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Title: INCREASED EOSINOPHIL PROTEIN X EXCRETION IN URINE FROM PATIENTS WITH INTERSTITIAL CYSTITIS

Aim of the study:

Interstitial Cystitis (IC) is a chronic inflammatory disease of unknown etiology. IPD-1151T, a new immunoregulator that supress helper T cell mediated allergic responses, including IgE production and eosinophil inflammation have shown some promise in the treatment of IC (1) suggesting a role of eosinophils in IC. Activated human eosinophils secrete four well characterized cytotoxic proteins, eosinophil-derived neurotoxin (EDN)/ eosinophil protein X (EPX), eosinophil cationic protein (ECP), eosinophil peroxidase (EPO) and major basic protein (MBP). Increased urinary level of ECP has been found in urine from patients with IC (2). However, a possible role for EPX in IC has never been investigated. In the present study urinary excretion of EPX was measured in morning urine from patients with IC at the day of cystoscopy with biopsies and healthy subjects.

Methods:

Morning urine samples were collected from nine healthy women and nine patients with diagnosed IC according to NIDDK criteria. Urine samples from IC patients were collected at the day for control cystoscopy with biopsies. Aliquots of each specimen were immediately centrifuged and the supernatants were stored at – 80 ^{o}C until assayed. U-EPX was measured with radioimmunoassay. All determinations were performed in duplicate and normalized to urine creatinine.

Results:

The levels of EPX was significantly raised in morning urine from patients with IC compared with controls. Mean urinary excretion of EPX were 109.7 ∀70.4 μg/mmol creatinine and 43.7 ∀22.0 μg/mmol creatinine in IC patients and controls, respectively (p = 0.01). Biopsies revealed chronic inflammation with lymphocytes and plasma cells in the lamina propria. Only few eosinophils and mast cells were seen in the lamina propria. In 4 patients biopsies eosinophils were found inside small vessels often attached to the endothelium. No eosinophils were seen in the detrusor.The mean mast cell count in detrusor biopsies was 44 mast cells per mm^2. All urine cultures were negative.

Conclusions:

Release of the neurotoxic EPX from eosinophils in the urinary bladder may play a role in the pathogenesis of IC. Crossing the endothelial barrier eosinophils may degranulate as part of their activation and thus become undetectable in routine sections.

References:

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