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EXPRESSION LEVEL OF ANTI-APOPTOTIC PROTEIN Bcl-2 IN BLADDER PAPILLOMAS

Shodiev O'lmas Mustafayevich
Bukhara State Medical Institute

Summary
In this work, the level of expression of the anti-apoptotic protein Bcl-2 was determined at different stages of bladder papilloma. The results showed that in the control group, this protein was expressed at a low level only in the basal layer of the epithelium lining the bladder. At the initial I stage of papilloma development during the metaplastic process in the changing epithelium, the expression of Bcl-2 protein increases to a high level in the cells of the basal layer of the epithelium with acanthosis At the II stage of papilloma, all cells of the epithelial layers are metaplastic and arranged vertically, the Bcl-2 protein is expressed at a relatively higher level in the cells of the basal and intermediate layers, and at the III stage of papilloma, the expression of this protein is even stronger.

Keywords: bladder, papilloma, cystitis, immunohistochemistry, Bcl-2 protein.

УРОВЕНЬ ЭКСПРЕССИИ АНТИАПОПТОЗНОГО БЕЛКА Bcl-2 В ПАПИЛЛОМАХ МОЧЕВОГО ПУЗЫРЯ

Шодиев Улмас Мустафаевич
Бухарский Государственный медицинский институт

Резюме
В данной работе определяли уровень экспрессии антиапоптотического белка Bcl-2 на разных стадиях папилломы мочевого пузыря. Результаты показали, что в контрольной группе этот белок экспрессировался на низком уровне только в базальном слое эпителия, выстилающего мочевой пузырь. На начальном I этапе развития папилломы при метапластическом процессе в изменяющемся эпителии экспрессия белка Bcl-2 повышается до высокого уровня в клетках базального слоя эпителия с акантозом. При II стадии папилломы все клетки эпителиальных слоев метапластичны и расположены вертикально, белок Bcl-2 экспрессируется на относительно более высоком уровне в клетках базального и промежуточного слоев, а при III стадии папилломы экспрессия этого белка еще сильнее.

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Ключевые слова: мочевой пузырь, папиллома, цистит, иммуногистохимия, белок Bcl-2.

СИЙДИК ПУФАГИ ПАПИЛЛОМАСИДА АНТИАПОПТОЗ ОҚСИЛ Bcl-2 НИНГ ЭКСПРЕССИЯЛАНИШ ДАРАЖАСИ

Шодиев Улмас Мустафоевич
Бухоро давлат тиббиёт институти

Аннотация.
Ушбу ишда сийдик пуфаги папилломасининг ҳар хил даврларида антиапоптоз оқсил Bcl-2 экспрессияланиш даражаси аниқланган. Натижалар шуни кўрсатдики, назорат гуруҳида сийдик пуфаги қопловчи эпителийсида бу оқсил фақат базал қаватида кам даражада экспрессияланиши аниқланди. Папиллома ривожланишининг дастлабки I – даври, ўзгарувчан эпителийда метапластик жараённинг пайдо бўлиш даврида, эпителийнинг акантоз ривожланган базал қавати ҳужайраларида Bcl-2 оқсилиннинг экспрессияланиши юқори даражага кўтарилиши кузатилади. Папилломанинг II – даврида эпителийнинг барча қават ҳужайралари метаплазияланиб, вертикал ҳолда жойлашганлиги, уларнинг базал ва оралиқ қаватлар ҳужайраларида Bcl-2 оқсилиннинг нисбатан кўпроқ даражада экспрессияланиши, папилломанинг III – даврида бу оқсилнинг экспрессияланиши яна ҳам кучайганлиги кузатилади.
Калит сўзлар: сийдик пуфаги, папиллома, цистит, иммуногистохимия, Bcl-2 оқсил

