Best Basic Science Abstract

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INFLAMMATORY INFILTRATES SPECIFIC TO HUNNER TYPE INTERSTITIAL CYSTITIS

Hypothesis / aims of study

It has been demonstrated that Hunner type interstitial cystitis (HIC) is a distinct inflammatory disorder, while non-Hunner type IC (NHIC) was of a scarcely inflamed entity (1). Historically mast cell infiltration has been recognized as a histological feature specific to HIC, but sceptical views toward the mastocytosis in IC have been recently reported (2). In this study, we compared inflammatory infiltrates among HIC, NHIC, non-IC cystitis, and 'normal' bladder samples to determine an HIC-specific inflammatory cell infiltration.

Study design, materials and methods

In total 133 specimens of the bladder were used in this study; 62 of HIC, 38 of NHIC, 15 of non-IC cystitis, and 18 of morphologically normal bladder. Diagnosis of IC and differential diagnosis of HIC and NHIC were made according to the clinical guidelines for interstitial cystitis and hypersensitive bladder syndrome (3). Two bladder specimens were obtained from 31 patients with HIC, including one from the Hunner lesion and one from a non-lesion area. In all other patients, one specimen was analysed. Fifteen non-IC chronic cystitis specimens were obtained from seven patients with non-specific chronic cystitis, and eight patients with non-muscle invasive bladder cancer. These specimens showed roughly the same degree of chronic inflammation as the HIC specimens. Diagnosis of chronic cystitis was made according to the histological evidence of non-malignant chronic inflammation represented by predominant stromal infiltration of lymphoplasmacytic cells, edema, and fibrosis. Eighteen morphologically normal bladder specimens were obtained from 17 patients with bladder cancer and one patient with leiomyoma of the urinary bladder. This comprised the 'normal control' group. We performed immunohistochemical detection of infiltrating T-lymphocytes, B-lymphocytes, plasma cells and mast cells using anti-CD3, CD20, CD138 and mast cell tryptase antibodies, respectively. Quantitative analysis of lymphoplasmacytic and mast cell infiltration was performed using image analysis software. Mast cell numbers were evaluated separately in the entire area and detrusor muscles of the specimen. Of the two specimens from each HIC case, one with higher mast cell numbers was selected and used throughout the study. Correlation between cell numbers was examined.

Results

Demographics and characteristics in patients with IC are shown in Table 1. Gender distribution showed significant female predominance in the IC group (28 versus 3 in HIC, and 27 versus 11 in NHIC, respectively) compared with the non-IC group (7 versus 8 in non-IC cystitis, and 5 versus 13 in normal control, $p < 0.001$, respectively). The mean age was 68.5 (range 38 – 88), 55.9 (20 – 83), 72.5 (54-85) and 64.3 (40-78) years in the HIC, NHIC, non-IC cystitis, and normal control groups, respectively. Patients with NHIC were significantly younger than those with HIC and non-IC cystitis ($p = 0.01$, respectively). A similar degree of lymphoplasmacytic infiltration was observed between HIC and non-IC cystitis specimens, and between NHIC and normal control specimens, respectively (Fig. 1A). Likewise, no significant differences in the number of mast cells were observed between HIC and non-IC cystitis specimens, and between NHIC and normal control specimens, respectively (Fig. 1B). Detrusors were included in 18, 20, 12 and 13 specimens from the HIC, NHIC, non-IC cystitis and normal control, respectively. There were no significant differences in the number of mast cells in detrusor muscles between IC and non-IC groups (Fig. 1C). The number of mast cells significantly correlated with that of lymphoplasmacytic cells (spearman's $\rho = 0.46$, $p<0.001$, Fig. 1D).

