

517 Angiogenesis in bladder tissues are strongly correlated with urinary frequency and bladder pain in patients with interstitial cystitis



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INTRODUCTION

To clarify the pathophysiology of urinary frequency and bladder pain usually seen in interstitial cystitis (IC) patients with or without Hunner lesions (HIC or NHIC), we examined the correlation among bladder inflammation, angiogenesis, fibrosis and denudation of urothelium in bladder biopsied tissues using immunohistochemistry, and O'Leary-Sant scores including symptom indexes (OSSI), problem indexes (OSPI) and visual analog scale (VAS) pain scores.

METHODS

Bladder biopsied tissues were collected from 12 HIC female patients, 12 NHIC female patients and 12 age-matched female patients (controls) with stress urinary incontinence and pelvic organ prolapse. Immunohistochemical staining of tissue necrotic factor- α (TNF- α), mast cell tryptase, vascular endothelial growth factor (VEGF), CD31, transforming growth factor- β (TGF- β), SLUG associated with epithelial mesenchymal transition and E-cadherin as well as Masson trichrome staining were examined in bladder tissues of each group, and the ratio of each staining per whole tissues (TNF- α , mast cell tryptase, VEGF, CD31, TGF- β , SLUG, E-cadherin) or muscle layers (Masson trichrome) was measured with Image J software (Fig. 1).

In addition, all participants completed OSSI, OSPI and VAS pain score questionnaire, and the significant correlation between the expression of TNF- α , mast cell tryptase, VEGF, CD31, TGF- β , collagen, SLUG or E-cadherin, and OSSI, OSPI and VAS pain scores was examined, respectively.

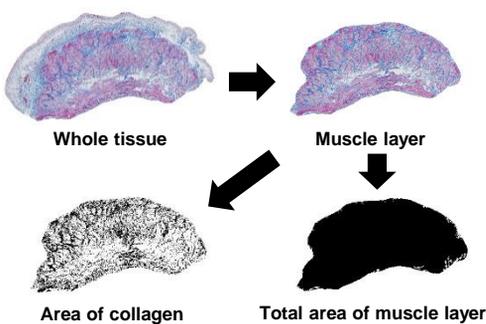


Fig. 1 Digital image analysis - Masson trichrome

RESULTS

The expression of TNF- α , VEGF, CD31, TGF- β and SLUG was significantly increased in NHIC and HIC patients compared with controls whereas the significant increases in the expression of mast cell tryptase and collagen were observed in HIC patients compared with controls and NHIC patients (mast cell tryptase) or compared with controls (collagen). On the other hand, the expression of E-cadherin was significantly decreased in HIC patients compared with controls and NHIC patients (Fig. 2). In addition, the increased expression of CD31 in bladder tissues were strongly correlated with OSSI ($r=0.81$), OSPI ($r=0.76$) and VAS pain scores ($r=0.76$) (Table).

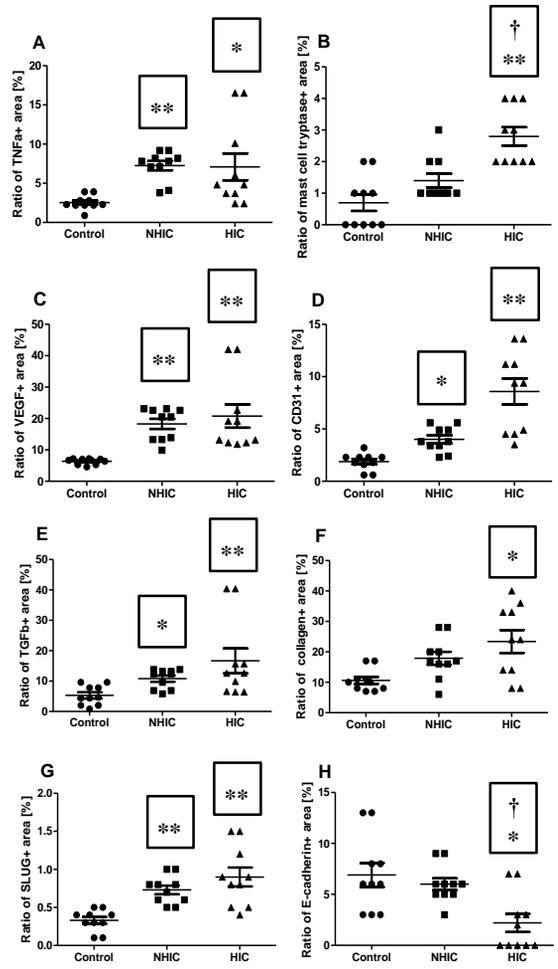


Fig. 2 The expression ratio of TNF- α (A), mast cell tryptase (B), VEGF (C), CD31 (D), TGF- β (E), collagen (F), SLUG (G) and E-cadherin (H)

Table The correlation of TNF- α , mast cell tryptase, VEGF, CD31, TGF- β , collagen, SLUG and E-cadherin with OSSI, OSPI and VAS pain scores

	OSSI	OSPI	VAS
TNF- α	0.41	0.58	0.51
Mast cell tryptase	0.59	0.69	0.74
VEGF	0.55	0.64	0.62
CD31	0.81	0.76	0.76
TGF- β	0.44	0.54	0.48
Collagen	0.39	0.53	0.44
SLUG	0.59	0.63	0.61
E-cadherin	-0.46	-0.40	-0.48

CONCLUSIONS

Bladder inflammation evident as the increased expression of TNF- α and mast cell tryptase, **angiogenesis** evident as the increased expression of VEGF and CD31, **fibrosis** evident as the increased expression of TGF- β and collagen, and **denudation of urothelium** shown by the increased expression of SLUG (epithelial mesenchymal transition) and the decreased expression of E-cadherin in bladder tissues were significantly correlated with urinary frequency and bladder pain. Especially, neovascularization evident as the increased expression of CD31 is likely to be a strong contributing factor to OSSI, OSPI and VAS pain scores in IC patients.

These results suggest that angiogenesis in IC bladder tissues are strongly correlated with urinary frequency and bladder pain in patients with NHIC and HIC. Therefore, angiogenesis would be a potential therapeutic target for controlling these urinary symptoms in IC patients.