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LOCALISATION OF MATRIX METALLOPROTEINASES 2 AND 8 WITHIN THE BLADDER IN INTERSTITIAL CYSTITIS AND PAINFUL BLADDER SYNDROME

Aims of study

Interstitial cystitis (IC) is an uncommon and poorly understood inflammatory bladder disease. One theory of pathogenesis involves breakdown of the glycosaminoglycan (GAG) layer lining the bladder allowing ingress of noxious chemicals to initiate an inflammatory response. Matrix metalloproteinases are a family of proteolytic enzymes which can digest GAGs and other glycoproteins of ground substance. We have previously shown a possible association between elevated MMP-2 activity and IC *in vitro*. An immunocytochemical (ICC) study of the localisation of MMP-2 and MMP-9 in bladder biopsies from patients with IC as defined by the NIDDK[1], patients with the painful bladder syndrome, and control patients (undergoing colposuspension) was conducted to examine the cellular localisation of MMP-2 and any differences between groups of patients.

Methods

Stored blocks of bladder biopsies were used to cut new sections for ICC against MMP-2. Biopsies were taken from patients having cystoscopy as an investigation for the frequency/urgency syndrome. Patient biopsies were classified as IC if the NIDDK criteria were met, or as painful bladder syndrome (PBS) if the criteria were not fully met. Control biopsies were obtained from women having surgery for urodynamic stress incontinence. 5µm sections were cut and stained with mouse monoclonal antibody to MMP-2 (Neomarkers, CA, USA). Positive staining was visualised using the DAB/peroxidase method. Intensity of staining of urothelium, suburothelial mesenchyme, blood vessels and detrusor muscle was assessed semi-quantitatively using the H-score[2]. For MMP-8, positive cells were counted within the urothelium, mesenchyme and muscle layers. Comparisons between groups were made using non-parametric statistical methods. Comparisons between groups were made using non-parametric statistical methods.

Results

34 patient blocks were identified, of whom 7 (21%) met the NIDDK criteria for IC. 18 samples from control patients were available. In all sections the urothelium did not stain for MMP-2. Staining in the sub-urothelial mesenchyme, blood vessels and destrusor muscle was variable in intensity. Mesenchyme staining was absent in 12 sections (5 control and 7 PBS). Median H score in mesechyme was 0.5 (0.02 – 2.1) in positive sections, with no difference between groups. Endothelial staining was absent in 13 biopisies (7 controls and 6 PBS). Median H score was 0.4 (0.05 – 1.5) in the remainder, with no difference between groups. 7 biopsies had no muscle. In the remaining 45, no staining was seen in 2 PBS biopsies. Median H score was 1.25 (0.05 - 2.5) with no differences between groups.

MMP-8 staining was limited to polymorphonuclear leucocytes (PNML). Three patterns of staining were identified: absent or scanty stained cells; stained PNML marginalised within blood vessels; stained PMNL filling the majority of blood vessels, and PMNL filling the vessels with cells also present in the extravascular mesenchyme. The pattern of staining seen bore no correlation with the classification of biopsies as control, FUS or IC.

Conclusions

MMP-2 does not appear to be present in urothelium, regardless of disease category. The presence of MMP-2 staining within the submucosal layers of the bladder is variable, although present in the majority of samples. Detrusor muscle demonstrated the highest intensity of staining. We were unable to detect differences in localisation of MMP-2 between control and case bladders, suggesting that MMP-2 is not implicated in the mechanism of aetiology of IC or PBS.

The localisation of MMP-8 positive cells was variable, but did not bear any relation to the disease state of the biopsies. These data support our previous work that leucocyte numbers are not discriminatory between disease states.

References

1. Hanno P, Levin RM, Monson FC, et al. Diagnosis of interstitial cystitis. J.Urol. 1990; 143: 278-281.

2. Lessey BA, Ilesanmi AO, Lessey MA, Riben M, Harris JE, Chwalisz K. Endometrial epithelium express integrins differentially throughout the menstrual cycle: implications for implantation, contraception, and infertility. Am.J.Reprod.Immunol. 1996; 35: 195-204.