

# Journal of Nephrology

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## Refractory diffuse podocytopathy

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This case illustrates the clinical course, diagnostic challenge and management difficulties associated with adult-onset severe nephrotic syndrome secondary to diffuse podocytopathy, with needs for bilateral nephrectomy as a last resource of therapeutic measure.

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Hypothesis

We present the case of a 25-year-old Caucasian male evaluated for nephrotic syndrome (NS). Three-years ago he was diagnosed with antiphospholipid syndrome (APS) after an unprovoked deep-vein thrombosis. Immunologic-markers were compatible with APS and systemic lupus erythematosus [ANA 1/1280 homogeneous-pattern, anti-dsDNA (Feia); 25 UI/mL, anti-C1q; 23.6 UI/mL and normal complement levels]. At the time he presented with microscopic hematuria (2-5 RBC/HPF) with no proteinuria; while renal function was normal. Since then, he has been on warfarin and had no new thrombotic event. The patient has no known family history of autoimmune nor renal disease. He presented with one-month progressive facial and peripheral edema and fatigue. He denied respiratory or urinary complaints, arthralgia or rash. Urine output was preserved. The patient had intermittent use of non-steroidal anti-inflammatory drugs (NSAIDs) for recurring headaches and denied drugs or alcohol consumption. At presentation he weighed 78 kg (significant increase during three months), had decreasing murmur at lung-bases and evidence of anasarca with laboratory evidence of NS (albumin 2.0 g/dL, total-cholesterol 405 mg/dL and triglycerides 317 mg/dL) and severe proteinuria (24-hour urine = 40 g/d). His urine showed microscopic hematuria, granular and lipid-casts with oval-fat bodies. Renal-ultrasound showed symmetric normal-sized heterogeneous kidneys with loss of cortico-medullary transition with no evidence of hydronephrosis. Abdominal-CT angiogram showed no evidence of thrombosis.

Repeat immunology showed positive ANA 1/320 with a fine- speckled pattern, normal C3 and C4, negative anti-dsDNA and C1q, and positive anti-Sm (62 U/mL). He was started on low-sodium diet, angiotensin-converting enzyme inhibitor and high-dose corticosteroids with the presumptive diagnosis of NSAID's related minimal-change disease. After a month of refractory therapy with associated worsening renal function, he was submitted to percutaneous renal biopsy. Biopsy was representative with fourteen glomeruli with tenuous mesangial hypercellularity. Interstitium showed no inflammatory infiltrate nor fibrosis and vascular structures were preserved. Renal tubules had changes compatible with acute tubular necrosis. Immunofluorescence (albumin, C3, C4, C1q, IgA, IgG and IgM) revealed granular deposits at the mesangium and tubular cytoplasm exclusive for C3. Electron microscopy showed diffuse foot process effacement and occasional mesangial deposits. Reticular aggregates were observed. Complement and podocytopathies genetic study did not identify any alteration. The patient presented a protracted course refractory to multiple immunosuppressive therapies consisting of two months of high-dose corticotherapy, one month mycophenolate mofetil (1 g twice daily), rituximab (1000 mg, 2 doses) and cyclosporine for approximately 20 days. Then hemofiltration was conducted with the intent of reducing residual diuresis, which was accompanied by a significant improvement of weight and edemas (from a maximum of 90 kg to 67 kg), however proteinuria continued (>30 g/d). He also incurred in a cycle of

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gentamicin with the same purpose, suspended after fifteen days due to vestibular-syndrome. As a last solution he was submitted to bilateral laparoscopic-nephrectomy and integrated on a regular hemodialysis program. The renal biopsy (Figure 1) of the nephrectomy showed a pattern consistent with diffuse and segmental glomerulosclerosis, mainly in the corticomedullary junction.

Up to 10% of adults with minimal-change disease appear to be glucocorticoid-resistant. This is most often due to insufficient glucocorticoid therapy (less than 16 weeks) or incorrect diagnosis (focal segmental glomerulosclerosis that is missed by sampling-error, or one of the variants of idiopathic NS other than focal segmental glomerulosclerosis) (1-6). We classified this case as a refractory diffuse podocytopathy. Nephrectomy is a last resort. There are multiple options such as chemical (NSAIDs, gentamicin), embolization and surgery. The prothrombotic-risk associated with post-embolization inflammatory reaction in a patient with APS made us opt for a surgical approach (7,8). He is a candidate for transplantation, taking into account the risk associated with primary FSGS relapse (9).

