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RELATIONSHIP BETWEEN PENILE / URETHRAL PAIN AND PATHOLOGICAL CHAGES OF THE PROSTATIC URETHRA IN PATIENTS WITH INTERSTITIAL CYSTITIS / PAINFUL BLADDER SYNDROME

Hypothesis / aims of study

Majority of interstitial cystitis / painful bladder syndrome (IC/PBS) patients are female and only 10% are male. IC/PBS often presents with lower urinary tract symptoms and bladder pain. In male IC/PBS patients, penile/urethral pain and discomfort are also their major symptoms.

Hydrodistension and transuretheral resection of Hunner's lesion are often applied in order to obtain a symptomatic improvement for bladder pain. However in those male patients, penile/urethral pain and discomfort sometimes do not improve in despite of those treatments.

In this study, we investigated whether inflammation spreads to the urethra as well as bladder mucosa in IC/PBS patients and examined the relationship between symptoms and histological findings of the urethra.

Study design, materials and methods

IC/PBS patients who were compatible with the NIDDK criteria were included. They completed O'Leary and Sant's indices, IPSS, CLSS (core lower urinary tract symptom score) and VAS questionnaire and underwent cystoscopy followed by biopsy and hydrodistension under spinal anesthesia. CLSS question 9 shows severity of bladder pain and question 10 shows severity of urethral pain (minimum score 0 and maximum score3) (ref. 1).

Bladder and prostatic urethra biopsies have been collected from eight male patients with IC/PBS and six control male patients. The biopsy specimens were stained with H&E and examined for epithelial denudation, submucosal edema and infiltration of inflammatory cells. These findings were graded by a score from 0 (none), 1(a little), 2(moderate), to 3(severe). The density (number per 1 square mm) of inflammatory infiltrates including mast cells was counted under microscopy. Immunohistochemistry (IHC) staining for NGF, CXCR3 and VEGF were also examined. The staining pattern was evaluated in epithelial cells both in terms of staining intensity and localization of positive cells. In terms of staining intensity, samples were subdivided into three categories: 1 (low), 2 (intermediate) and 3 (high). These histological slides were examined by four investigators. Data were analysed using the Mann-Whitney U test.

Results

A total of 14 cases (8 IC/PBS patients and 6 controls who are with low-risk solitary superficial bladder cancer and without prostatic involvement) were collected. Table 1 summarizes ages, symptom scores and histological findings of the IC/PBS urethral and bladder specimen and control urethral biopsy specimens. O'Leary and Sant's symptom index was 16.3 on average and problem index was 13.5 in IC/PBS patients. In the IC/PBS group, average scores of Q9 were 2.25 and average scores of Q10 was 2.25, which were significantly ($p<0.05$) higher than those (0.17 and 0.33, respectively) in the control group. Denudation of epithelium and infiltration of inflammatory cells of IC/PBS is remarkably increased compared to those of controls ($p<0.05$). Expression of NGF as determined by IHC showed a score of 2 in 25% and 3 in 75% of IC/PBS cases and a score of 1 in 33% and 2 in 16.7% were shown in control group; the difference between the two groups was statistically significant ($p<0.05$). Expression of CXCR3 was shown as a score of 2 in 75% and 3 in 25% of IC/PBS cases and a score of 1in 50% and 2 in 50% of the control group ($p=0.028$). Expression of VEGF was shown as a score of 2 in 37.5% and 3 in 62.5% of IC/PBS cases and a scores of 1 in 50% and 2 in 50% of the controls ($p<0.05$).

Interpretation of results

Urethral mucosa of IC showed characteristic histopathological features including denudation of epithelium, submucosal inflammation, and edema. The urethral mucosa of controls did not show those features in comparison with IC/PBS. Analysis of immunohistochemical staining also showed that staining intensity of NGF, VEGF and CXCR3 were increased in IC/PBS urethra compared to controls.

Concluding message

The results of this study suggest that not only bladder, but also urethra might be affected by inflammation. This may contribute to development of symptoms such as urethral/perineal pain and discomfort.

Table1. Results of the immunohistochemical staining on prostatic urethra from 8 IC/PBS patients and 6 controls

patient no.	*Age*	*OSSI*	*OSPI*	*CLSS Q .9 (pain in the bladder)*	*CLSS Q.10 (pain in the urethra)*	*denudation of epithelium **	*infiltration of monocytes **	*NGF ***	*CXCR3 ***	*VEGF ***
IC 1	69	20	16	3	3	2	2	3	2	3
2	57	15	11	0	2	3	3	3	2	2
3	71	13	14	2	0	3	2	2	3	3
4	67	18	14	2	3	3	3	3	2	2
5	69	19	16	3	3	3	3	3	2	3
6	61	19	16	3	2	3	3	3	2	3
7	67	17	12	3	3	3	3	3	3	3
8	70	9	9	2	2	3	3	2	2	2

Mean	66.4	16.25	13.5	2.25	2.25	2.75	2.75	2.75	2.25	2.63
Control 1	64	NA	NA	0	0	1	1	0	2	2
2	67	NA	NA	0	0	0	1	0	1	1
3	82	NA	NA	0	0	1	1	1	2	1
4	70	NA	NA	0	1	1	2	1	2	2
5	65	NA	NA	0	0	0	1	0	1	1
6	77	NA	NA	1	1	0	0	2	1	1
Mean	70.8	-	-	0.167	0.33	0.5	1	0.67	1.67	1.5
p value	0.51	-	-	0.006	0.008	0.0014	0.0017	0.002	0.028	0.005

NA: not applicable *: 0: normal, 1: weak, 2: intermediate, 3: severe **: 1: low, 2: intermediate, 3: high

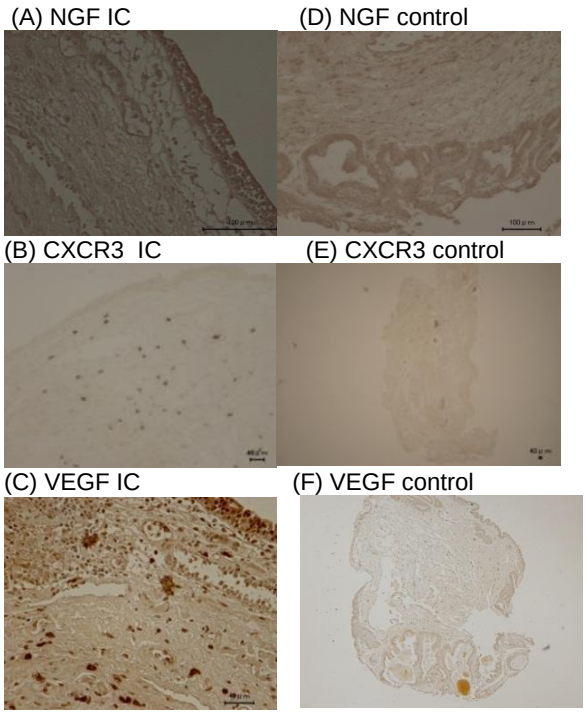

Figure 1 Represenatative immunohistochemistry staining of prostatic urethral specimens taken from IC patients (A, B and C) and control patients (D, E, and F) for NGF (A and D)CXCR3 (B and E) , and VEGF (C and F)expressions

References
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