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PAINFUL BLADDER SYNDROME: DO THE DIFFERENT HISTOPATHOLOGICAL FEATURES CORRELATE?

Hypothesis / aims of study

Painful bladder syndrome is defined as a clinical entity of chronic pelvic pain, pressure or discomfort perceived to be related to the urinary bladder, and accompanied by at least one other urinary symptom such as persistent urge to void or frequency. Confusable diseases as the cause of the symptoms must be excluded [1,2]. The exact prevalence of painful bladder syndrome is unclear, but some authors suggest it has been widely underestimated so far [3]. Moreover, evidence is increasingly pointing towards the existence of several subtypes of this disease [1-3]. The precise pathophysiological mechanisms of painful bladder syndrome remain unknown, though current understanding of the disease links aberrant differentiation of the urothelium, neural upregulation and mastocytosis to its development. For diagnosis of painful bladder syndrome, ESSIC (European Society for the Study of Interstitial Cystitis/Painful Bladder Syndrome) recommended a specific diagnostic work-up, as well as performing cystoscopy with hydrodistension and bladder biopsies [1]. This study evaluates correlation between the histological findings in bladder biopsies handled following ESSIC recommendations. We also evaluate the importance of the histological findings in painful bladder syndrome compared to the cystoscopic findings.

Study design, materials and methods

All included patients consulted our third line referral centre with symptoms of painful bladder syndrome that were at least six months present. Other confusable diseases were ruled out by thorough history, clinical examination, urine analysis and imaging. Only cases who scored more than 12 on the O' Leary-Sant Interstitial Cystitis Symptom and Problem indices and had a score than 7 on a visual analogue scale for pain were included. All patients underwent cystoscopy with hydrodistention, During this procedure at least three deep biopsies were taken, including detrusor muscle, from those areas with the most apparent bladder wall lesions. The biopsies were examined by the same pathologist. For the cell countings different stains were used, but the Leder stain was used most frequently. A cut-off point of 28 mast cells/mm² was used for the diagnosis of detrusor mastocytosis. Data from our database were analysed using SPSS software. To assess correlations between cystoscopic and biopsy parameters, different methods were used. The correlation between ordinal variables in our database, such as urinary epithelial damage and inflammatory infiltrate, was measured using Gamma statistics. To compare mastocytosis with other biopsy parameters, on the other hand, we used the Anova test. Where significant differences were found, comparative judgment was used. In the latter case, to correct multiple testing, a number of tests were used, such as the Tukey test.

Results

In this study 15 men and 93 women were included. The median age was 53 years, ranging from 28 to 82 years. Correlation analysis using the methods described above showed a significant correlation between urothelial damage and inflammatory infiltrate (Gamma value = 0.465, $p = 0.006$). Significant correlations were also found between urothelial damage and detrusor mastocytosis (Tukey corrected ANOVA, $p < 0.001$). Surprisingly, in this study, no correlations were found between inflammatory infiltrate and detrusor mastocytosis (ANOVA, $p = 0{,}202$). The cystoscopic parameters (glomerulations, bleeding, mucosal tears, bladder capacity and Hunner's lesion) showed no significant correlations with histological features of bladder biopsies (Table 1).

Interpretation of results

The ESSIC working group made recommendations for the diagnostic work-up of painful bladder syndrome. These guidelines recommend cystoscopic hydrodistention and bladder biopsies. In this study an attempt was made to find correlations between the different cystoscopic and histological features as set by the ESSIC. The results show significant correlations between some histological features: urothelial damage, inflammatory infiltrate and detrusor mastocytosis. No correlations were found between cystoscopic and histological findings. These results can be related to those previously suggested by other authors. Possible drawbacks in this study are on the one hand that bladder wall fibrosis is not assessed in a standard way in our biopsies, on the other hand that the histopathological grading of inflammatory infiltrate in our biopsies is arbitrary, thus not reflecting an absolute count of the different inflammatory cell types. Our results show that painful bladder syndrome comprises a group of clinical entities showing different cystoscopic and histological features. In our opinion, both cystoscopy and bladder histology are essential keystones in the diagnostic work-up of painful bladder syndrome.

Concluding message

The exact etiology of the painful bladder syndrome remains elusive. In this study correlations were found between the presence of urothelial damage and the presence of inflammatory infiltrate, as well as between the presence of urothelial damage and detrusor mastocytosis. However, there were no other apparent correlations between the different cystoscopic and histological features as such. These findings emphasise the recommandations stated in the ESSIC guidelines that both cystoscopic and bladder biopsies are mandatory tools in the diagnostic approach of painful bladder syndrome.

Table 1: p-values calculated for correlations between pathological features and cystoscopic findings. (x = gamma statistics used, xx = ANOVA used)

	Cystoscopic findings	**Pathological features**

Pathological features	*Glomerulations*	*Bleeding*	*Urothelial damage*	*Inflammatory infiltrate*
Urothelial damage	0.442 (x)	0.153 (x)		0.006 (x)
Inflammatory infiltrate	0.145 (x)	0.537 (x)	0.006 (x)	
Detrusor mastocytosis	0.967 (xx)	0.675 (xx)	< 0.001 (xx)	0.202 (xx)

References

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What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
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Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**