IN FABRY DISEASE PODOCYTURIA IS ELEVATED IN UNTREATED vs TREATED ADULT PATIENTS AND DOES NOT CORRELATE WITH PROTEINURIA OR RENAL FUNCTION

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PURPOSE

To assess the degree of podocyturia in Fabry treated (agalasidase β 1m/kg EOW) vs untreated patients vs controls.
To correlate podocyturia with proteinuria and with GFR.

METHODS

Prospective controlled study

GROUP 1: CONTROLS
N = 11

GROUP 2: FABRY PATIENTS
N = 17

All patients on ACEi or ARBs

GROUP 2 A
N = 12: AGALASIDASE β 1 mg/Kg/15 days iv

GROUP 2 B
N = 5: Declined therapy

Variables: Age, gender, hypertension, diabetes, proteinuria, eGFR according to MDRD-4, podocyte count per 10 x20 microscopy power fields and number of podocytes/gram of urinary creatinine. All patients presented genetic mutations linked with the severe (classic) phenotype.

RESULTS

VARIABLE	GROUP 1 CONTROLS N = 11	GROUP 2 FABRY N =17	P
AGE (years)	48 ± 17.11	41 ± 12.5	NS
GENDER (males)	45%	47%	NS
HYPERTENSIVES	0	3	< 0.0001
DIABETICS	0	0	NS
PROTEINURIA (g/day)	0.09 ± 0.1	1.46 ± 1.06	< 0.0001
eGFR MDRD4 ml/min	92.73 ± 21.62	54.35 ± 41.62	0.01
PODOCYTE COUNT/10 x20	0.37 ± 0.30	1.00 ± 0.82	0.0089
PODOCYTES/gram urinary Creatinine	50.00 ± 28.88	87.53 ± 17.79	< 0.001

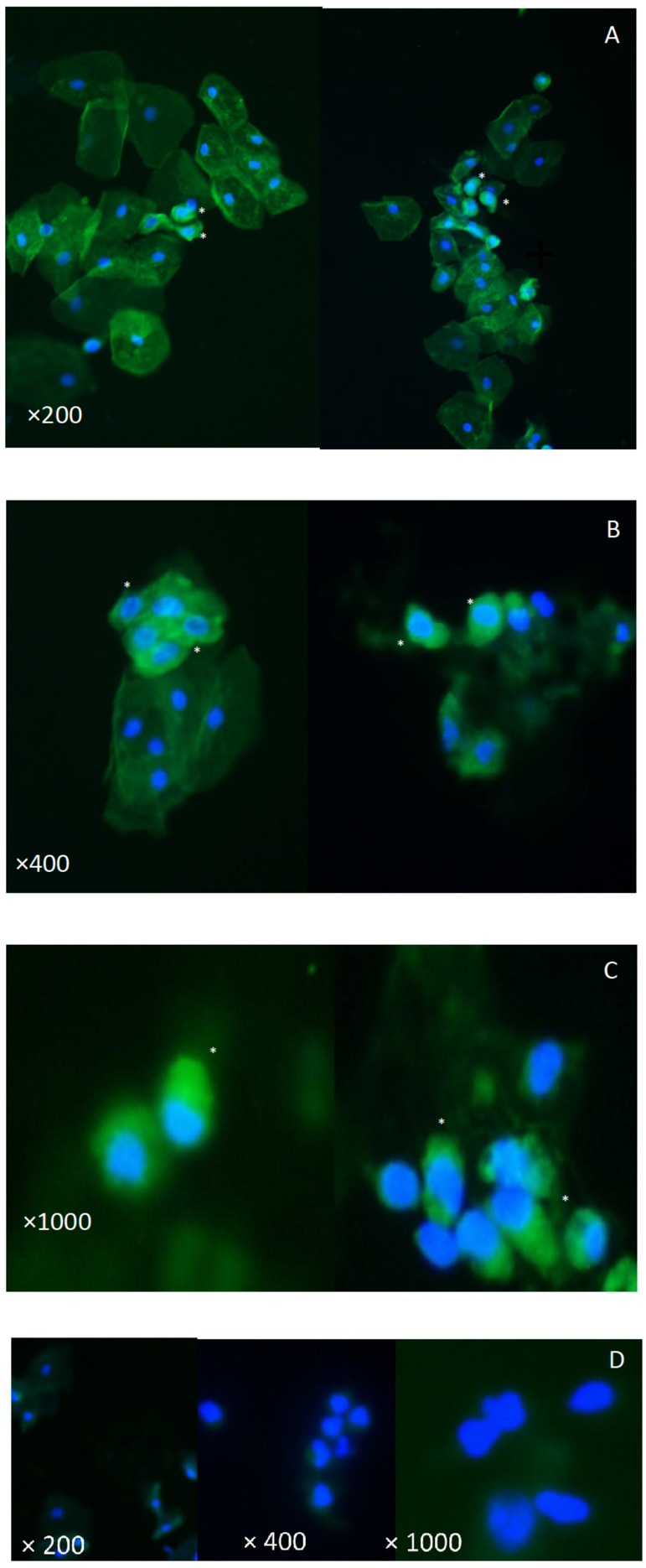
VARIABLE	GROUP 1A TREATED N = 12 *	GROUP 2 UNTREATED N = 5	P
AGE (years)	43.42 ± 12.01	36.4 ± 13.67	NS
GENDER (males)	47%	42%	NS
HYPERTENSIVES	3 (25%)	0	< 0.0001
DIABETICS	0	0	NS
PROTEINURIA (g/day)	1.70± 1.19	0.90 ± 0.40	< 0.0001
eGFR MDRD4 ml/min	54.25 ± 37.36	54.60 ± 35.58	NS
PODOCYTE COUNT/10 x20	0.55 ± 0.25	2.09 ± 0.63	< 0.0001
PODOCYTES/Gram Ur Creatinine	61.80 ± 44.90	149.26 ± 32.68	< 0.0001

