PREDICTING PROGRESSION OF C3 GLOMERULOPATHY: HISTOLOGICAL AND CLINICAL MARKERS

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INTRODUCTION AND AIMS

The term C3 glomerulopathy describes proliferative glomerulonephritis, characterized by the presence of glomerular deposits composed of C3 in the absence of significant amounts of Ig implicating hyperactivity of the alternative complement pathway. The full spectrum of histologic change observed in C3 glomerulopathy has yet to be defined and pathologic predictors of renal outcome within this patient population remain largely unknown. This study aimed to evaluate histological and clinical risk factors for C3 glomerulopathy progression to end stage renal disease (ESRD).

METHODS

A total of 48 patients [26 (54.2%) male, mean age:34±14 year, mean follow up of 46±39 months] with kidney biopsies fulfilling criteria for C3 glomerulopathy between 2001 and 2013 were reviewed. Histopathologic, demographic, and clinical data were recorded and predictors of ESRD were determined using the Cox proportional hazards model. The impact of histological (glomerular sclerosis, crescents, intensity and pattern of staining for C3, IgA, IgG, IgM, kappa, lambda, C1Q, fibrinogen) and clinical (age, gender, systolic blood pressure (SBP), eGFR, serum creatinine, hemoglobin (Hgb), albumin, C3, C4, proteinuria, hematuria) markers on progression of C3 glomerulopathy analyzed using Cox regression.

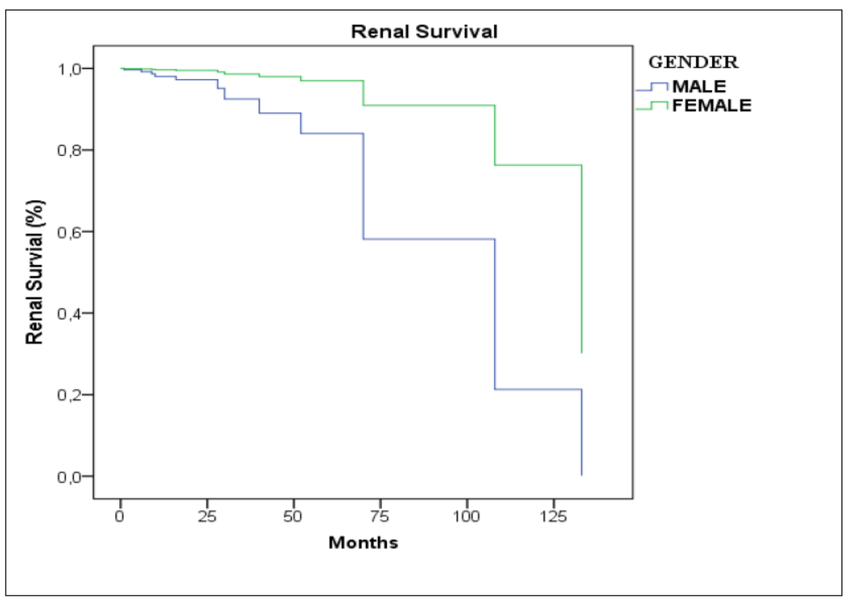
RESULTS

Patients typically presented with hematuria (81%) and proteinuria (100%). Kidney biopsy mainly showed a membranoproliferative pattern (n=14, 70%), although both mesangial proliferative (n=13, 27%) and diffuse endocapillary proliferative (n=1, 2%) glomerulonephritis were noted. The mean eGFR of patients at baseline was 75 44 ml/min/1.73 m^2. Of 39 patients with available follow-up data, 12 (31%) progressed to ESRD after a median of 28 months (Table 1). Only a patient (2%) had a family history of kidney disease and progressed to ESRD. In the cox regression analysis, although the intensity and pattern of C3 staining were not found to be associated with progression to ESRD, percentage of crescents (HR:1.16, p=0.013) and glomerulosclerosis (HR:1.24, p=0.011), severity of interstitial fibrosis as histological markers were found to be associated with progression to ESRD. Age (HR:0.853, p=0.002), male gender (HR:9.807, p=0.044) and eGFR (HR:0.907, p=0.001) at baseline were the clinical markers predicted ESRD in the Cox regression analyses (Fig. 1).

Table 1. Clinical and laboratory findings at the time of renal biopsy in patients progressed to ESRD.

	ESRD (n=12)	Others (n=27)	*P* value
Male/Female	8/4	12/15	NS
Age (years)	30 ± 11	33 ± 12	NS
Systolic BP (mmHg)	133 15	135 17	NS
eGFR (mL/min/1.73 m^2)	40 17	88 43	**<0.001**
Hemoglobin (g/dL)	10.7 2.1	11.2 1.9	NS
Creatinine (mg/dL)	2.37 1.47	1.32 ± 1.07	**0.017**
Albumin (g/dL)	2.85 1.01	3.06 0.66	NS
Proteinuria (g/day)	5.36 4.17	4.41 3.02	NS
% of crescents	29 38	12 20	NS
% of glomerulosclerosis	25 19	10 13	**0.02**

Figure 1. Cox- regression renal survival of patients according to gender (HR:9.87, p=0.044)



CONCLUSIONS

This study identifies important clinicopathologic markers predicting the progression of C3 glomerulopathy to ESRD. Higher percentage of crescents and glomerulosclerosis, severity of interstitial fibrosis as histological markers and younger age, male gender and lower eGFR at the time of biopsy as clinical markers predicted ESRD.

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