A familial case of minimal change disease emerging during a concurrent steroid course

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Introduction

Nephrotic syndrome is characterized by proteinuria, hypoalbuminemia, hyperlipidemia, and edema. The most common causes of nephrotic syndrome include membranous nephropathy, focal segmental glomerulosclerosis, and minimal change disease (MCD). Gold standard diagnosis of MCD requires kidney biopsy with electron microscopy showing effacement of foot processes in the glomeruli allowing protein to enter the urine. The cause of effacement is unknown but is theorized to be due to immune dysregulation. Minimal change disease accounts for 15% of idiopathic nephrotic syndrome in adults.

Clinical Case

We present a case of a 70-year-old man diagnosed with MCD, with family history of MCD in his brother.

- **Presenting symptoms**: 2-week history of edema
  - 15-20 lb weight gain, foamy urine, & fatigue
  - Recently diagnosed with giant cell arteritis (GCA) on prednisone taper (30 mg at presentation)
- **Physical exam:**
  - 3+ bilateral lower extremity pitting edema and periorbital edema

Test	Patient Value	Reference Range
Protein	4.4 g/dL	6-8.5 g/dL
Albumin	2.1 g/dL	3.2-4.9 g/dL
Creatinine	1.17 mg/dL	0.7-1.4 mg/dL
24-hour urine protein	>600 mg/dL	5-25 mg/dL
Urine protein/ Tvolume	9,900 mg	<150 mg/Tvol
Urinalysis	3+ protein, 3 RBCs, 3 WBCs, 19 hyaline casts	0-5 RBCs, 0-5 WBCs, 0-5 hyaline casts
ANA, anti-dsDNA, c-ANCA, p-ANCA	negative	negative
Anti-RNP	1.5 AI	0-0.9 AI

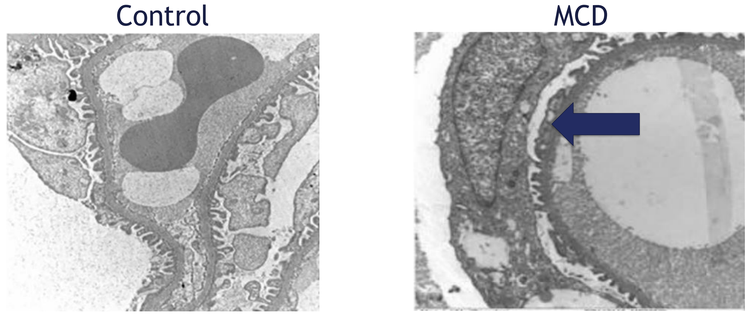
Clinical Case

- **Kidney biopsy:**
  - Podocyte effacement characteristic of MCD
- **Treatment:**
  - Prednisone increased to 60 mg
  - Pantoprazole 40 mg for ulcer prophylaxis
  - Aspirin 81 mg for venous thromboembolism (VTE) prophylaxis
    - Hypoalbuminemia <2.5 g/dL
  - Sulfamethoxazole-trimethoprim 800-160 mg for pneumocystis pneumonia prophylaxis

Diagnosis

- **Classic symptoms of MCD**
  - Foaming urine
  - Lower extremity and periorbital edema
  - Weight gain, fatigue, ascites and pleural effusions (in severe cases)
  - Symptoms can develop within days-weeks
- **Lab Findings**
  - **Urine studies**: Proteinuria >3.5 grams/day, Fatty casts and oval fat bodies
    - Loss of thyroglobulin
    - Loss of IgG: risk of infection
    - Loss of anticoagulants (antithrombin III, protein C, protein S): risk of thrombosis
  - Hypoalbuminemia & hyperlipidemia
  - Serum creatinine and BUN: Usually normal
- **Invasive Testing**
  - **Definitive diagnosis:** renal biopsy
  - **Electron microscopy (EM):** characteristic effacement of podocyte foot processes

Figure 1: EM showing podocyte effacement in MCD



From "In situ evaluation of podocytes in patients with focal segmental glomerulosclerosis and minimal change disease" by da Silva, C. A. et al., 2020, PLOS One, Copyright © 2020 da Silva et al

Discussion

- **Causes**
  - MCD is not typically familial
    - Both patient and brother diagnosed at similar age (~70), suggesting genetic contribution
  - Iatrogenic: associations with NSAID use which patient was using for headaches from GCA
- **Genetic Factors:**
  - Studies suggest involvement of kidney ankyrin repeat-containing (KANK) family proteins
  - Ongoing research to identify additional genes
- **Treatment:**
  - MCD is treated with high-dose corticosteroids
  - The patient was already on steroids (prednisone for GCA), concerns about steroid-resistant MCD

References

da Silva, C. A., Monteiro, M. L. G. D. R., Araújo, L. S., Urzedo, M. G., Rocha, L. B., Dos Reis, M. A., & Machado, J. R. (2020). In situ evaluation of podocytes in patients with focal segmental glomerulosclerosis and minimal change disease. PloS one, 15(11), e0241745. https://doi.org/10.1371/journal.pone.0241745

Hull R P, Goldsmith D J A. Nephrotic syndrome in adults BMJ 2008; 336 :1185 doi:10.1136/bmj.39576.709711.80

Kopp, J. B., Anders, H. J., Susztak, K., Podestà, M. A., Remuzzi, G., Hildebrandt, F., & Romagnani, P. (2020). Podocytopathies. *Nature reviews. Disease primers*, *6*(1), 68. https://doi.org/10.1038/s41572-020-0196-7

Saleem, M. A., & Kobayashi, Y. (2016). Cell biology and genetics of minimal change disease. *F1000Research*, *5*, F1000 Faculty Rev-412. https://doi.org/10.12688/f1000research.7300.1

Vivarelli, M., Massella, L., Ruggiero, B., & Emma, F. (2017). Minimal Change Disease. *Clinical journal of the American Society of Nephrology : CJASN*, *12*(2), 332–345. https://doi.org/10.2215/CJN.05000516

Zabala Ramirez, M. J., Stein, E. J., & Jain, K. (2023). Nephrotic Syndrome for the Internist. *The Medical clinics of North America*, *107*(4), 727–737. https://doi.org/10.1016/j.mcna.2023.03.006