Prevalence of DNAJB9 positivity in our cohort of patients with fibrillary glomerulonephritis

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Aim

DNAJB9 is a heat-shock protein recently found to be the most abundant antigen in kidney specimens of patients with fibrillary glomerulonephritis (FGN).[1] The presence of DNAJB9 seems to be highly specific and sensitive for FGN.[2] The aim of this study was to investigate clinical and histological features and DNAJB9 positivity of the patients in our cohort of FGN.

Methods

The Registry of kidney biopsies at Department of Renal Pathology and Electron Microscopy, Dubrava University, Zagreb, between 2009 and 2021, was retrospectively reviewed for samples with FGN. Demographic, clinical and pathologic data of FGN patients were analyzed and additional immunohistochemistry (IHC) for DNAJB9 was performed on paraffin-embedded tissue. In order to define patients with FGN, we used following criteria: presence of Congo Red-negative glomerular deposits that were organized into randomly oriented straight fibrils 10-30 nm in diameter without distinct hollow core by EM and stained with antisera to immunoglobulin heavy and light chains by IF.

Results

We identified 17 adults (4 males) with FGN. Table 1 shows relevant demographic and clinical features of our cohort. The most common pattern of glomerular injury based on light microscopy was mesangial GN (13 patients). Light chain restriction was present in four samples of whom two had clear evidence of monoclonal gammopathy (MG) (case 14 and 16) and later were treated due to overt multiple myeloma. IHC for DNAJB9 was positive (Figure 1) in all cases except case 12 and 16. Case 12 did not have light chain restriction as well as evidence of MG or other systemic disease with kidney involvement.

Conclusions

In our cohort of patients with FGN, 88% of kidney samples expressed DNAJB9 positivity by IHC regardless of presence of light chain restriction, MG or systemic diseases with possible kidney involvement.

Table 1 Demographic and clinical characteristics of patients at the time of kidney biopsy.

Case No.	Sex	Age (y)	Year of diagnosis	AH	Proteinuria (g/day)	Full nephrotic syndrome	Microscopic hematuria	eGFR (ml/min/1.73 m^2)	Associated medical conditions
1	M	59	2010	+	3.4	-	+	64	HF/DMT2
2	F	55	2010	+	-	-	+	75	-
3	F	49	2011	+	1.7	-	-	54	SLE
4	F	58	2011	+	0.5	-	+	48	-
5	F	62	2012	+	-	-	+	45	-
6	M	59	2013	+	0.6	-	+	63	LC/DMT2
7	F	54	2013	+	9.8	+	-	64	-
8	F	61	2013	+	3.5	+	+	31	-
9	F	29	2014	-	-	-	+	77	SLE
10	F	54	2014	-	-	-	+	62	-
11	M	60	2014	+	13.7	+	-	36	DMT2
12	F	67	2015	+	1.5	-	+	79	-
13	F	73	2016	+	8.5	+	-	51	DMT2
14	F	77	2017	+	3.5	-	+	13	MG, LC, DMT2
15	F	65	2018	+	1.6	-	+	46	-
16	M	64	2018	+	5.4	+	+	56	MG, DMT2
17	F	63	2018	+	5.8	+	-	49	-
Mean [range]		59 [29-77]			4.6 [0.5-13.7]			54 [13-79]	

AH, arterial hypertension; HF, heart failure; DMT2, type 2 diabetes mellitus; SLE, systemic lupus erythematosus; LC, lung carcinoma; MG, monoclonal gammopathy.

Table 2 Pathohistological features of 17 patients with fibrillary glomerulonephritis.

	Light Microscopy (LM)							IF and IHC				Electron Microscopy	
Case No.	No. of glomeruli	Glomerular pattern by LM	IFTA (%)	GGS (%)	FSGS (%)	ah[a]	AFI[b]	IgG	C3	Light chain	DNAJB 9	Fibril diameter (nm)	Podocyte foot process effacement[c]
1	14	MesGN	20	0	0	2	2	2+	+/-	κ&λ	+	13 ± 3	+
2	30	MesGN	0	20	0	0	0	2+	2+	κ&λ	+	11.5 ± 1.3	-
3	5	MesGN	0	0	0	0	0	+/-	-	κ	+	13 ± 4	++
4	11	N	30	27	18	3	2	+/-	+/-	κ&λ	+	15 ± 2	-
5	17	MesGN	15	29	0	2	1	3+	2+	κ&λ	+	20 ± 4	+[e]
6	13	MesGN[d]	10	8	0	1	0	2+	2+	κ&λ	+	17.6 ± 4	+
7	20	MGN	30	10	20	0	0	2+	+	κ&λ	+	10.2 ± 2	+++
8	18	MesGN[d]	15	11	6	2	2	2+	+	κ&λ	+	16.5 ± 2	+++
9	32	N	0	6	0	0	0	+	+	κ&λ	+	14 ± 2	-[e]
10	23	MesGN	5	0	0	2	1	2+	0	κ&λ	+	14.9 ± 0.9	+
11	19	MesGN	65	32	26	3	3	3+	2+	κ&λ	+	13 ± 4	+
12	11	MesGN	15	11	4	3	2	+	-	κ&λ	-	16.1 ± 2.4	++
13	11	MesGN	10	27	0	3	1	3+	+	κ&λ	+	11 ± 2	+++
14	10	MesGN	50	30	0	3	0	2+	+	κ	+	12 ± 1.1	-
15	8	MesGN	30	25	25	3	0	+	+	κ&λ	+	11 ± 1.1	-
16	24	MesGN	10	25	0	3	0	3+	2+	κ	-	13 ± 2	+++
17	17	DPGN	40	29	18	0	2	+	2+	λ	+	19 ± 2	+++

LM, light microscopy; GGS, global glomerulosclerosis; FSGS, focal segmental glomerulosclerosis; MesGN, mesangial GN; N, normal; MGN, membranous GN; DPGN, diffuse proliferative endocapillary GN.

