LONG-TERM PERITONEAL DIALYSIS TREATMENT IS ACCOMPANIED WITH HIGH EXPRESSION OF B CELL ASSOCIATED GENES

Parikova A.[1], Hruba P. [2], Krediet R.T. [3], Struijk D.G. [3], Krejcik Z. [4], Stranecky V. [5], Viklicky O. [1]

1 Dept. of Nephrology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic. 2 Transplant Laboratory, Institute for Clinical and Experimental Medicine, Prague, Czech Republic. 3 Dept. of Nephrology, Academic Medical Center University of Amsterdam, The Netherlands. 4 Institute of Haematology and Blood Transfusion, Prague, Czech Republic. 5 Institute of Inherited Metabolic Disorders, Prague, Czech Republic.

INTRODUCTION and AIM

Permanent stimulation of the peritoneum during peritoneal dialysis (PD) is associated with chronic inflammation resulting in angiogenesis and fibrogenesis. Mainly macrophages, but also T cells have been shown to be involved in the pro-fibrotic response through the release of profibrotic mediators. The ongoing inflammation and extracellular matrix turnover seem to be critical processes in the development of severe complication of PD, encapsulating peritoneal sclerosis.

The aim of the study was to identify and compare genes potentially involved in peritoneal alterations during PD treatment by gene expression profiling of peritoneal cells in short- and long-term PD patients.

METHODS

Peritoneal effluent of the long-dwell (median 9, range 8-13 hours) of 33 stable PD patients was centrifuged to obtain peritoneal cells. The whole transcriptome of 20 patients treated less than 2 years and 13 patients treated more than 2 years was compared using Illumina Human HT-12 v4 Expression BeadChips . Differentially expressed genes were defined as those with a mean expression > 3.5, a fold change > 2 and a p value <0.05.

A 4-hour 3.86% glucose peritoneal equilibration test (PET), including temporary drainage after 1 hour for assessment of free water transport was performed on the day after the long-dwell collection in all patients. Peritoneal transport characteristics were assessed in both groups and compared using Mann-Whitney-U test.

Symbol	Definition
CD79A	encodes protein component of B lymphocyte antigen receptor
CD24	encodes a protein that is expressed on mature granulocytes and B cells and modulates growth and differentiation signals to these cells
BLK	encodes protein which has a role in B-cell receptor signaling and B-cell development. The protein also stimulates insulin synthesis and secretion in response to glucose
TCL1A	expressed in immature $CD4^-$ $CD8^-$ T cells and in several stages of developing B cells. *TCL1A* is also expressed in activated peripheral lymphocytes, promoting cell proliferation and survival by activating protein kinase B

RESULTS

Patient characteristics and transport parameters are shown in Table 1. In the long-term group 57 genes were up-regulated. In an enrichment analysis aimed to identify genes and pathways expressed differently between the short- and long-term group, genes involved in the immune system process (p= 1.70E-5), immune response (p=2.0E-3), cell activation (p=1.3E-3), leuko- and lymphocytes activation (p=2.6E-3, p=3.5E-3) were found to be substantially up-regulated in the group treated more than 2 years. Among the most up-regulated genes in the group treated > 2 years with more than 3-fold higher expression compared to patients treated < 2 years were the B cell associated genes: *BLK, CD79A, CD24, TCL1A (Fig).*

