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ROLE OF CAJAL CELLS IN THE GENESIS OF REFRACTORY OVERACTIVE BLADDER IN WOMEN

Hypothesis / aims of study

Recent studies have shown that the Cajal cell-like interstitial cells are found in the muscles of many organs - myocardium, Fallopian tubes, gallbladder, pancreas, in the addition to gastrointestinal tract [1, 2] as well as in the urogenital system organs - renal pelvis and ureter, bladder, urethra, prostate, penile corpora cavernosa. That's why it has been hypothesized, that these cells provide spontaneous myogenic activity of the surrounding smooth muscle cells by their pacemaker activity [2]. That's why the objective of our work was to identify the morphological features and the expression of CD117 in bladder tissues in women with refractory OAB and chronic cystitis.

Study design, materials and methods

We performed a morphological study of 16 biopsy specimens of the bladder wall from women with chronic cystitis, and 14 specimens from women with OAB and analysed immunohistochemical marker (CD117). The mean age of the patients was 40.6 ± 10.4 years. Mean age of the OAB and chronic cystitis patients was 38.0 ± 5.4 and 41.8 ± 2.3, respectively. The absence of significant age differences ($p = 0.45$) allowed the valid comparison of morphological characteristics in both groups.

Results

The morphological study of biopsy specimens revealed typical pathological features: in the cystitis group, the biopsy specimens typically included the bladder mucosa surface layers with squamous cell metaplasia in the form of multilayered squamous epithelium (MSE) with the signs of atrophy, the underlying stroma had diffuse lymphocytoplasmocytic infiltration, sclerosis, vessel walls hyalinosis, plethora and muscle fiber atrophy. In the OAB group the histological findings were different: the biopsy specimens more often included the bladder mucosa surface layers covered with multirowed epithelium (MRE) or MSE metaplasia with hyperkeratosis, in the submucosal layer, we found oedema, sclerosis, thin-walled vessels, focal inflammatory infiltration, as well as focal muscle fiber hypertrophy. We found significant differences in the several morphological parameters. The chronic cystitis patients had more significant epithelial atrophy and atrophy of muscle layer while the OAB patients demonstrated significantly more expressed stromal oedema and the muscle layer hypertrophy ($p<0.01$).The chi-square intergroup comparisons revealed statistically significant differences in the occurrence epithelium and muscle layer atrophy in the chronic cystitis patients and stromal oedema and the muscle layer hypertrophy in OAB patients ($p<0.05$).). The evaluaton of CD117 expression in inflammatory infiltrate in the stroma revealed high content of the marker in cells in the both groups ($p\geq0.05$), the OAB patients tended to have higher marker expression, particularly in stromal cells, suggesting a higher number of pacemaker cells in the bladder wall. Thus, we found smooth muscle hypertrophy in OAB patients and, in contrast, smooth muscle atrophy in chronic cystitis patients, as well as higher expression of CD117 in OAB patients.

Interpretation of results

Our study demonstrated that despite similar symptoms of chronic cystitis and overactive bladder: frequent urination (more than 8 times a day and more than 2 times during the night), urgent urination, small to medium volumes of urine per each urination, discomfort during the urination, etc., the histological findings are different. The multirowed epithelium was commonly found in the biopsy specimens from the bladder wall of the OAB patients, while squamous cell metaplasia was more frequent in chronic cystitis, the epithelium and muscle layer atrophy were more pronounced in the chronic cystitis patients; stromal oedema and muscle layer hypertrophy were characteristic to the OAB patients. Nevertheless the both groups demonstrated signs of inflammation: marked lymphoplasmocytic infiltration of the stroma, blood vessels hyalinosis and plethora, stromal oedema and sclerosis. Moreover, immunohistochemical analysis of CD117 expression in the infiltrating inflammatory cells in stroma revealed a high marker concentration in the both groups. Since CD117 is also a marker of cells with pacemaker activity, a high concentration of CD117 + cells in the stroma supports the theory, that due to their pacemaker functions these cells provide spontaneous myogenic activity of adjacent smooth muscle cells [2], leading to their hypertrophy. Moreover, this fact explains the differences in the clinical presentation, for example, urgency and pollakiuria are more frequent in chronic cystitis patients during the disease exacerbation, while this symptom is relatively stable and persistent in OAB patients. These differences are apparently associated with a larger number of cells with pacemaker activity in OAB patients, since we discovered an evident tendency towards higher CD117expression in OAB patients compared to those with chronic cystitis. Apparently, these cells are inactive in patients with unexacerbated chronic cystitis, which is indirectly confirmed by the muscle cells atrophy in histological findings.

Concluding message

The study findings support the hypothesis of OAB inflammatory genesis [3] and can be used to optimize of treatment strategies in these patients.

However, this was a pilot study with limited materials; therefore further studies in this area are necessary.

References

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Disclosures
Funding: This was an independent study and the funding support was from the Scientific Centre of Obstetrics, Gynecology and Perinatology named after V.I. kulakov Ministry of Health. **Clinical Trial:** Yes **Public Registry:** No **RCT:** No **Subjects:** HUMAN **Ethics Committee:** Ethics Committee for Biomedical Research at the Scientific Centre **Helsinki:** Yes **Informed Consent:** Yes