#### Author's contribution

Conceptualization: JO and SS.

Writing—Original Draft Preparation: JO, IS and JF.

Writing—Review and Editing: JT, SS and AC (6th author).

Supervision: TM, JL and AC (9th author).

All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

#### Conflicts of interest

The authors declare that they have no competing interests.

#### Ethical issues

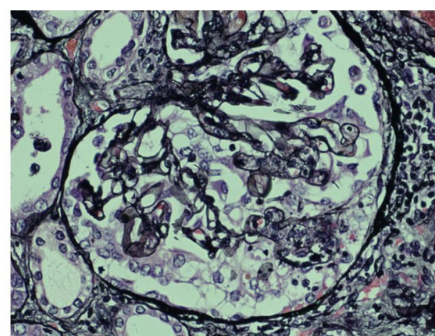
This report was conducted based on the World Medical Association Declaration of Helsinki. A written informed consent was obtained from the patient for publication as a hypothesis. Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors, having nothing to declare.

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#### References

1. Szeto CC, Lai FM, Chow KM, Kwan BC, Kwong VW, Leung CB, et al. Long-term outcome of biopsy-proven minimal



**Figure 1.** Glomerulus showing segmental collapse of capillaries, hypertrophy and hyperplasia of overlying podocytes (Jones methenamine silver stain,  $\times 100$ ; nephrectomy sample).

- change nephropathy in Chinese adults. *Am J Kidney Dis.* 2015;65:710-8. doi: 10.1053/j.ajkd.2014.09.022.
2. Maas RJ, Deegens JK, Smeets B, Moeller MJ, Wetzels JF. Minimal change disease and idiopathic FSGS: manifestations of the same disease. *Nat Rev Nephrol.* 2016;12:768-76. doi: 10.1038/nrneph.2016.147.
3. Deegens JK, Dijkman HB, Borm GF, Steenbergen EJ, van den Berg JG, Weening JJ, et al. Podocyte foot process effacement as a diagnostic tool in focal segmental glomerulosclerosis. *Kidney Int.* 2008;74:1568-76. doi: 10.1038/ki.2008.413.
4. Hommos MS, De Vriese AS, Alexander MP, Sethi S, Vaughan L, Zand L, et al. The Incidence of Primary vs Secondary Focal Segmental Glomerulosclerosis: A Clinicopathologic Study. *Mayo Clin Proc.* 2017; 92:1772-1781. doi: 10.1016/j.mayocp.2017.09.011.
5. Yao T, Udwan K, John R, Rana A, Haghighi A, Xu L, et al. Integration of Genetic Testing and Pathology for the Diagnosis of Adults with FSGS. *Clin J Am Soc Nephrol.* 2019;14:213-223. doi: 10.2215/CJN.08750718.
6. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. *Kidney Int.* 2021;100:S1-S276. doi: 10.1016/j.kint.2021.05.021.
7. Olivero JJ, Frommer JP, Gonzalez JM. Medical nephrectomy: the last resort for intractable complications of the nephrotic syndrome. *Am J Kidney Dis.* 1993; 21:260-3. doi: 10.1016/s0272-6386(12)80743-8.
8. Takase HM, Contti MM, Nga HS, Bravin AM, Valiatti MF, El-Dib RP, et al. Nephrectomy Versus embolization of non-functioning renal graft: a systematic review with a proportional meta-analysis. *Ann Transplant.* 2018;23:207-217. doi: 10.12659/AOT.907700.
9. Uffing A, Pérez-Sáez MJ, Mazzali M, Manfro RC, Bauer AC, de Sottomaier Drumond F, et al. Recurrence of FSGS after Kidney Transplantation in Adults. *Clin J Am Soc Nephrol.* 2020;15:247-256. doi: 10.2215/CJN.08970719.