The Relevance of the Problem

Bcl-2 domain 6 protein is a homologous protein that slows down the process of apoptosis. This protein with with a molecular weight of 22 kDa, it is found in the cell and nuclear membrane, sarcoplasm and mitochondrial membrane. Overexpression of this protein inhibits the release of calcium ions and inhibits antioxidant activity by slowing down lipoperoxidation and NO-synthetase activity. The main function of Bcl-2 is to stop the release of cytochromes S, ATF, ATF through the pores, which are anti-apoptotic molecules from mitochondria. Why when Bcl-2 binds to the mitochondrial membrane, it closes the pores, interrupts pro-apoptotic signals, and apoptosis does not develop. Papilloma of the bladder can develop under the influence of various pathological factors, as a result of which, in chronic diseases that have developed in the bladder, cell death occurs, including the integumentary epithelium, due to the programmed process of apoptosis. But in most cases, due to chronic diseases, the process of cell apoptosis can slow down and stop. Therefore, in our study, we decided

to study the anti-apoptotic protein Bcl-2 in the lining epithelial cells of the bladder papilloma. Increased activity of Bcl-2 it is observed in a number of diseases of the bladder, including papillomas.

Due to the development of inflammatory and dysregenerative processes in the submucosal connective tissue layer of the bladder papilloma, differentiation of the cells of the integumentary epithelium is disrupted and often lags behind, the proliferative activity of the cells of the basal layer increases and the anti-apoptotic protein In them can activate the expression of Bcl protein-2. [5, 6, 7, 8]. Material and methods. Biopsies of the bladder mucosa obtained during cystoscopy were taken from 21 men and 18 women living in the Bukhara region with a history of papillomas. The age of the patients ranged from 18 to 84 years, the average age was 32.6 years. The duration of the disease in them ranged from 4 months to 6 years, on average 2.7 ± 0.9. Biopsies were fixed in 10% neutral formalin for 48 hours. Dehydration was carried out in alcohols of increasing concentration and in chloroform.

Histological sections were pre-stained with hematoxylin and eosin to determine their topography. Then a series of sections obtained from paraffin blocks were dewaxed, dehydrated, unmasked and stained for the presence of antigens on a special automated system Ventana Benchmark XT, Roche, Switzerland. Vcl2 was detected using antibodies

The results of the study and their discussion. In order to determine the pathomorphological and immunohistochemical changes occurring in the integumentary epithelium of the bladder papilloma, biopsies obtained from people without any pathology in the bladder were initially examined as a control group. Then pathomorphological and immunohistochemical changes of the mucous membrane and the integumentary epithelium of the bladder were studied in comparison with each other according to clinical and morphological forms and the timing of papilloma development.

It was determined that the epithelium covering the mucous membrane of the bladder of the control group consists of an ordinary multilayer variable epithelium, and its epithelial cells located in the basal layer are relatively large, hyperchromic, located in the basement membrane and most often the nuclei have an oval and elongated shape. In the surface layers of the multilayer epithelium, there is a relative sparsity of cells, smaller nuclei, lighter color, flattened location.

The results of an immunohistochemical study of the anti-apoptotic protein of epithelial cells showed that in the control group this protein was expressed at a very low level in the cytoplasm of some relatively young and cambial cells located in the basement membrane, and was not expressed. in the remaining cells of the

intermediate and surface layers (Fig. 1).

