

# #604 Hunner lesion histopathology with recurrence in biopsies of patients with interstitial cystitis/ Bladder pain syndrome after triamcinolone injection

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### Hypothesis / aims of study

Bladder interstitial cystitis (ICS), is a chronic, debilitating condition affecting the bladder and surrounding tissues, involving abnormalities in the bladder lining. The tissue is infiltrated with cells form the immune system, including antigen-presenting cells, B and T lymphocytes and mast cells. The nervous system is affected as well. Hunner lesions (HL) feature areas of inflammation troughout the organ and ulceration may be present, causing severe pain and bleeding. HL treatment relies on fulguration and/or injection of triamcinolone with corticosteroid injected into the bladder wall. The present study examined the histopathology of HL and the severity, progression, recurrence rate, and response to triamcinolone.

#### Study design, materials and methods

Retrospective chart review of 14 patient (median age of 65.66  $\pm$  16.15 years) with demographics, clinical characteristics, and treatment outcomes from January 2013 to November 2023 was performed. Bladder biopsies for patients with HL (n=6), Non-Hunner lesions (NHL)(n=3) and controls (UC)(n=4) were were stained with Hematoxylin and Eosin (H&E), Masson's Trichome, and Toluidine blue. Immunofluorescence was carried out using antibodies for p75<sup>NTR</sup>, TNF-α and CD68. Data was statistically analyzed using GraphPad Prism 9 and SPSS v27.0 softwares.

#### **Results and interpretation**

This study comprised a total of 14 participants, with a median age at This study comprised a location 14 participants, with a median age at biopsy of  $65.67 \pm 16.15$  years, who were monitored for an average duration of  $5.4 \pm 4.40$  years. Bladder biopsies were obtained from 13 out of the 14 individuals (12 females, 1 male) with HL IC/BPS (n=6), N-HL IC/BPS (n=3) and UC (n=4). The number and location of HL varied among patients, ranging from one to six lesions, rendeminantly located at the demonscription and to rendeminantly predominantly located at the dome, posterior, and posterolateral walls. Patients with HL had higher rates of autoimmune diseases compared to those with NHL and UC. All patients with HL experienced baseline lower urinary tract symptoms (LUTS) and underwent various therapies, including medical oral therapy (3/5 patients) and fulguration with laser/electrocautery (5/5 patients). Among the patients with HL, 5 out of 7 (71.4%) received intravesical injection of triamcinolone at the lesion sites, with 3 patients requiring multiple re-treatments due to symptom recurrence up to 3-6 times. One out of the 7 patients underwent simple cystectomy without a triamcinolone injection trial. Clinical questionnaire scores for Overactive Bladder Symptom Score (OABSS), International Consultation on Incontinence Questionnaire - Short Form (ICIQ-SF), and Incontinence Impact Questionnaire - Short Form (IIQ-7) were not significant between the groups. Blood neutrophil-to-lymphocyte ratio (NLR) was assessed as it is recognized as a potential indicator of systemic inflammation and has been studied in IC/BPS patient cohorts. Histopathological analysis revealed acute and chronic inflammatory changes along with extensive denudation in the HL group, exhibiting more mast cells and fibrosis in the subgroup that received multiple triamcinolone injections. Preliminary results of immunostaining indicated cells positive for TNF-alpha,



	Ctl	HL	NHL
	n=6	n=6	n=3
Sub-epithelial inflammation			
Grade 0	3	0	3
Grade 1	2	5	0
Grade 2	1	1	0
Lymphoid aggregate			
Absent	3	1	3
Present	3	5	0
Plasma rich cell areas			
Absent	4	3	3
Present	2	3	0
Neutrophilic infiltration			
Absent	3	5	3
Present	3	1	0
eosinophilis infiltration			
Absent	5	6	3
Present	1	0	0
Full thickness epithelium			
Absent	3	5	0
Present	3	1	3
Epithelial denudation/loss			
Grade 0	3	1	3
Grade 1	3	4	0
Grade 2	0	1	0

Table 1. Hematoxylin-eosin scores



Fig 2. Biopsies from controls (Ctl), patients with IC displaying HL or NHL were stained with toluidine blue. Mast cells were present in every sample (arrows) at the level of the lamina propria and urothelium, being most abundant in HL. Bar = 50 microm



Fig 3. Biopsies from patients with IC displaying Hunner's lesions were stained for p75NTR, (left) CD68 (middle) and TNF-alpha (right). Receptor p75 was found expressed inside Hunner's lesion while staining for CD68 and TNF-alpha could be found only in the areas surrounding the lesions.



Fig 4. Number of mast cells counted on Toluidine blue staining and density of signal in Masson's trichrome staining. ANOVA one way, \*P<0.05, \*\*P<0.01 compared to control.

#### Conclusions

Microscopic examination of the biopsies by classic histology staining provide an insight into the development of the pathology. Individuals diagnosed with BPS/IC with HL, who undergo treatment with triamcinolone, display more pronounced clinical manifestations, pathological features, and positive immunostaining for CD68, p75<sup>NTR</sup> and TNF-alpha, when compared to patients with NHL and UC. Further investigations with a larger patient cohort are imperative to validate and substantiate these results.

## DISCLOSURE The authors have no potential conflict of interest.