

Title: Clinical Course of Fibrillary Glomerulonephritis

Investigators:

Michaela D Restivo (PI)

Andrew S. Bomback (Co-investigator)

Gerald B. Appel (Co-investigator)

Jai Radhakrishnan (Co-investigator)

Abbreviated title: Fibrillary glomerulonephritis

Research procedure: Analysis of existing data

Study Description:

- 1. Study Purpose:** Fibrillary glomerulonephritis (GN) is a rare cause of renal failure in adults that can progress rapidly to end stage renal disease. Presently, no therapies have been proven to improve survival or change disease course. Therapy is largely determined by rate of disease progression and histologic findings on light microscopy. Less aggressive clinical and pathologic disease is treated conservatively with renin angiotensin system (RAS) blockade, dietary and lifestyle modifications, blood pressure control and close follow-up for possible renal replacement therapy; while patients with more aggressive disease are treated with immunosuppression - usually corticosteroids and/or calcineurin inhibitors¹². Pathologically, fibrillary GN is characterized by the deposition, visualized on electron microscopy, of randomly arrayed medium sized fibrils in the basement membrane and mesangium of glomeruli. Immunofluorescence reveals presence of IgG immunoglobulin in 97% of fib GN biopsies with demonstration of immunoglobulin in visualized fibrils³. Consequently it is hypothesized that the pathogenesis of Fib GN may relate to the abnormal activation of B cells⁴; thus the use of B cell targeted therapies such as the anti-CD20 monoclonal antibody rituximab may prove effective in its treatment. Rituximab has previously been used with some success in other potentially B cell-related nephritides including idiopathic membranous nephropathy⁵⁶⁷ and Hepatitis C-associated mixed cryoglobulinemia⁸. A recent series of 3 cases of fibrillary GN at Columbia demonstrated that rituximab therapy was associated with decreased proteinuria and preserved renal function during 27 months of follow up⁹. It is unclear, at present, whether this therapy is more effective than alternative immunosuppressant therapy, whether individual patient factors influence effectiveness of therapy, and how therapy may alter long-term prognosis and progression to end stage renal disease.

This retrospective chart review seeks to:

1. To compare changes in proteinuria among patients with fibrillary GN treated with rituximab versus other therapies (conservative therapy, alternative immune-suppressing regimens).
2. To determine whether clinical and/or histopathologic characteristics predict disease progression or response to rituximab therapy for fibrillary GN

2. **Study Design and Statistical Procedures:** This is a retrospective chart review which will include collection of epidemiological, clinical, biochemical and pathological data. The data will be evaluated by unpaired between groups t-tests (rituximab therapy vs. other therapy) to determine whether rituximab therapy affects proteinuria; and by univariate and multivariate analyses to determine whether there are epidemiological, clinical or histopathologic predictors of treatment outcome.
3. **Study Procedures:** Charts of patients diagnosed with fibrillary glomerulonephritis by kidney biopsy at Columbia University between 1995 and 2010 qualify for this review. Epidemiological, clinical, biochemical and pathological data will be collected and evaluated by unpaired between groups t-tests (rituximab therapy vs. other therapy) to determine whether rituximab therapy affects outcomes; and by univariate and multivariate analyses to determine whether there are epidemiological, clinical or histopathologic predictors of treatment outcome.
4. **Study Drugs or Devices:** None, not applicable
5. **Study Questionnaires:** None, not applicable
6. **Study Subjects:** We will include all patients diagnosed with fibrillary glomerulonephritis whose kidney biopsy was read at Columbia University, between 1995 and 2010.
7. **Recruitment:** Not applicable
8. **Confidentiality of Study Data:** Data will be collected from patient charts and contained on a 128-bit encrypted password-protected Excel file. The database will not include individually identifiable data for confidentiality purposes. Patients' identification will be replaced by a randomly assigned number. The key linking patient identity to the data number will be maintained separately by the Principal Investigator on a different password-protected computer. Once data collection is complete, all identifiers will be destroyed at the earliest opportunity.
9. **Potential Risks:** As this is a retrospective chart review, the only risk is the possibility of loss of confidentiality. However, this is unlikely due to the measures already in place to safeguard patient identity.
10. **Potential Benefits:** This study offers no direct benefit to the patients whose charts are being reviewed. However study results may yield improvement in future care of patients with fibrillary glomerulonephritis.
11. **Alternatives:** not applicable

¹ Radhakrishnan J, Uppot R, Colvin R. Case 5-2010: A 51 year old man with HIV infection, proteinuria and edema. *New England Journal of Medicine*, 2010; 362:636-46.

² Rosenstock JL, Markowitz GS, Valeri AM, Sacchi G, Appel GB, D'Agati VD. Fibrillary and immunotactoid glomerulo- nephritis: distinct entities with different clinical and pathologic features. *Kidney Int* 2003;63:1450-61.

³ Iskandar S. Falk R. Charles Jeanette J. Clinical and pathologic features of fibrillary glomerulonephritis. *Kidney International*, 1992; 42:1401-1407.

⁴ Collins, M. Sankar N. Chung M. SLoand J. Golman B. Appel G. Povin B. Rituximab Treatment of Fibrillary Glomerulonephritis. *Amerjican Journal of Kidney Dlsease*, 2008. 52(6):1158-1162

⁵ Remuzzi G. Chiurciu C. Abbate M. Brusegan V. Botempelli M. Ruggeneti P. Rituximab for idiopathic membranous nephropathy. *Lancet*, 2002; 360:923-934.

⁶ Fervenza FC. Cosio FG. Erickson SB. Rituximab in idiopathic membranous nephropathy. *Kidney International*, 2008; 73:117-125.

⁷ Ruggenenti P. Chiruchiu C. Brusegan V. Abbate M. Perna A. Filippi C. Remuzzi G. Rituximab in Idiopathic Membranous Nephropathy: A One-Year Prospective Study. *J Am Soc Nephrol*, 2003. 1851-1857.

⁸ Quartuccio L. Soardo G. Romano G. Zaja F. Scott A. De March G. Fabris M. Ferracciolo G. DeVita S. Rituximab treatment for glomerulonephritis in HCV-associated mixed cryoglobulinemia: efficacy and safety in the absence of steroids. *Rheumatology*, 2006; 45:842-846.

⁹ Collins, M. Sankar N. Chung M. SLoand J. Golman B. Appel G. Povin B. Rituximab Treatment of Fibrillary Glomerulonephritis. *Amerjican Journal of Kidney Dlsease*, 2008. 52(6):1158-1162