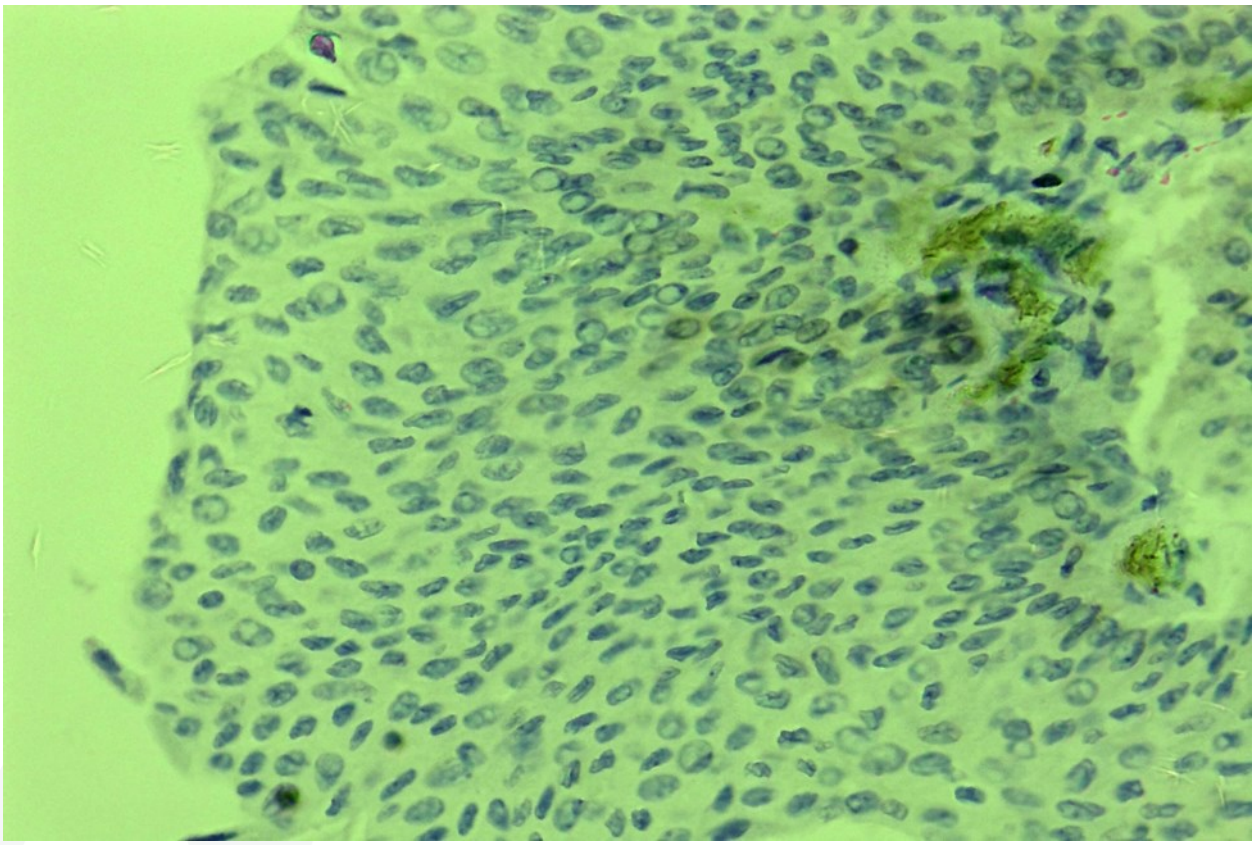

Figure 1. Bladder, norm, Bcl-2 protein is expressed at a low level in some cells of the basal layer. Coloring: immunohistochemistry. Evasion: 10x40.

The next task of the study was to study the level of expression of the anti-apoptotic protein Bcl-2 as the proliferative activity of epithelial cells increased during different periods of papilloma, and the following data were revealed. It is known that the initial period of papilloma development is determined by the appearance of metaplastic processes in the changing epithelium. At the same time, the number of multilayer epithelial layers increases, the epithelium of the surface layers flattens and, due to an increase in the amount of glycogen and proceratin in the cytoplasm of cells, acquires a bubble-like appearance As a result of an immunohistochemical study, it is determined that due to the increased proliferative activity of the multilayer variable epithelium of the bladder, a strong acanthosis develops in the basal part, its germination by bundles into the connective tissue layer under the basal epithelium layer is observed.

