

RENAL-LIMITED PR-3 ANTIBODY POSITIVE VASCULITIS AND THIN BASEMENT MEMBRANE NEPHROPATHY PRESENTING AS RPGN

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INTRODUCTION

➤ Renal-limited ANCA-positive vasculitis is an exceedingly rare condition with involvement of other organ systems becoming a distinct possibility with disease progression

CASE BACKGROUND

➤ A 27 year old with no significant past medical history presents to the emergency department with the vague abdominal pain, ten-pound weight loss, petechial rash on the abdomen and feet, sparing the soles, and occasional copper-colored urine

➤ These symptoms occurred one month after an assumed viral upper respiratory infection (URI) with low-grade fever, cough, rhinorrhea

➤ Patient received his second dose of an mRNA COVID vaccine two weeks prior to symptom onset

➤ At time of presentation, taking 600 mg Ibuprofen one to two times daily to treat abdominal pain

HOSPITAL COURSE

➤ Initial workup revealed:

	Pertinent Laboratory Findings	
Measurement	Result	Normal Range
WBC (K/mcL)	6.1	4.0 – 11.0
HGB (g/dL)	8.7	13.0 – 17.0
MCV (fl)	80	78 – 100
Creatinine (mg/dL)	9.0	0.67 – 1.17
BUN (mg/dL)	71	6 – 20
Albumin (g/dL)	3.0	3.6 – 5.1

➤ The patient was admitted to the hospital, and further investigation revealed microscopic hematuria, nephrotic-range proteinuria, positive serum anti-PR-3 antibody, no major electrolyte imbalances, and negative HIV antigen, HBsAg, and HCV antibody, as well as abnormal echogenicity of bilateral renal parenchyma with no evidence of hydronephrosis on ultrasound

➤ The patient subsequently underwent renal biopsy revealing:

➤ Crescentic glomerulonephritis with 18% of glomeruli demonstrating either global or segmental scarring

➤ Thin Basement Membrane Nephropathy

➤ He was initiated on IV fluids, high dose steroids and rituximab, stabilized

➤ Discharged with a plan for continued immunosuppression and close monitoring of kidney function.

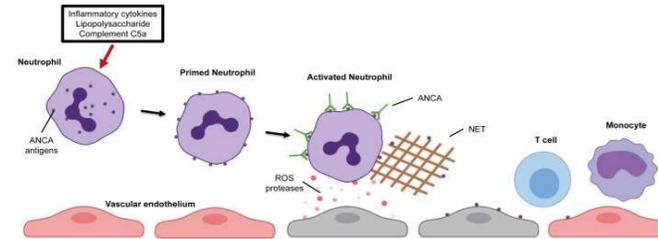


Figure 1. Pathogenesis of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis. ANCA autoantigen proteinase 3 (PR-3) is normally sequestered in the granules of neutrophils. Environmental stimuli result in neutrophil priming, with movement of PR3 and MPO to cell surface

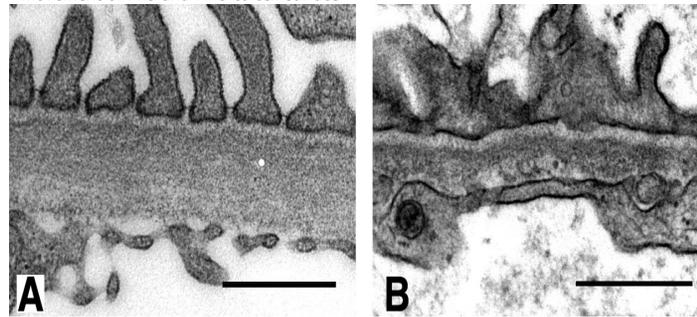


Figure 2. Ultrastructural nature of the glomerular basement membrane in thin basement membrane nephropathy (TBMN). (A) In the normal adult male kidney, one can see a uniformly wide glomerular basement membrane (GBM) located between the fenestrated endothelial cells and the podocyte foot processes. (B) In TBMN, the GBM does not reveal any structural abnormalities, but it is characteristically thinned, sometimes having only approximately half of the thickness in a normal kidney (A).

