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EXPRESSION LEVEL OF KI-67 PROLIFERATIVE MARKER IN CELLS OF URINARY BLADDER POLYPS AND PAPILLOMA TISSUES

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Abstract: This article presents information on the expression level of proliferative marker KI-67 in bladder polyp and papilloma tissue cells. Although the proliferative activity of cells was low only in the basal layer of the covering epithelium of the bladder polyp and papilloma that we studied, it was confirmed by the brownish expression of the Ki-67 marker in the nuclei of stroma tissue cells. Morphologically, the location of the Ki-67 marker in the nucleus of the lining epithelial cells, in both the nucleus and nucleolus of the stromal tissue cells, confirms that these cells are in different phases of proliferative and mitotic activation, i.e. G1, S, G2, M levels.

Keywords: bladder, polyp, papilloma, proliferative marker.

The urgency of the problem.

Ki-67 is a marker of cell proliferation and is expressed at different levels in all cell activation phases, i.e. G1, S, G2, M. From the initial phase of cell activation, G1 to M phase, this marker increases and reaches a maximum by the metaphase of mitosis. In the early G1 phase, the Ki-67 marker is located at the centromere of the satellite DNA and at the telomere of the chromosome. In the middle phases of cell activation, the Ki-67 marker appears in the nucleus, and by the G2 phase, it is expressed both in the nucleus and in the karyoplasm. When the cell enters post-mitotic G0, the Ki-67 marker is degraded by proteosomes, undergoes complete catabolism, and is not expressed in interphase cells. Therefore, this immunohistochemical marker is of great importance not only in tumor processes, but also in hyperplasia, metaplasia, regeneration, dysplasia, which continues with cell proliferation, as it shows the activity of cell proliferation.

Cell proliferation index can be calculated based on the Ki-67 marker. A total of 500 cells were counted in the calculation, and it was determined how many of them had the positive expression of this marker in the nucleus, and what percentage of all cells were positive. 1) 10% - low level, 2) 10-20% - medium level, 3) more than 20% is considered high level expression.

The purpose of the study. Taking into account the above discussions, the aim of this study was to determine the proliferation index of cellular structures in the tissues of polyps and papillomas, which are benign tumors of the bladder, by the expression level of the immunohistochemical marker Ki-67 and the proliferation index.

Research materials and methods. For the immunohistochemical study of bladder polyp and papilloma benign tumors, histological preparations prepared from 5 polyps and 6 papilloma tumors were first deparaffinized, dehydrated, demasked, and the expression level of antigens responsible for proliferation in cells was performed in a specialized and automated system, i.e. Ventana Benchmark XT, Roche, Switzerland. Polyp was examined in samples 18114/19 and 18112/19 and papilloma in samples 2213/15 and 2217 with the help of antibody that detects Ki-67 antigen immunologically. In both processes, the level of expression of this antigen in different areas of tissue structures G.G. It was calculated using a computer-programmed polyautomatic method of autocorrelation and evaluated in percentages.

Research results. The results of the investigation showed that the expression of the cell proliferation factor was found to have different indicators in the epithelial cells and interstitial cells of the tumors we studied. The proliferative index of Ki-67, an immunohistochemical marker of bladder polyp epithelial cells, was 7.16ë0.13, which was confirmed to be low (Table 1). The proliferative index of Ki-67, an immunohistochemical marker of connective tissue cells of the interstitial tissue in the polyp stroma, was observed to be relatively high (18.64ë1.41), and morphologically, it was found that the Ki-67 marker was expressed in the nuclei of the majority of histiocytic cells in the epithelial stroma covering the polyp in a dark brown color (Figure 1). In this case, the expression in both the karyoplasm and the nucleolus of the lining epithelial cell nuclei confirms that the cells are in the middle phase of activation, that is, in the G2 phase.

So, the covering epithelium in the bladder polyp shows a slow development compared to the stromal cells, a low level of proliferation, almost no metaplasia and dysplasia of the epithelial cells.

