396

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CHANGES IN EXTRACELLULAR MATRIX COMPONENTS OF BLADDER DETRUSOR IN RELATION TO BLADDER HYPERTROPHY AND COMPLIANCE IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA

AIMS OF STUDY

With the use of ultrasound estimated bladder weight (UEBW) as a measure of bladder hypertrophy, the pathophysiology and clinical implications of bladder hypertrophy caused by infravesical obstruction have been described in patients with benign prostatic hyperplasia (BPH) (1,2). In our previous study, the significant increase in the ratio of connective tissue-to-smooth muscle was found in relation to the degree of bladder hypertrophy in BPH patients (3). These results prompted us to further evaluate the changes in extracellular matrix components (collagen types I and III, fibronectin), in relation to bladder hypertrophy and urodynamic findings in BPH patients.

METHODS

Thirty-four patients with BPH (71.4±7.9 years) underwent subcapsular prostatectomy, and a full-thickness specimen of anterior bladder wall was obtained at surgery. An informed consent regarding the sampling of bladder wall was obtained prior to surgery. As normal controls, cadaver bladders excised on autopsy in 13 men (68.5±18.0 years) with no urinary tract diseases were used. In all cases, international prostate symptom score, post-void residual urine volume, maximum flow rate, bladder compliance, prostate volume, transition zone volume were obtained prior to surgery. UEBW was measured using transabdominal sonography with a 7.5 MHz probe. From the thickness of the anterior bladder wall and the intravesical volume, UEBW was calculated supposing the bladder to be sphere (1).

Bladder wall specimens were fixed in 10% formalin before embedding in paraffin. On thin sections stained by the Masson-trichrome method, the ratio of connective tissue to smooth muscle (c/m) was obtained by dividing the sum of the connective tissue area by sum of the smooth muscle area using a computer assisted color image analysis system. In addition, serial sections in each sample were used for immunohistochemistry for collagen types I and III and fibronectin using rabbit anti-human monoclonal collagen types I and III and fibronectin antibodies, respectively. Similarly, the ratio of collagen type III-immunoreactive area-to-collagen type I-immunoreactive area (collagen III/I) and the ratio of fibronectin-immunoreactive area-to-non-immunoreactive

area (f/n) were obtained.

RESULTS

In controls, the c/m, collagen Ⅲ/Ⅰ and f/n ranged from 20.9 to 30.0% (25.4±2.4%), from 22.2 to 43.1% (33.0±5.9%) and from 27.0 to 54.9% (41.8±9.1%), respectively. An age correlated significantly with c/m ($r=0.629$, $p<0.05$), but not with collagen Ⅲ/Ⅰ and f/n. In BPH cases, UEBW ranged from 21.0g to 126.1g (47.9±25.4g), showing a significant negative linear relationship with compliance. All cases with low compliant bladders (<10ml/cmH2O) had UEBW of 60g or more. When analyzed together, there was no significant difference in c/m between controls and BPH cases. However, c/m in BPH patients with UEBW of 60g or more was significantly greater than that in control cases. There was also a significant difference in c/m between BPH cases with UEBW of 60g or more and those with UEBW less than 60g. In all but 1 case (96%, 24/25), with UEBW of less than 60g, c/m was less than 30%, while in all 9 cases with UEBW of 60g or more c/m was 30% or more ($p<0.0001$).

As for collagen Ⅲ/Ⅰ and f/n, statistically significant differences were noted between control and BPH cases. In addition, both collagen Ⅲ/Ⅰ and f/n in BPH cases with UEBW of 60g or more were significantly greater than those with UEBW of less than 60g. In those cases with considerable bladder hypertrophy as evaluated by UEBW (60g or more), infiltration of collagen type Ⅲ into smooth muscle and fibronectin were more prominent than control and other BPH cases.

There were significant relationships between c/m and collagen Ⅲ/Ⅰ ($r=0.601$, $p<0.0005$), between c/m and f/n ($r=0.676$, $p<0.0001$) and between collagen Ⅲ/Ⅰ and f/n ($r=0.684$, $p<0.0001$). When analyzed together in 34 BPH cases, UEBW correlated significantly with all morphometric measures (c/m, $r=0.744$, $p<0.0001$; collagenⅢ/Ⅰ, $r=0.698$, $p<0.0001$; f/n, $r=0.733$, $p<0.0001$). Among urodynamic measures obtained, bladder compliance was the only one correlating significantly with c/m ($r=0.673$, $p<0.0001$), collagen Ⅲ/Ⅰ ($r=0.475$, $p<0.05$) and f/n ($r=0.590$, $p<0.001$). There was also a significant correlation noted between f/n and postvoid residual urine volume ($r=0.514$, $p<0.01$).

CONCLUSIONS

These results suggest that abnormal increase of connective tissue accompanied with increased levels of collagen type Ⅲ and fibronectin could contribute to advanced bladder hypertrophy with the loss of elasticity of the bladder wall in patients with infravesical obstruction.

REFERENCES

1. Urology **47**:942, 1996 2. J Urol **158**:89, 1997 3. J Urol **161**:827, 1999