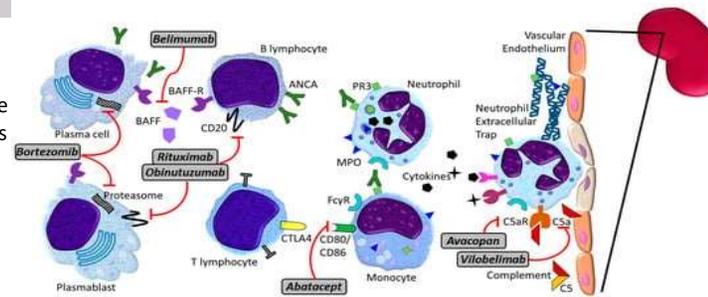


Figure 3. Immune drivers and potential therapies of ANCA-associated vasculitis. Abbreviations: ANCA: anti-neutrophil cytoplasmic antibodies. BAFF: B lymphocyte activating factor. C5a: complement factor 5 fragment a. NETs: neutrophil extracellular traps. MPO: myeloperoxidase. PR3: leukocyte proteinase 3.

HOSPITAL COURSE, CONT.

➤ He unfortunately presented again to the hospital 1 month later after monitoring of his renal function showed progressive worsening.

➤ A repeat renal biopsy revealed progression of the disease to 56% of glomeruli with global scarring. The patient was prepared for hemodialysis due to progression of disease resulting from failure of treatment

DISCUSSION

➤ A rising creatinine with hematuria should be treated as a medical emergency when developing over days to weeks

➤ This case illustrates a patient diagnosed with rapidly progressive glomerulonephritis due to two separate pathological process

➤ Glomerular scarring due to autoimmune vasculitis (Figure 1)

➤ Thin basement membrane nephropathy (Figure 2)

➤ It remains unclear whether the COVID mRNA vaccine is implicated as a trigger in the pathogenesis of this diagnosis

➤ Disease pathogenesis is further confounded by preceding viral URI, although there was no evidence of post-infectious immune complexes on renal biopsy

➤ B-cells produce ANCA, B-cell Activating Factor (BAFF), Neutrophil Extracellular Traps (NETs) and Complement 5a (C5a) (Figure 3) which are implicated in vascular inflammation

➤ Rituximab is the only currently approved therapy for ANCA-associated vasculitis

➤ Rituximab targets CD20 and halts differentiation of B lymphocytes into plasma cells, thus reducing downstream inflammation

➤ Bortezomib, belimumab, abatacept, and avacopan represent therapies that could have potential benefit in the treatment of ANCA-associated vasculitis (Figure 3)

➤ The kidney is typically the slowest organ to respond to immunosuppressive therapy in ANCA-associated vasculitides

REFERENCES

- Falk, R. J., Merkel, P. A., & King Jr, T. E. (2021). *Granulomatosis with polyangiitis and microscopic polyangiitis: Clinical manifestations and diagnosis*. UpToDate. https://www.uptodate.com/contents/granulomatosis-with-polyangiitis-and-microscopic-polyangiitis-clinical-manifestations-and-diagnosis?search=epidemiology+of+renal+vasculitis&ionRank=1&usage_type=default&anchor=H3476397968&source=machineLearning&selectedTitle=4~107&display_rank=4#H3476397968.
- Woodworth, T., Abuelo, J., Austin, H., Esparza, A. & (1987). *Severe Glomerulonephritis with Late Emergence of Classic Wegener's Granulomatosis*. *Medicine*, 66 (3), 181-191.
- Seo, P., & Stone, J. H. (2004). The antineutrophil cytoplasmic antibody-associated vasculitides. *The American Journal of Medicine*, 117(1), 39–50. <https://doi.org/10.1016/j.amjmed.2004.02.030>
- Geetha, D., Jefferson, J.A. (2019). ANCA-Associated Vasculitis: Core Curriculum 2020. *American Journal Of Kidney Disease*. <https://doi.org/10.1053/j.ajkd.2019.04.031>
- Almaani S, Fussner LA, Brodsky S, Meera AS, Jayne D. ANCA-Associated Vasculitis: An Update. *Journal of Clinical Medicine*. 2021; 10(7):1446. <https://doi.org/10.3390/jcm10071446>