FOXP3+ REGULATORY T-LYMPHOCYTES IN THE INTRARENAL INFILTRATES OF PROTEINURIC PRIMARY GLOMERULOPATHIES

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Objective

The finding of FOXP3+ regulatory T-lymphocytes (Tregs) in allograft biopsy samples from renal transplant recipients has been associated with lessening immune injury. However, there are sparse data on the presence and role of FOXP3+ Tregs in primary glomerulopathies of native kidneys. We assessed the immunohistochemical expression of FOXP3+ Tregs in IgA nephropathy (IgAN), focal segmental glomerulosclerosis (FSGS) and membranous glomerulopathy (MGN).

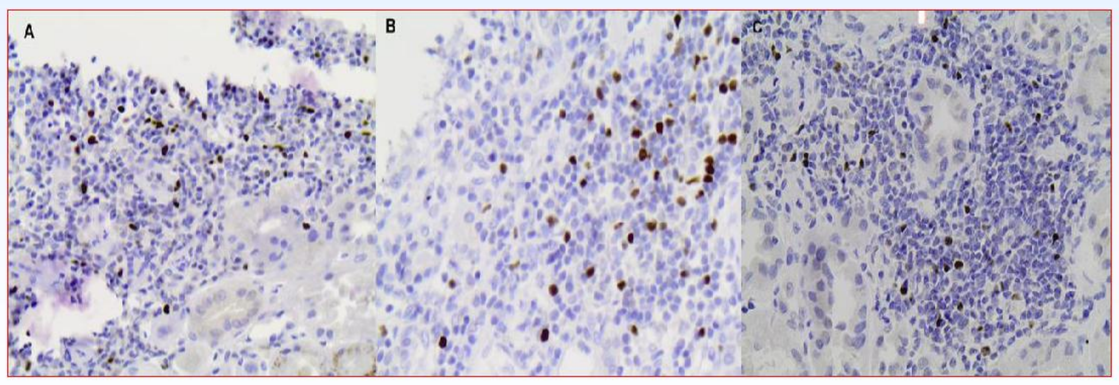

Figure 1. FOXP3+ Tregs in: A: IgA nephropathy, B: Focal segmental glomerulosclerosis, C: Membranous glomerulopathy.

Methods

A total of seventy-one biopsies (twenty-eight from patients with IgAN, twenty-two with FSGS and twenty-one with MGN), conducted due to proteinuria as main indication, were retrospectively analyzed. FOXP3+ Tregs, CD4+ and CD3+ T-lymphocytes per tissue mm^2 were counted, using digital analysis, in interstitial and periglomerular hotspots of inflammatory infiltration. Their absolute counts and ratios were correlated with histopathologic parameters and clinical outcome measures.

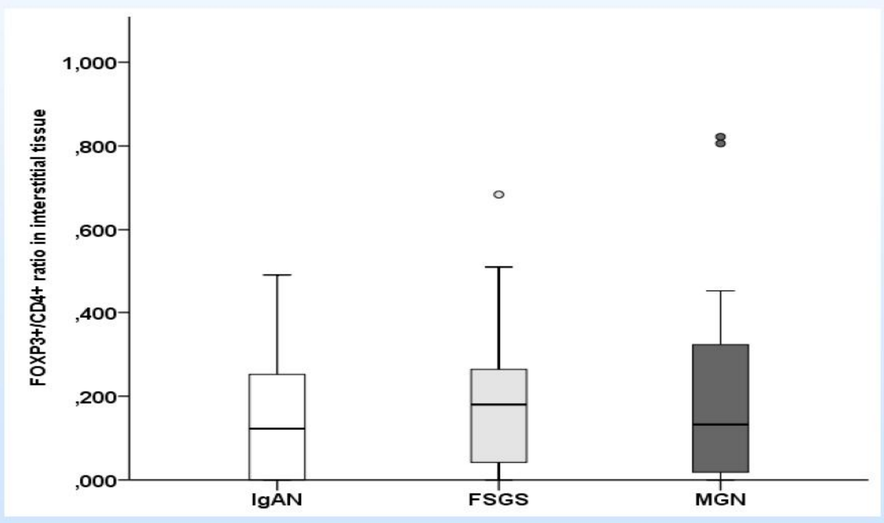

Figure 2.

Results

FOXP3+ Tregs were identified in the renal tissue in 64% of IgAN, 77% of FSGS and 76% of MGN (p>0,05) (fig. 1). No statistically significant difference was found between FOXP3+/CD4+ ratios in the interstitial tissue (fig. 2, p>0,05 for all comparisons). Higher interstitial FOXP3+ Tregs counts were found in patients without vascular hyalinosis compared to those with (1.814±2.160 versus 831±696, p: 0,029, table 1). A similar pattern was also observed for segmental sclerosis but it did not reach statistical significance. In patients that exhibited FOXP3+ Tregs interstitial infiltration and a high FOXP3+/CD4+ ratio (above the mean value), eGFR>60 ml/min was significantly more common in multivariate analysis (OR: 4,80, 95% CI: 1.2 –17,91, p: 0.019, table 2).

	FOXP3+ Tregs absolute count in interstitial tissue (per mm^2)		p value
Segmental sclerosis or not	1.047±858	1.477±2.315	NS
Global glomerulosclerosis or not	1.265±1.548	632±286	NS
Interstitial fibrosis ≥25% or <25%	1.462±1.766	718±462	NS
Interstitial inflammation dense or sparse	1.476±1.738	777±837	NS
Vascular hyalinosis or not	831±696	1.814±2.160	0,029

Table 1.

	eGFR ≥ 60 ml/min/1,73 m^2			Proteinuria ≥ 3,5 g/day		
	OR	95% CI	p value	OR	95% CI	p value
FOXP3+/CD4+ ratio in interstitial tissue						
Low	1			1		
High	4,80	1,29 - 17,91	0,019	0,93	0,29 - 3,00	0,902

Table 2.

Conclusion

The presence of intrarenal FOXP3+ Tregs in primary glomerulopathies seems to be rather frequent and increased expression may be associated with less histologic lesions. Raised FOXP3+/CD4+ ratio in the interstitial tissue independently predicts better renal function.

References

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