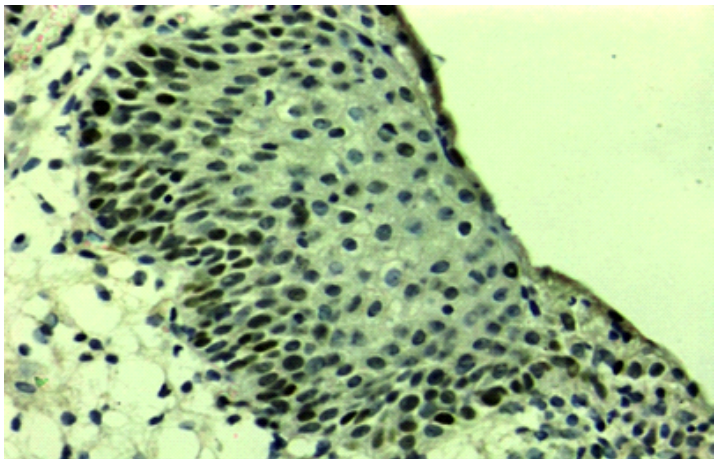


Figure 1. Polyp (864/21 samples), expression level of Ki-67 marker in the nuclei of covering epithelial cells, 17.5%. Floor -x20.

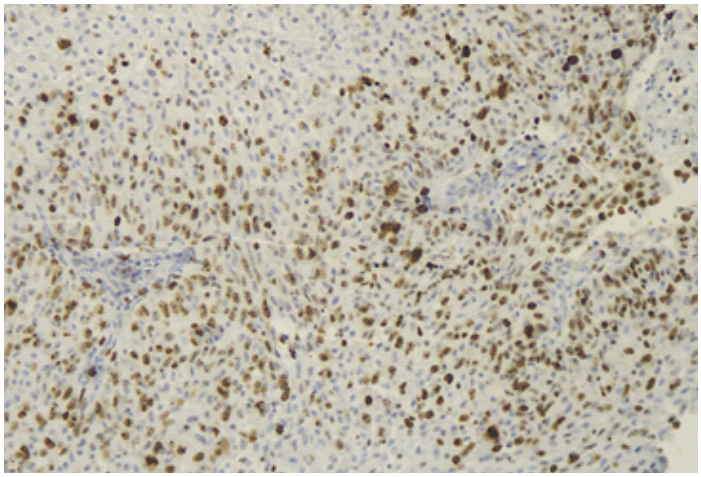


Figure 2. Polyp (specimen 18114/19) Diffuse expression of nuclei of stromal cells, 58%. Floor: x20

Immunohistochemical examination of bladder papilloma tissue for Ki-67 cell proliferation marker showed that it is expressed in epitheliocyte cells located mainly in the basal layers of the covering epithelium at various levels, that is, from light brown to dark brown. In this case, it is determined that some of the positively stained epithelial cells have an enlarged nucleus and a dark positive result, while others are relatively lighter stained and much smaller in size. It was observed that the number of immunohistochemically positive epithelial cells was 24.7% of the total number of covering epithelia, this indicator was slightly higher than the expression of the Ki-67 marker of the covering epithelium of bladder polyp, i.e. it increased by 7%.

Since bladder papilloma usually begins after the development of inflammatory and dysregenerative processes in the bladder wall, the proliferative inflammatory process prevails in the papilloma stroma, at the same time the proliferative activity of both covering epithelial and stromal cells increases, as a result of which the expression of the Ki-67 marker increases. In the immunohistochemical examination of the Ki-67 marker, it was found that in some cases of papilloma, the Ki-67 marker, which shows the proliferative activity at a low level, was expressed in the cellular structures (). In this case, some epithelial nuclei were relatively enlarged and gave a dark positive result, while others were relatively lighter and stained at the level of fragmentation. Quantitatively, the number of epithelia positively stained with the Ki-67 marker was found to be higher than the total number of epithelia of the gland. In most cases, it was found that the marker indicating cell proliferation was expressed in the cells of the basal layer of the covering epithelium, including in the nuclei of some epitheliocytes, it was expressed in a light brown color, while in others it was expressed in a relatively dark brown color (Fig. 3).