Table 1. Demographics and characteristics in patients with interstitial cystitis (IC)

	Hunner type IC	Non-Hunner type IC	*p* value
No. (male / female)	31 (3 / 28)	38 (11 / 27)	0.07
Mean age at the time of biopsy (years)	68.5 ± 11.1 [38 – 88]‡	55.8 ± 17.8 [20 - 83]	<0.01*
Age at onset of IC (years)	65.3 ± 10.3 [38 - 80]	52.6 ± 17.6 [15 - 81]	<0.01*
OSSI†	13.2 ± 4.0 [7 - 20]	12.0 ± 3.6 [3 - 20]	0.30
OSPI†	11.6 ± 3.6 [3 - 16]	10.8 ± 3.8 [1 - 16]	0.42
VAS†	6.7 ± 2.4 [1 - 10]	6.0 ± 2.9 [0 - 10]	0.46
Urinary frequency	16.3 ± 5.4 [7 - 30]	15.6 ± 7.4 [4 - 42]	0.36
Average voided volume (mL)	109.8 ± 41.7 [40 - 220]	125.4 ± 81.1 [30 - 400]	0.92
Maximum voided volume (mL)	168.0 ± 58.6 [50 - 300]	219.3 ± 112.9 [50 - 500]	0.08
Maximum bladder capacity at bladder distension (mL) with a pressure of 80 cmH_2O at the time of biopsy	526.7 ± 180.4 [200 - 900]	698.7 ± 181.0 [400 - 1200]	<0.001**

†OSSI / OSPI: O'Leary and Sant's symptom index and problem index, VAS: visual analogue scale (for pain)
Values are expressed as mean±SD [range]
*$p<0.01$, **$p<0.001$ significant difference by Wilcoxon rank-sum test

Fig. 1. Quantitative analysis of the number of lymphoplasmacytic cells (A) and mast cells in biopsy specimens (B: entire areas C: detrusor muscles) and correlation between lymphoplasmacytic cells and mast cells in all specimens (D)

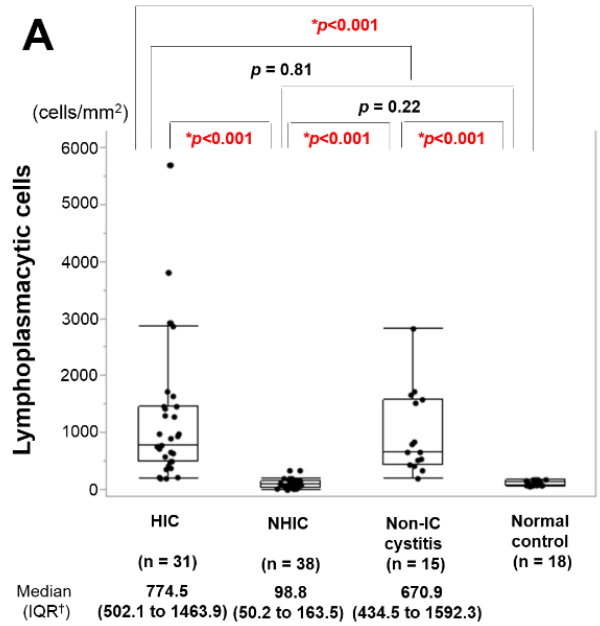

Figure 1A: Lymphoplasmacytic cell infiltration in biopsy soecimens (The total count of CD3-+CD20-+CD138-positive cells)