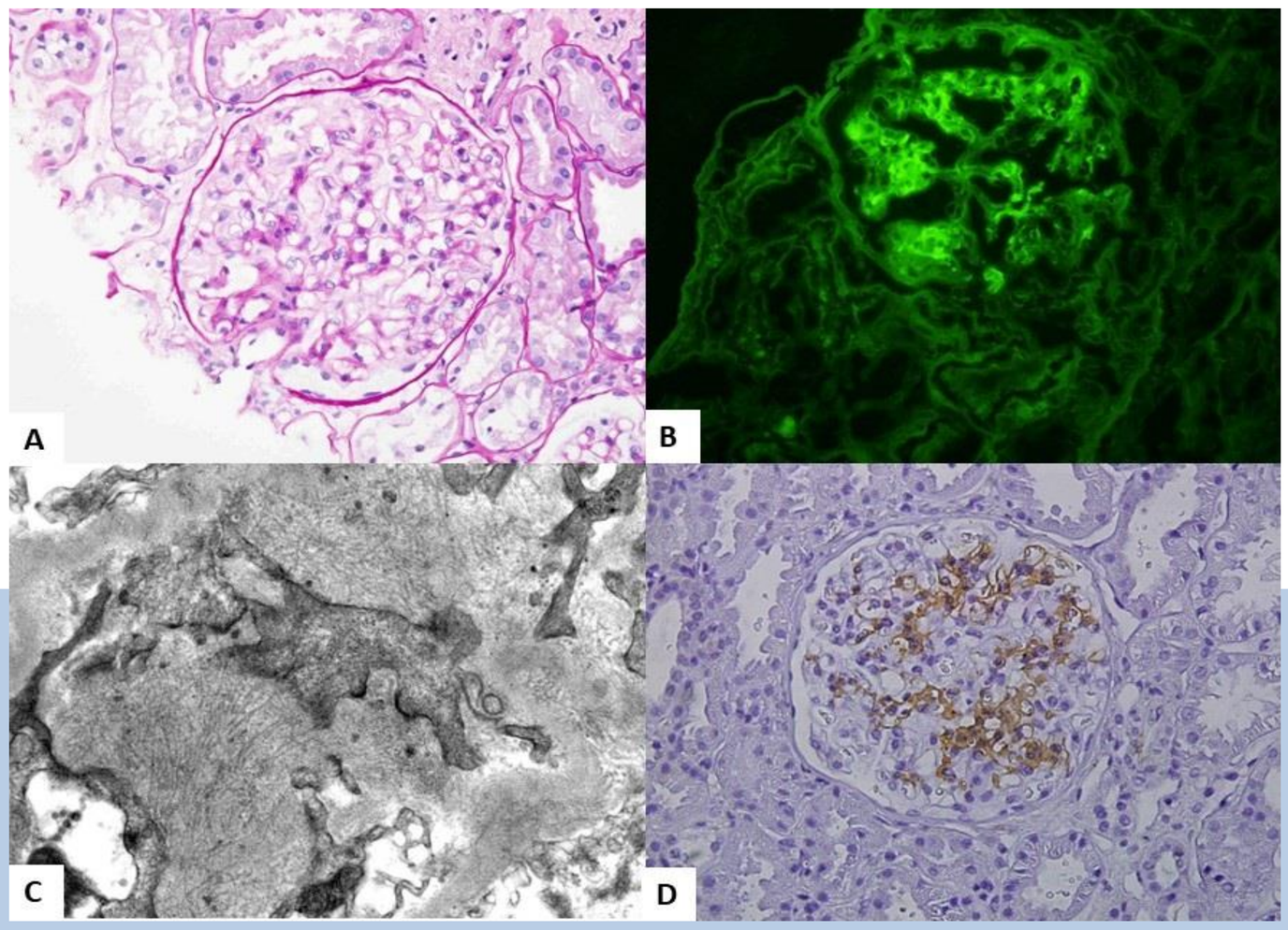

Figure 1 Kidney biopsy findings in case 9. A) Glomerulus with normal morphology. PAS stain, magnification x400. B) Immunofluorescent analysis showing smudgy IgG positivity. Magnification x400. C) Fibrillary deposits in mesangium. TEM x25000. D) Positive DNAJB9 immunohistochemistry stain in glomerulus, x400.

Abbreviations: *[a]Scored as: 0-absent, 1-mild, 2-moderate, 3-severe, [b]Scored as: 0-absent, 1-mild, 2-moderate, 3-severe, [c]Effacement scored as: - (absent), + (focally, in < 50 % of podocyte process surface), ++ (50 - 80 %), +++ (diffuse, > 80 %), [d]Accompanied by mesangial hypercellularity, [e]Additional finding of thin glomerular basement membrane.*

References: [1]Dasari S, et al. J Am Soc Nephrol. 2018;29:1–6.
[2]Nasr SH, et al. Kidney Int Reports. 2018;3:56–64.