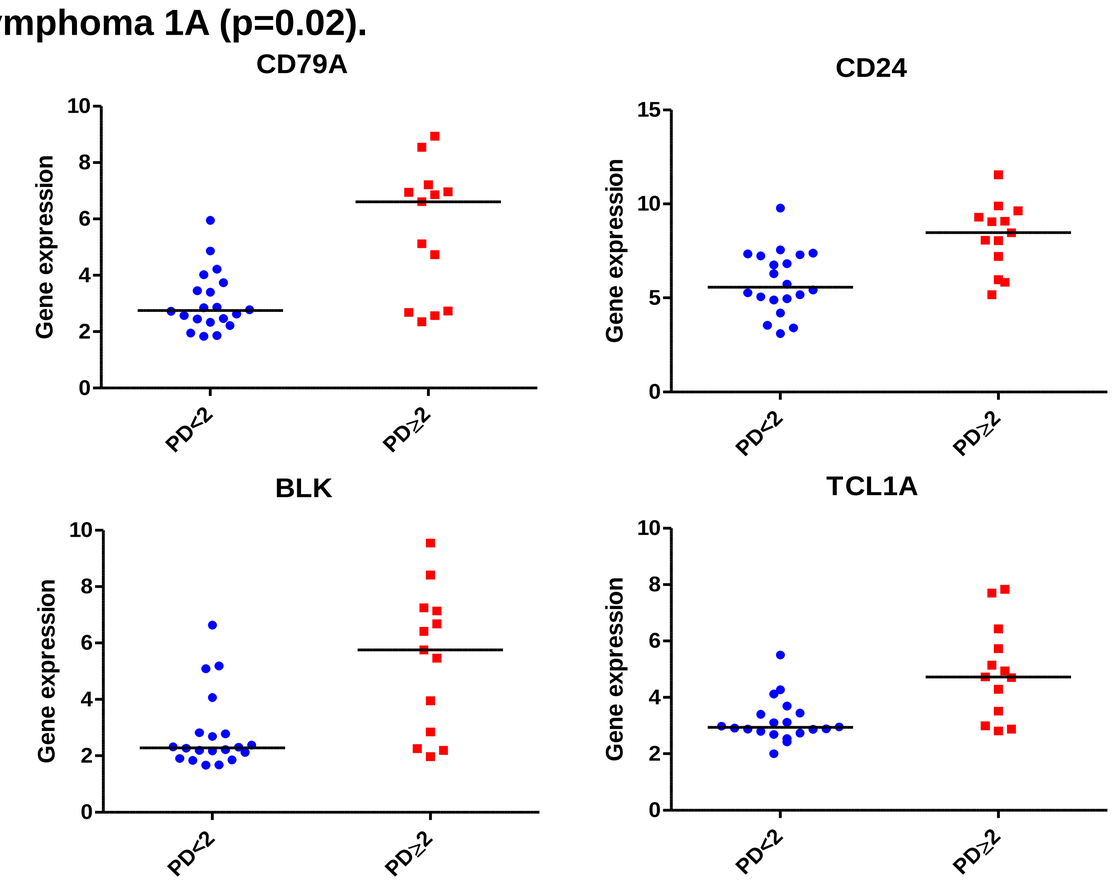
Table 1

Patient characteristics and transport parameters in short-term and long-term group. Medians and ranges are given.

	PD<2 years n=20	**PD>2 years n=13**	**p-value**
PD duration (months)	6(2-21)	43(24-68)	<0.01
Age (years)	46(29-69)	61(33-74)	0.02
Male/Female	10/13	9/4	0.72
Net ultrafiltration (mL)	305(-150-810)	630(0-880)	0.22
D/P creatinine	0.80(0.60-0.91)	0.77(0.58-0.87)	0.67
D/P sodium $_{60}$	0.9(0.8-1.1)	0.9(0.8-0.9)	0.74
NUF $_{0-60}$ (mL)	300(200-500)	350(200-700)	0.55
SPT $_{0-60}$ (mL)	174(63-380)	177(36-556)	0.87
FWT $_{0-60}$ (mL)	119(68-300)	144(16-314)	0.62

Fig.

Comparison of B cell associated genes between patients treated less and more than 2 years. *CD79A:* CD79a molecule , immunoglobulin-associated alpha (p=0.02). *CD24*: cell adhesion molecule (p=0.03). *BLK*: B lymphoid tyrosin kinase (p=0.03). *TCL1A*: T-cell leukemia/lymphoma 1A (p=0.02).



CONCLUSION

Peritoneal dialysis treatment provokes activation of immune system response, especially B cell related transcripts. B cell activity may be involved in long-term peritoneal membrane alterations. Whether this activity is associated with the alteration of peritoneal membrane function is the subject of ongoing research.

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