significant proteinuria, acute renal failure, or nephrotic syndrome, with some of these events potentially being reversible if identified early [5, 6].

Likewise, the cases described by Azar et al. [7] and Chen et al. [8] strengthen the connection between sunitinib use and the development of nephropathy, emphasizing the need for timely intervention during the clinical course. The authors concluded that continuous 24-hour monitoring of serum creatinine and urine protein is vital for early detection of nephrotoxicity and proper treatment decisions. In summary, the data shown in the graph and tables support a causal link between sunitinib treatment and the observed glomerular injury. Renal improvement after adjusting the VEGF inhibitor dose further supports this hypothesis. As proposed by Kakeshita et al.1 and Overkleeft et al. [9], active surveillance in patients receiving these agents constitutes a fundamental strategy to prevent irreversible kidney damage and preserve the continuity of cancer treatment.

Alongside adjusting the sunitinib dose, it is crucial to consider additional pharmacological strategies to reduce kidney damage and manage hypertension linked to VEGF inhibitors. The prevalence of these side effects can range from 20% to 90%, depending on the potency and dose of the chemotherapeutic agents. This condition is also reversible, resolving when the medication is stopped, and its pathophysiology involves inhibition of VEGF's vasodilatory capacity, increased levels of the vasoconstrictor endothelin-1, greater production of reactive oxygen species, and microvascular rarefaction. In this context, angiotensin II receptor antagonists (ARBs) are effective options for both blood pressure control and the reduction of proteinuria. ARBs not only lower blood pressure but also offer renoprotective benefits by decreasing intraglomerular pressure and modulating the kidney's inflammatory and fibrogenic responses [10 -15]. In patients with glomerulopathy caused by VEGF inhibitors, the use of ARA II can help preserve renal function and support the continuation of cancer treatment. Therefore, incorporating these strategies into a multidisciplinary approach can enhance clinical outcomes, reduce complications, and improve patient quality of life.

Conclusions

This case shows focal and segmental glomerulosclerosis linked to sunitinib use, with proteinuria reversing after stopping the drug.

Abbreviations

ANA: antinuclear antibodies.
FSGS: Focal and segmental glomerulosclerosis.

Supplementary information

The supplementary materials have not been provided.

Acknowledgments

Does not apply.

Authors' contributions

Jorge Oswaldo Quinchuela Hidalgo: Conceptualización, administración del proyecto, supervisión, validación, visualización, escritura, revisión y edición.
Andrés Arias Casierra: Conceptualización, metodología, investigación.
Paúl Araujo: Conceptualización, metodología, investigación.
Verónica Remache: Conceptualización, metodología, investigación, Escritura – Borrador original.
Cindy Mafla: Metodología, investigación, Escritura – Borrador original.
Pamela Landeta: Conceptualización, metodología, investigación.
Hernán Roincón: Conceptualización, metodología, investigación.
All the authors read and approved the final version of the manuscript.

Financing

The study was self-financed by the authors. The patient's insurance company assumed the costs of hospitalization and hemodialysis treatments.

Availability of data or materials

Does not apply.

Declarations

Ethics committee approval and consent to participate

It does not apply to clinical cases.

Consent for publication

The authors have the written permission of the patient for publication.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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DOI: Digital Object Identifier. **PMID**: PubMed Identifier.

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