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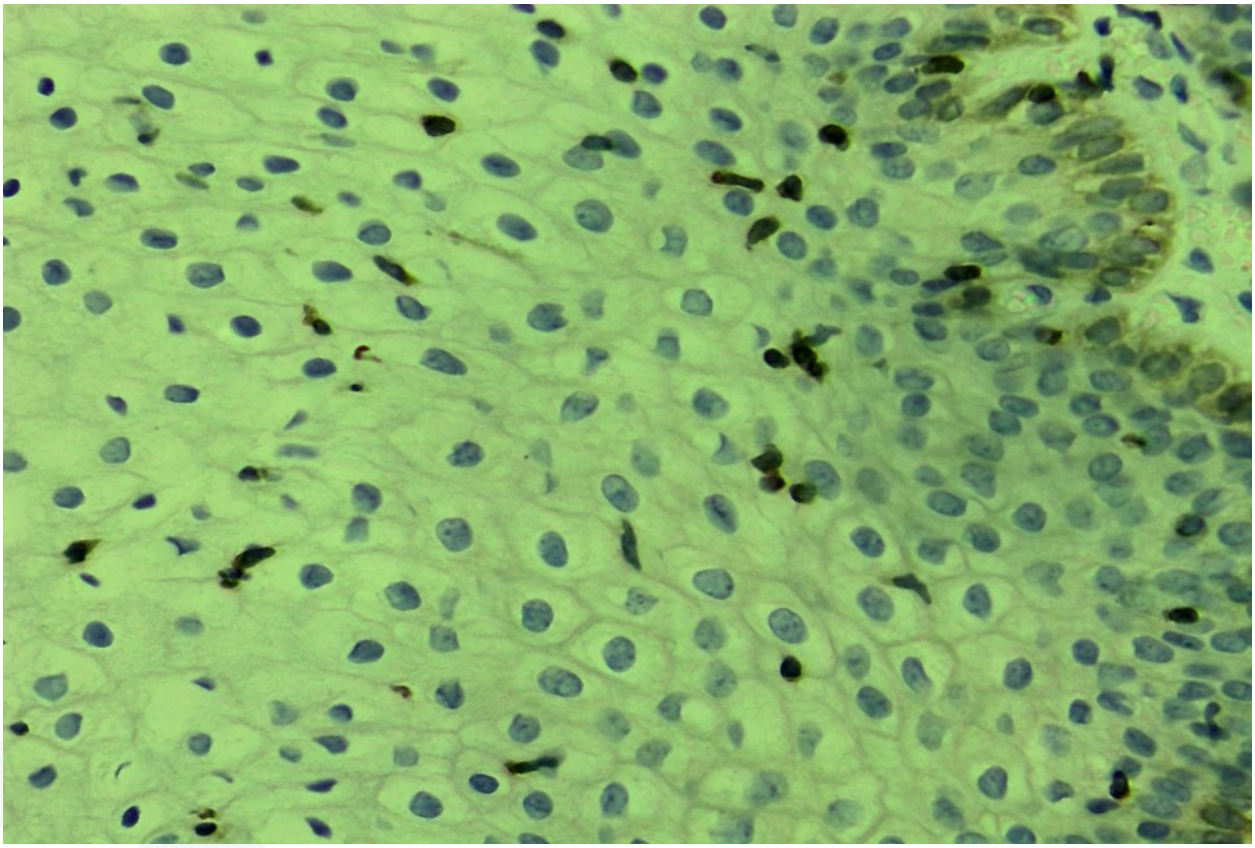

Figure 2. Bladder, grade I papilloma, Bcl-2 protein is expressed in some cells of the basal and intermediate layers. Coloring: immunohistochemistry. Evasion: 10x40.

