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IgA NEPHROPATHY: ASSOCIATIONS BETWEEN THE OXFORD CLASSIFICATION, CLINICAL PRESENTATION AND IMMUNOHISTOLOGY

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INTRODUCTION

Heterogeneity of IgA nephropathy (IgAN) morphological presentation is associated with different clinical presentation, prognosis and eventually pathogenesis of the disease. In 2009, the Oxford Classification (Ox.C.) proposed the use of 4 histological parameters with prognostic significance: mesangial proliferation (M), segmental sclerosis (S), endocapillary proliferation (E), interstitial fibrosis/tubular atrophy (IF/TA) (T). Immunohistology findings were excluded. The aim of this study was to evaluate the potential associations between clinical presentation, immunohistology, and each of these parameters.

METHODS

Renal biopsies performed between 2003 and 2010 in a single center were evaluated to retrieve the diagnosis of IgAN. A total of 42 patients were identified. Each biopsy was reclassified according to Ox.C: M0/M1; S0/S1; E0/E1; T0/T1/T2, and presence of crescents (C0/C1) was added. The following parameters were evaluated at biopsy time: age, history of hypertension (HTN), history of macroscopic hematuria, serum IgA (elevated if >350mg/dL), immunofluorescence (IF) (positive IgG, IgA and IgM if >1+, positive C3 and C1q if >= 1+), creatinine clearance (CCr, ml/min/1.73m^2), and proteinuria (Uprot, g/24h). Associations between these parameters were analysed using Student t-test, Mann-Whitney test and Fischer exact test, as appropriate.

RESULTS

Positivity for mesangial proliferation (M1), segmental sclerosis (S1), endocapillary proliferation (E1), IF/TA (T1 and T2) and crescents (C1) was identified in 59%, 42,6%, 30,9%, 30,9% (T1 16,6%, T2 14,3%), and 30,9% of the biopsies, respectively.

OXFORD CLASSIFICATION PARAMETERS AND PRESENTATION

Age (43±16 y), history of HTN (48%), macroscopic hematuria (33%), and elevated serum IgA (48,6%), were not found to be associated with M1, S1, E1, T1 or C1. S1 was associated with higher Uprot (p=0,033), and T2 with lower CCr (p=0,024), when compared to S0 and T0-1, respectively (Table 1).

Tabela 1* – Oxf.C. Parameters and Kidney Disease Presentation

	Uprot g/dia	p	CCr ml/min/1.73m2	p
M0	4,02 ± 3,15	0,148	54 (32-81)	0,077
M1	2,00±1,84		72 (60-105)	
S0	1,98 (0,87- 3,31)	0,033	87±41	0,057
S1	4,13 (1,95- 5,22)		64±31	
E0	3,13 (1,52-4,43)	0,281	78±38	0,195
E1	4,16 (1,58-8,76)		61±41	
T0-1	2,59 (1,2-5,0)	0,412	77±39	0,024
T2	3,71 (3,0-4,6)		40±13	
C0	2,59 (1,1-4,5)	0,126	80±39	0,103
C1	4,2 (2,4-5,6)		58±39	

IMMUNOHISTOLOGY

Concerning IF, positivity for IgG, IgA, IgM, C3 and C1q was identified in 0%, 100%, 31,0%, 88,1%, e 26,2% of the cases, respectively. No association was found between immunohistology findings and age, HTN, hematuria and serum IgA. Association with Oxf. C. histological parameters and clinical presentation is described in Table 2 and 3, respectively.

Table 2 – Immunohistology and Oxf.C. Histological Parameters

	IgM++ %	p	C1q+ %	p
M0	41,7	0,469	15,4	0,262
M1	27,6		37,5	
S0	27,3	0,741	23,8	0,491
S1	35,0		35,3	
E0	28,6	0,720	15,4	0,022
E1	38,5		53,8	
T0-1	29,4	0,659	28,7	1
T2	42,8		16,7	
C0	35,7	0,493	20,7	0,056
C1	23,1		54,5	

Table 3 * – Immunohistology and Kidney Disease Presentation

	Uprot g/dia	P	CCr ml/min/1.73m2	P
IgM+	7,37 ± 5,54	0,001	54,43 ± 28,59	0,040
IgM-	2,40 ± 1,53		81,47 ± 41,99	
C1q+	6,16 (2,44-12,2)	0,039	69,33 ± 37,37	0,734
C1q-	2,59 (1,49-4,22)		74,34 ± 42,41	

* (Table 1 and 3) – Values are expressed as mean ± s.d or median (range)

CONCLUSIONS

Clinical parameters (age, HTN, macroscopic hematuria), as well as serum IgA, did not show to have association with a particular morphological pattern of IgAN according to Oxf.C. In opposition to the Oxf.C. support data, the presence of crescents was identified in a significant percentage of the patients biopsies. Nevertheless, disease presentation was not significantly different in these patients. Also differently to what was present in the Oxf.C. data, positivity for S1 was only associated with higher proteinuria, and the presence of IF/TA>25% was associated only with lower CCr.

On the other side, IF findings, not included in Oxf.C., demonstrated to be relevant in this analysis. C1q positivity, traducing eventual activation of classical complement pathway (usually not related with IgAN), was associated with more proliferative forms of the disease, and IgM positivity was associated simultaneously to both higher Uprot and lower CCr, a fact not observed for each of the 4 histological parameters of Oxf.C.

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