PODOCYTES INJURY MARKERS IN PATIENTS WITH CHRONIC GLOMERULONEPHRITIS (CGN)

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INTRODUCTION

Podocyte (Pdc) injury and decrease in glomerular Pdc number leads to proteinuria (PU) and nephrotic syndrome (NS) that eventually progresses to glomerulosclerosis. Detection of Pdc injury by measurement of podocyturia and Pdc-specific protein in the urine has been used to estimate ongoing glomerular damage. Heat shock protein-27 (HSP-27) is one of the intracellular protective proteins, which involved in maintaining of Pdc cytoskeleton and foot processes, it can reveal in the urine during Pdc injury.

THE AIM

was to evaluate excretion of markers of podocyte injury: nephrinuria (NU), podocyturia (PdcU) and HSP-27 urinary level in patients (pts) with different CGN course.

METHODS

73 CGN pts were studied: 20 – with inactive CGN (I group), 23 active CGN – with proteinuria (PU) > 1 g/d (II group), 30 - with NS (III group), including 7 pts with severe NS (anasarca, PU higher than in pts with moderate NS (9,76 [6; 12] g/d vs 4,2 [3; 7,5] g/d), hypoalbuminemia < 20 g/L), and 7 pts - with NS and impaired renal function. 8 healthy subjects were studied as control. PdcU was estimated by urinary flow cytometry, the urinary levels of nephrin and HSP-27 by ELISA. WT-1 renal expression (as a nuclear marker of podocyte) was assessed by immunohistochemical morphometry. Response to immunosuppressive therapy was evaluated in 23 pts depending on the initial level of NU and Pdc

RESULTS

The PdcU, NU and HSP-27 levels in active CGN pts were higher then in control group, in pts III group – significantly higher than in II group (Tab 1).

The urinary HSP-27 in pts with active CGN correlated directly with PU (Rs = 0,27, p < 0,05) (Fig.1) and negatively with the level of serum albumin (Rs = -0,22, p = 0,07).

In CGN patients with severe NS (anasarca, PU to 12 g/d, hypoalbuminemia < 20 g/L) PdcU and urinary HSP-27 level were higher (168/μl [19; 782] and 2,28 ng/ml [0,93; 4,02] respectively) compared to CGN pts with moderate NS (7,87 /μl [4,2; 30], and 1,07 ng/ml [0,71; 1,72] respectively, p < 0,01). Direct correlation between PdcU and NU (Rs = 0,9, p < 0,05) establishes ongoing Pdc injury. At the same time, correlation between urinary HSP-27, PdcU (Rs = 0,42, p < 0,01) (Fig. 3) and NU (Rs = 0,32, p < 0,05) in NS confirms close connection between Pdc damage and protective mechanisms.

82% pts with low NU and PdcU (< level 17ng/ml and 20/μl) had NS remission during 6 month of active immunosuppressive therapy. On the other hand, 67% pts with high NU or PdcU (>17ng/ml or 20/μl) had the resistance to immunosuppressive drugs, given from 9 month to 2 years (Fig. 2). In tissue WT-1 expression was lower (podocytopenia) by severe NS course with the worst therapy response (Fig. 4).

Table 1. Urinary excretion of heat shock protein-27 (HSP-27) , nephrinuria (NU) and podocyturia level in patients with CGN (n=73)

Patients groups	N	HSP-27 urinary level (ng/ml)	Podocyturia (cells/μl)	NU (ng/ml)
I. Inactive CGN	20	0,72 [0,65;0,98] *	6,2 [3,7;6,8] *	8,1 [6,6; 10,3]
II. Active CGN with PU 1-3 g/d	23	0,76 [0,68;1,14] * °	6,77 [3,2;17,4] * °	9,5 [7,6; 12,9] *
III. Active CGN with NS	30	1,1 [0,73; 1,83] °	16 [8;38,4] * °	16,2 [9,9;25,7] * °
Healthy control	8	0,73 [0,66;0,96]	0 [0;6]	7,9 [1,7;9,5]

* - p<0,05 vs «III patients group» °- p<0,05 vs «healthy control»

