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SUBUROTHELIAL MYOFIBROBLASTS INFILTRATION IN SPONTANEOUSLY HYPERTENSIVE RATS

Hypothesis / aims of study

Although chronic bladder inflammation related to bladder ischemia is considerd to have causative role in emergence of over active bladder (OAB) (1), the pathophysiolosy is still unclear. Recent study have shown increased gap junction formation in the suburothelium myofibroblasts in biopsies from humans with OAB (2), suggesting that myofibroblasts might have a role in development of idiopathic OAB. On the other hand myofibroblasts is promoted by various stimulation such as oxidative stress and cytokines (3). Therefore, to assess the involvement of myofibroblast in pathogenesis of OAB in bladder ischemia, we investigated alteration of histopathology and cytokines expression using spontaneously hypertensive rats (SHRs) as OAB model related to bladder ischemia.

Study design, materials and methods

Twenty-week-old (n=4) male SHRs and age-matched Wistar-Kyoto rats controls were used. Single voiding volume and urinary frequency were analyzed using metabolic cage system. After voiding monitoring, bladder was harvested for analysis of histopathology and mRNA expression. Masson's trichrome stain was performed to evaluate alteration of collagen fiber in the bladder. In addition, immunohistostaining for αSMA was performed to identify myofibroblasts. Expression levels of IL6, IL8, TNFα mRNA in the bladder were investigated by real-time quantitative PCR. Statistical analysis was performed using Mann-Whitney U test. P value less than 0.05 was considered statistically significant.

Results

In voiding function analysis, single urine volume was significantly decreased and voiding frequency was significantly increased in SHRs compared to control. In histological evaluation, increased suburothelial collagen fiber was shown in SHRs compared to control group. Immunohistostaining revealed suburothelial positive staining for αSMA. In RT-qPCR analysis, mRNA expression level of IL6, IL8 and TNFα was significantly increased in SHRs compared to Control in the bladder (Figure1).

Interpretation of results

In the present study SHRs exhibited frequent urination in association with suburothelial myofibroblast infiltration evidenced by positive staining of αSMA. Furthermore we demonstrated, in SHRs, upreguration of IL6, IL8 and TNFα which could promote myofibroblast differentiation. These results suggest that cellular damage due to oxidative stress related to bladder ischemia may induce secretion of inflammatory cytokines such as IL6, IL8 and TNFα leading to suburothelial myofibroblast infiltration implicated in development of OAB.

Concluding message

We demonstrated that frequent urination in association with suburothelial myofibroblast infiltration which may have a role in development of OAB using SHRs. Therefore, further clarification of molecular mechanism associated with myofibroblast in emergence of OAB may lead to new therapy for idiopathic OAB.

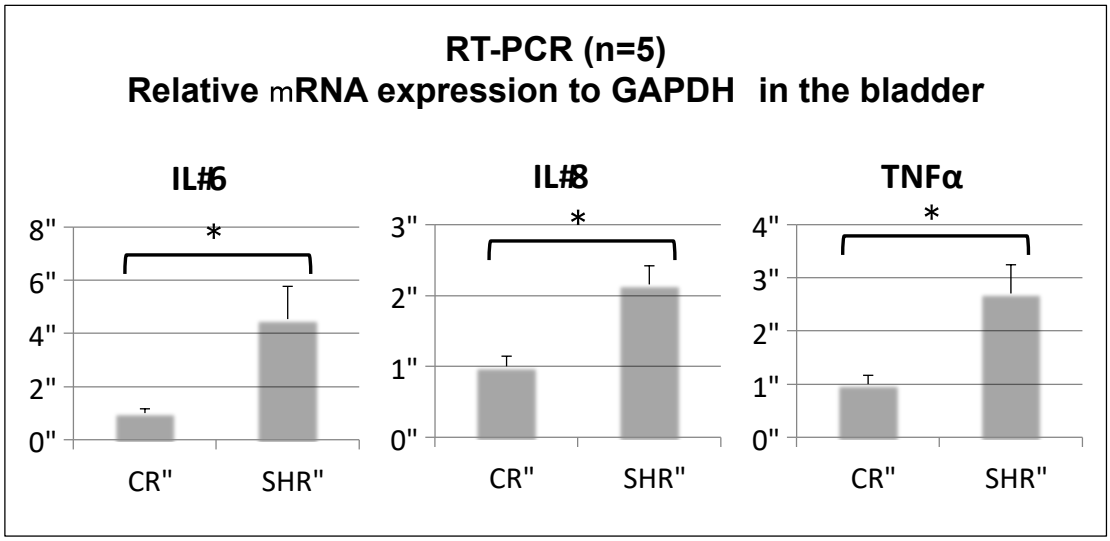

Figure 1 Relative mRNA expression to GAPDH in the bladder

* p < 0.05 Mann–Whitney U test

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Disclosures
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