Fibrillary glomerulonephritis with mixed connective tissue disease controlled with Rituximab

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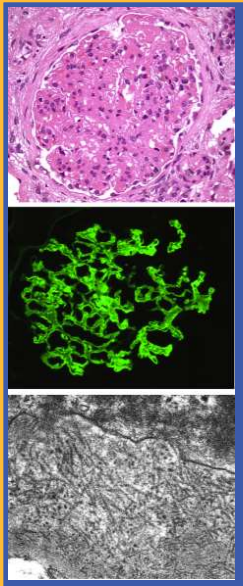
Learning Objectives

- To present a case of fibrillary glomerulonephritis (FGN) with mixed connective tissue disease (MCTD) controlled with rituximab
- To learn about FGN and its potential treatment with rituximab

Case Description

- FGN is a rare glomerular disease found in 0.5%-1% of native kidney biopsy series. It is usually associated with underlying malignancy (chronic lymphocytic leukemia, B cell lymphoma), hepatitis C infection or certain autoimmune diseases mostly found in Graves' disease, systemic lupus, Crohn's disease, and idiopathic thrombocytopenia purpura. In general, renal involvement in MCTD is infrequent at early stage, but is often observed and complicates the clinical course where the membranous and mesangial proliferative glomerulonephritis have been reported.
- We report an 80 year-old female, Ms. S with history of MCTD with scleroderma, interstitial lung disease, hypertrophic cardiomyopathy, as well as prior diagnosis of rheumatoid arthritis and lupus at her 50s, who has developed chronic kidney disease due to FGN. Patient initially presented in nephrology clinic with hypertension, renal insufficiency and sterile pyuria. Occasional mild proteinuria and cellular casts were observed and thought to be tubulointerstitial nephropathy. Renal biopsy later revealed fibrillary and immune complex mediated glomerulonephritis. Extensive fibrillary deposits by electron microscopy warrant a diagnosis of FGN. Rituximab was initiated afterward since 2016 for empirical FGN treatment although the data are limited and have inconsistent outcomes. Patient also has been on long-term Azathioprine for MCTD and lisinopril for Raynaud phenomenon. Her kidney function has remained stable at her baseline range of 1.1-1.5 since 2006. Urinalysis stays grossly negative except occasionally trace protein and sterile pyuria. She is currently following up with nephrology clinic every 6 months.



Light Microscope: Mesangial Hypercellularity and expansion by amorphous eosinophil materials associated with fibrillary deposits

Immunofluorescence: Ill-defined, smudged positive staining with IgG, C3, Kappa and lambda over mesangial and glomerular capillary wall

Electron Microscope: Extensive podocyte foot process effacement. Randomly oriented fibrils within subepithelial space and mesangial matrix.

Figure 1. Renal biopsy in FGN [1]

Reference:
1. Rosenstock J., Markowitz G. S. et al., Fibrillary Glomerulonephritis: An Update. Kidney International Reports (2019) 4, 917-922
2. Hogan J., Bomback A. et al., Rituximab Treatment for Fibrillary Glomerulonephritis. Nephrol Dial Transplant (2014) 29: 1925-31

Discussion

- FGN is a rare proliferative form of glomerular disease featured by randomly oriented, non-branching fibrillar deposits. The positive staining with IgG, C3, Kappa and lambda light chains strongly suggests fibrils' composition with a complex of antibodies and antigens. Negative congo red staining helps differentiate from amyloidosis, but not exclusive to each other.
- Patients with FGN usually have coexistent autoimmune disease (11%), diabetes (24%), malignancy (9%) and hepatitis C (13%). Our patient Ms. S only has history of MCTD, as well as malignancy of lingual squamous cell carcinoma which occurred recently after FGN was treated and stabilized.
- She originally presented with renal insufficiency, absence to 1+ proteinuria and sterile pyuria to nephrology clinic dated back to 2009, and was thought to have underlying tubulointerstitial nephropathy given her history of MCTD. She was under biannual monitor only with intermittent Epogen administration for mild anemia, Imuran for scleroderma and lisinopril for hypertension. In 2016, given worsening Cr and proteinuria, biopsy was requested and led to the diagnosis of FGN in setting of arteriolosclerosis from chronic scleroderma. Rituximab was initiated after discussing with her rheumatologist. Her kidney function labs have been stable since then without proteinuria.
- Rituximab is proposed for FGN treatment due to the presence of polyclonal immunoglobulin deposits. Most reported treatment successes have preserved renal function. It is hypothesized that it only prolongs progression of renal disease and may not be effective after much decline of renal function. More studies are needed to delineate its effects, mechanism and prospects.

Conclusion

- To the best of our knowledge, FGN with MCTD is rarely observed and FGN often entails poor prognosis with fast progression to end-stage kidney disease (ESKD). Here, we report a case of well-controlled FGN by rituximab with MCTD. It would also be prudent for physicians to keep FGN under one of differential diagnosis for renal involvement in MCTD.