

## DEVELOPMENT OF BLADDER GLOMERULATIONS AFTER HYDRODISTENSION IN PATIENTS WITH UPPER URINARY TRACT UROLITHIASIS SUGGESTING CROSS TALK AND BLADDER INFLAMMATION OCCUR BETWEEN UPPER AND LOWER URINARY TRACT

### Hypothesis / aims of study

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a disease of chronic inflammation of bladder presented with urinary frequency, urgency, and bladder pain. Development of glomerulations after hydrodistension is considered being diagnostic of IC/BPS. However, lower urinary tract symptoms are also common in the patients with upper urinary tract (UUT) urolithiasis. The aim of this study was to investigate whether there is relationship between UUT urolithiasis and bladder inflammation.

### Study design, materials and methods

A total of 73 patients with UUT urolithiasis were enrolled and received cystoscopic hydrodistension before the stone surgery. Bladder tissues from 29 patients who developed glomerulations after hydrodistension were compared with 10 controls. Immunofluorescence (IF) staining of adhesive protein E-cadherin, tryptase (indicating mast cell activation), and TUNEL (indicating urothelial cell apoptosis) were performed. The IF intensity of E-cadherin was measured using an Image J method. The percentage of activated mast cells and apoptotic cells were measured and quantified as positive cell per area unit ( $4 \mu\text{m}^2$ ).

### Results

The mean age was  $57.0 \pm 12.5$  years old for the urolithiasis group and  $50.5 \pm 9.6$  for the controls. Fifty one of the 73 (70.0%) patients developed glomerulations after hydrodistension. Grade 1 glomerulations in 37 patients, grade 2 in 13, and grade 3 in 1 were noted without any bladder ulcer in these patients. In patients with stone position in middle or distal ureters, the percentage of glomerulations was significantly higher than those with stone positions in upper ureter or kidney ( $92.3\%$  (24/26) v  $57.4\%$  (27/47),  $p < 0.01$ ). After excluding the patients with pyuria (28 patients, 38.4%), the rate of glomerulations was still significantly higher in the patients with middle or distal ureteral stone than those with upper ureteral or renal stones ( $90.9\%$  v  $47.8\%$ ,  $p < 0.01$ ). In IF staining (Fig. 1), the distribution of E-cadherin in the bladder tissue of patients with UUT urolithiasis was significantly lower than controls ( $19.4 \pm 14.0$  v  $42.4 \pm 16.7$ ,  $p < 0.01$ ). The activated mast cell and apoptotic cell numbers in the bladder tissue of urolithiasis patients were both significantly higher than controls ( $13.5 \pm 7.0$  v  $1.3 \pm 1.2$  and  $2.3 \pm 1.9$  v  $0.1 \pm 0.3$ , respectively, both  $p < 0.01$ ).

### Interpretation of results

Development of glomerulations after hydrodistension is considered specific to IC/BPS before, and the mechanism is unknown. Urothelial dysfunction and suburothelial inflammation play important roles in IC/BPS bladders. In this study, glomerulation rate in overall urolithiasis patients was around 70%, independent of pyuria. Elevated urothelial dysfunction and suburothelial inflammation were also proven in the bladder tissue of these patients, implying the communication of inflammatory process between the upper and lower urinary tracts. Pelvic organ cross-sensitization has been observed before, and the convergent afferent pathway with neurogenic inflammation is the presumed mechanism. The higher glomerulation rate in patients with stone in more distal portion of UUT also suggests that more closer to the bladder got more chances of cross talk.

### Concluding message

Glomerulations after hydrodistension are not specific for IC/BPS. The incidence of glomerulations in patients with UUT urolithiasis is high, especially in those with stone position in the middle or distal ureter. Urothelial dysfunction, increased suburothelial inflammation and apoptosis are observed in the bladder tissue of patients with UUT urolithiasis, indicating the existence of cross talk of inflammation between UUT and LUT.

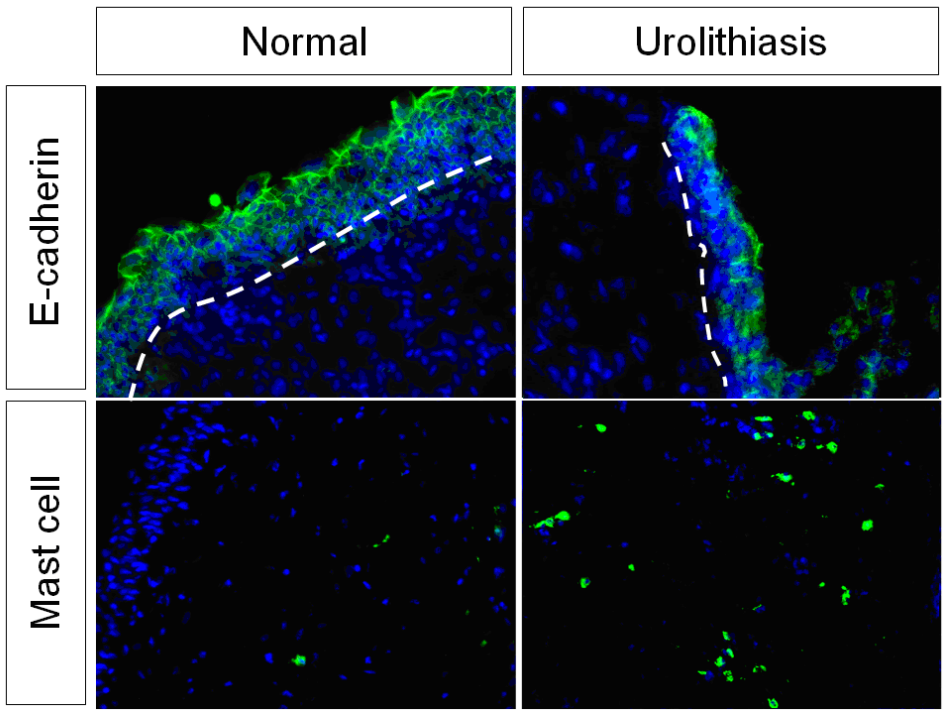


Fig. 1. Immunofluorescence staining in the bladder mucosa of patients with UUT urolithiasis and normal controls.

Disclosures

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