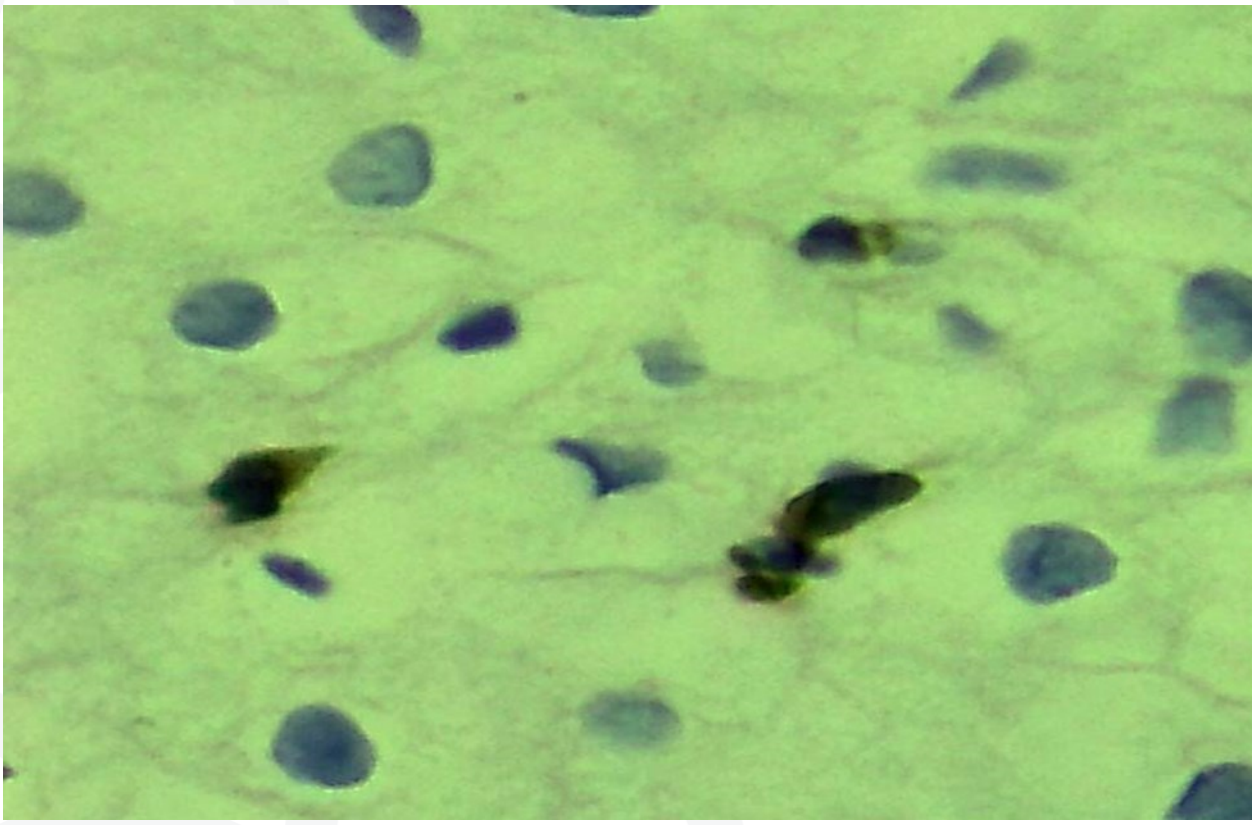

Figure 3. Bladder, grade I papilloma, Bcl-2 protein is expressed close to the nucleus of interstitial epithelial cells. Coloring: immunohistochemistry. Evasion: 10x100.

When considering the multilayer variable epithelium as a whole, Bcl-2 is expressed in the 1st row of cells of the basal layer at a low level in the form of light brown cytoplasmic inclusions (Fig. 2). As the hydropic dystrophy and vacuolization of the cytoplasm of cells of the middle and surface layers of the multilayer epithelium, local expression of Bcl-2 protein is observed in some of them. When examined under a microscope lens, it was revealed that at the first stage of papilloma of the mucous membrane of the bladder, except for the epithelium of the basal layer, the epithelium of almost all the middle and surface layers underwent metaplasia, that is, it became flattened and became vacuolized. due to hydropic dystrophy. As a result, Bcl-2 appeared in the nuclear envelope of the cytoplasm of some metaplastic cells, therefore, a brown inclusion is tightly defined in the nucleus (Fig. 3). This morphological and immunohistochemical condition indicates that epithelial cells have proliferated and produced an anti-apoptotic protein.