**** Mean time in therapy: 5.99 + 1.33 years***

CORRELATIONS

GROUP 2A FABRY TREATED PATIENTS	GROUP 2B FABRY UNTREATED PATIENTS
PODOCYTURIA-PROTEINURIA ρ = -0.47	
PODOCYTES/g ur cr-e GFR ρ = 0.56 P = 0.05	PODOCYTES/g ur cr-e GFR ρ = -0.41
	PODOCYTES/g ur cr- PROTEINURIA ρ = 0.67
	e GFR- PROTEINURIA ρ = -0.95 P < 0.01

Urinary immunodetection of podocytes by immunofluorescence employing synaptopodin



Urine smear showing the presence of synaptopodin positive cells, identified as podocytes (A-C White asteriks).
Urine smear without podocytes: controls (D)

CONCLUSIONS

FABRY SUBJECTS DISPLAY HIGHER LEVELS OF PODOCYTURIA THAN CONTROLS.
FABRY TREATED PATIENTS DISPLAY A NEGATIVE CORRELATION BETWEEN PODOCYTURIA AND PROTEINURIA AND A POSITIVE CORRELATION WITH GFR.
FABRY UNTREATED PATIENTS PRESENT SIGNIFICANT HIGHER PODOCYTURIA DESPITE BEING YOUNGER AND LOWER PROTEINURIA.
IN UNTREATED INDIVIDUALS, PODOCYTURIA IS INDEPENDENT OF PROTEINURIA OR RENAL FUNCTION.

THERAPY WITH AGALASIDASE β 1 MG/KG EOW MAY PROTECT AGAINST IRREVERSIBLE PODOCYTE LOSS AND MAY PRESERVE RENAL FUNCTION.
HIGHER LEVELS OF PROTEINURIA IN TREATED PATIENTS MAY INDICATE THE INITIATION OF THERAPY AT ADVANCED STAGES OF THE DISEASE.
PODOCYTURIA COULD BE EMPLOYED AS A BIOMARKER TO START THERAPY OR TO ASSESS RESPONSE TO THERAPY, BUT NEEDS TO BE VALIDATED.

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H) Clinical Nephrology, primary and secondary glomerulonephritis.

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