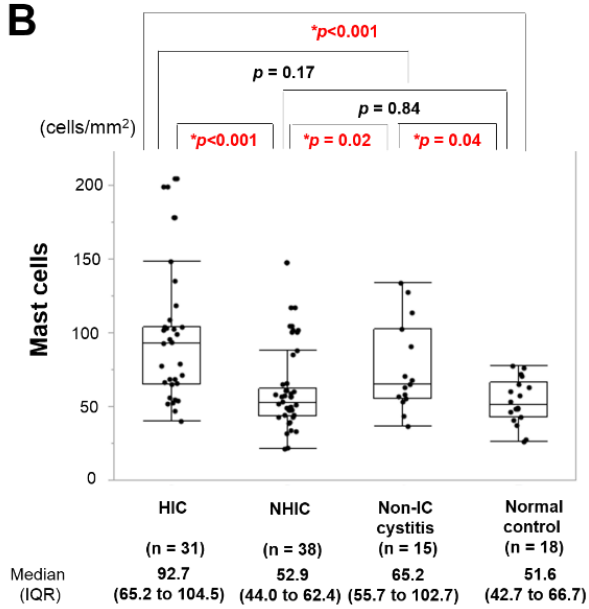

Figure 1B: Mast cell infiltration in biopsy specimens (entire areas) (The total count of mast cell tryptase-positive cells)

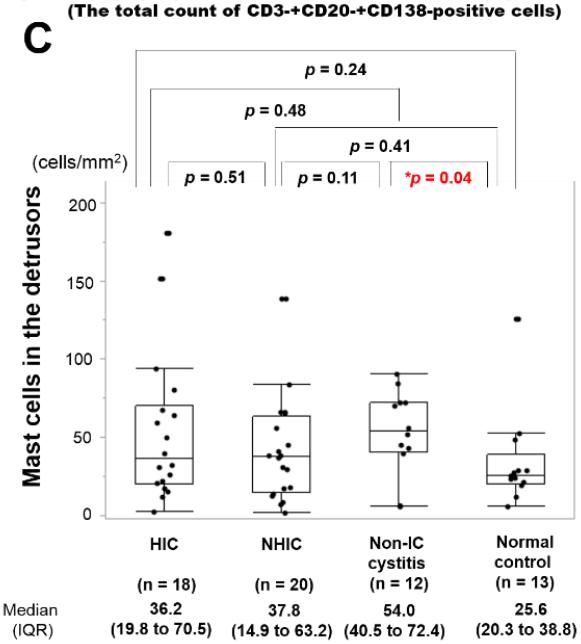

Figure 1C: Mast cell infiltration in detrusors in biopsy specimens (The total count of mast cell tryptase-positive cells)

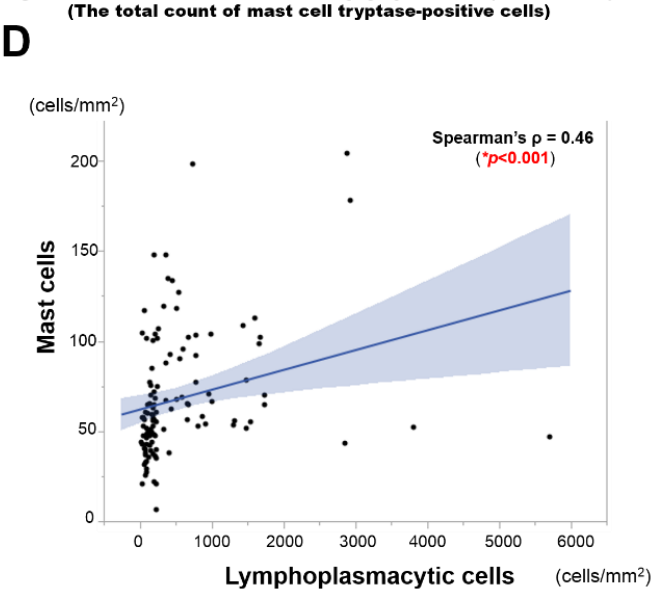

Figure 1D: Correlation between the number of mast cells and lymphoplasmacytic cells

* Significant difference by Wilcoxon rank-sum test
† Interquartile range

Interpretation of results

The results indicate that there is no difference in the number of mast cell tryptase-positive cells in either entire areas or detrusor muscles of IC biopsy specimens compared to non-IC biopsy specimens, suggesting that mast cell infiltration may be proportional to the degree of lymphoplasmacytic infiltration.

Concluding message

Infiltration of inflammatory cells but not mast cells may be a feature of HIC.

References

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Disclosures

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