POSSIBLE ROLES OF MAST CELLS IN MICE WITH CHRONIC PELVIC PAIN SYNDROME

Hypothesis / aims of study
Chronic pelvic pain syndrome (CPPS) severely affects QOL of the patients suffered from interstitial cystitis/bladder pain syndrome (IC/BPS) and irritable bowel syndrome (IBS). CPPS is often refractory to currently available therapeutic treatments. Previous studies have implicated that mast cells might be involved in the pathophysiology of IC and IBS\(^1\)-\(^3\), suggesting their contributions in the urinary symptoms in CPPS. In the present study, we examined the effects of mast cell deficiency on abnormalities in experimental IC and IBS models.

Study design, materials and methods
The mast cell-deficient WBB6F1-\(^{W/W}\) mice (\(W/W\)) and control WBB6F1-\(+/+\) mice (control) (\(n=10\) for each group) were obtained. Voiding frequency and voided volume (VV) were determined in these mice housed in metabolic cages. To establish an IC model, we intraperitoneally administered cyclophosphamide (CYP) at a dose of 300 mg/kg 4 hours before examination. For an IBS model, we applied a stress-induced colonic hypersensitivity model, in which animals were subjected to acute physical restraint within a small tube for 30 minutes. A combination of these two was used as an IC+IBS model. After the experiments, urinary bladders were removed. Sections were stained with toluidin blue for the detection of mast cells, as well as with HE for routine histological examination.

Results
There was no significant difference in body weight between \(W/W\) and control. The mean voiding volumes (VV) before experiments was significantly lower in \(W/W\) as compared to control. Following the acute physical restraint (IBS model), the relative changes in VV per void remained at the same levels (\(W/W\):110.7%; control: 118.6%). After the peritoneal injection of CYP (IC model), although VV per void were decreased in both \(W/W\) and control groups, the voiding capacity was better maintained in the former (\(W/W\): 32%; control: 19.2%). Similar results were obtained in the IC+IBS model (\(W/W\): 45.3%; control: 22.3%). Histological examination of the urinary bladder revealed no significant abnormalities in the IBS model either in \(W/W\) and control mice. In the IC and IC+IBS models, although mucosal ulceration and edematous thickening of the wall were noted in both \(W/W\) and control groups, the inflammatory changes were much less prominent in the former.

Interpretation of results
The mean VV before experiments was significantly lower in \(W/W\) as compared to control. In IBS model, the relative changes in VV remained at the same levels. In IC model, although VV were decreased in both \(W/W\) and control groups, the voiding capacity was better maintained.

Concluding message
The lack of significant changes in VV and histology in the IBS model indicated that the acute physical restraint stress itself is insufficient to induce urinary dysfunction and inflammatory changes. The decrease in VV and histological features of acute inflammation in the IC and IC+IBS models appeared to be well correlated. Our findings strongly suggest that the presence of mast cells in the urinary bladder might be an aggravating factor of inflammation associated with IC.

References

Disclosures
Funding: Grant-in-Aid for Scientific Research (C) KAKENHI #24590721 Clinical Trial: No Subjects: ANIMAL Species: mice Ethics Committee: The Asahikawa Medical University Institutional Animal Care