Fig 1. Correlation between urinary HSP-27 and PU level in pts with active CGN

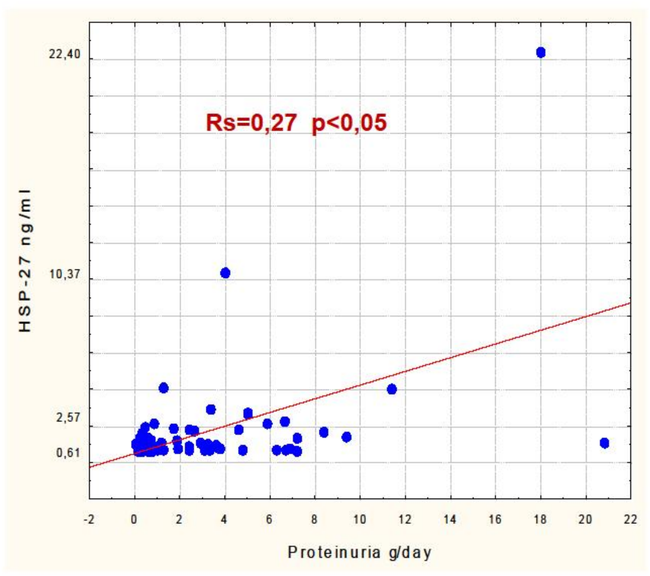


Fig 2. Podocyturia level and effects of therapy

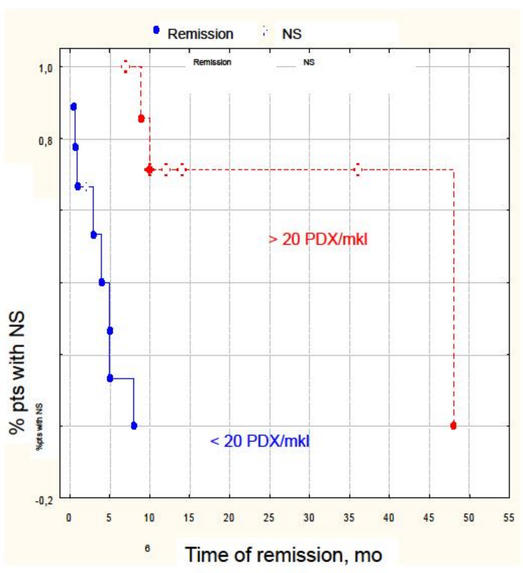


Fig 3. Correlation between urinary HSP-27 and PdcU level in CGN pts with NS

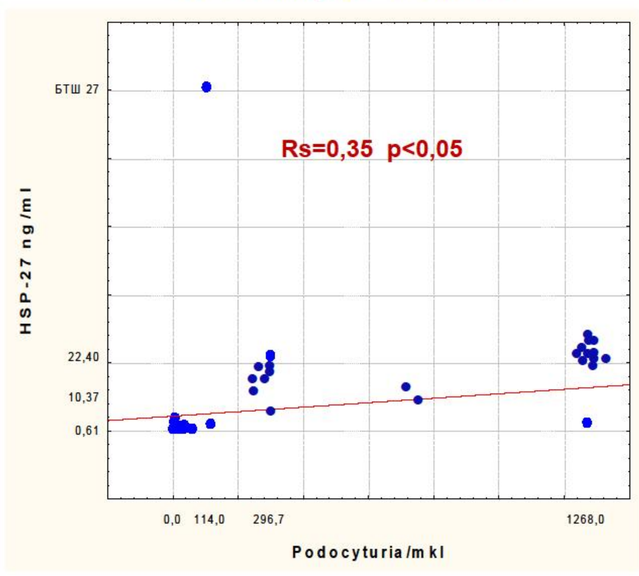
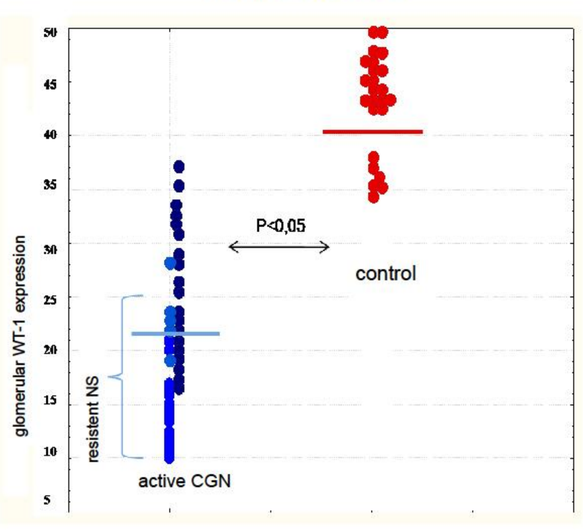


Fig 4. Glomerular WT-1 expression in pts with NS and without NS



CONCLUSION

These biomarkers are sensitive indicators Pdc injury and associated with high PU and NS severity. NU, PdcU may be useful noninvasive tests for assessment nephritis activity and prognosis.

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