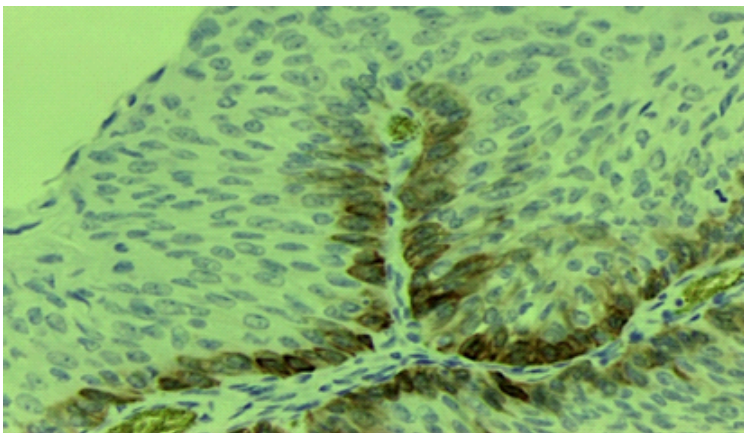
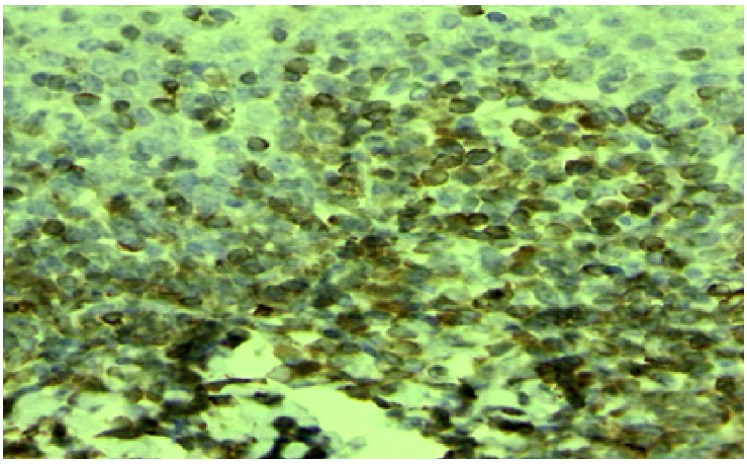


Figure 3. Papilloma (sample 3672/22), expression of Ki-67 in the basal layer of the covering epithelium, 12.8%, Cat: x20.



In the development of bladder papilloma, the development of chronic inflammation and dysregenerative processes in the unformed connective tissue of the submucosal layer is of great importance. As a result of the development of these general pathomorphological processes, both cellular and fibrous structures of the connective tissue in the bladder submucosa are proliferated and increased. Therefore, the main reason for the appearance of a benign tumor of the urinary bladder mucosa, such as papilloma, is the growth of submucosa connective tissue. Therefore, immunohistochemical examination of the marker Ki-67, which shows the proliferative activity of connective tissue cells that make up not only the epithelial lining of the bladder papilloma, but also the stroma, is of great importance and serves as the main fundamental information in the correct diagnosis of this process. In our material, i.e., in 6 cases of bladder papillomas, immunohistochemical examination revealed that the level of expression of the proliferative marker of Ki-67 cells (Fig. 4) was stronger than that of the covering epithelium. In this case, a total of 500 of the connective tissue cells in the stroma of the papilloma were counted, and how many of them expressed this marker at a positive level was calculated, and the result was 62.4%, and this indicator was observed to be 4.9 times higher than the indicator of the covering epithelium.

Summary

When polyps and papillomas from benign tumors arising in the mucous membrane of the bladder were examined at the immunohistochemical level, it was found that the Ki-67 marker in their covering epithelium was at a much lower level, and had significantly higher indicators in the stroma tissue structures.

Although the proliferative activity of cells was low only in the basal layer of the covering epithelium of the bladder polyp and papilloma that we studied, it was confirmed by the brownish expression of the Ki-67 marker in the nuclei of stroma tissue cells.

Morphologically, the location of the Ki-67 marker in the nucleus of the lining epithelial cells, in both the nucleus and nucleolus of the stromal tissue cells, confirms that these cells are in different phases of proliferative and mitotic activation, i.e. G1, S, G2, M levels.

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