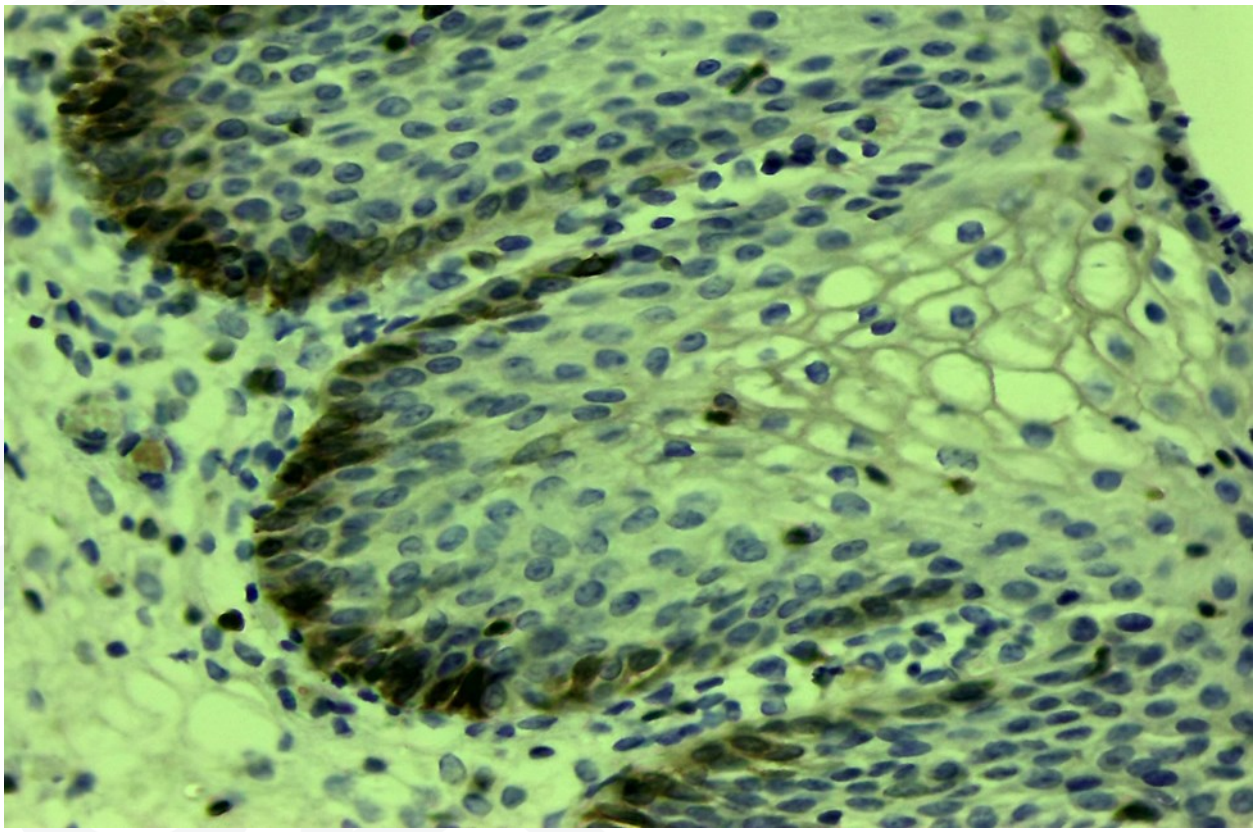

Figure 4. Bladder, grade II papilloma, Bcl-2 is expressed in the basal layer of 2-3 rows. Coloring: i mmunohistochemistry. Evasion: 10x40.

At stage II papilloma of the mucous membrane of the bladder, that is, when the appearance and shape of epithelial cells change, it is determined that the altered epithelium has turned into a multilayer flat epithelium and almost all of its cells are

located vertically. It is observed that the cells of the basal layer consist of a relatively small and dark-colored epithelium, the cells of the surface layers are relatively larger, edematous and enlarged in size due to an increase in keratogyalin in their cytoplasm. An immunohistochemical study during this II-period of the disease showed that, unlike the I-period, during this period, the Bcl-2 protein was expressed in a dark brown color in the cytoplasm of part of the cells of the 2nd-3rd row and intermediate layers. located in the basal layer (Fig. 4). This situation indicates an increase in the proliferative activity of the epithelium of the basal and intermediate layers during the II period of papilloma, the Bcl-2 protein adhered to the mitochondrial membrane and closed the pores, cutting off pro-apoptotic signals and causing apoptosis. indicates the cessation of its development. As mentioned above, during this period of the disease, the multilayer changing epithelium has an oval and elongated shape, located vertically. Positively expressed Bcl-2 interstitial cells also have an elongated shape, with a relatively narrow cytoplasm and light brown color.

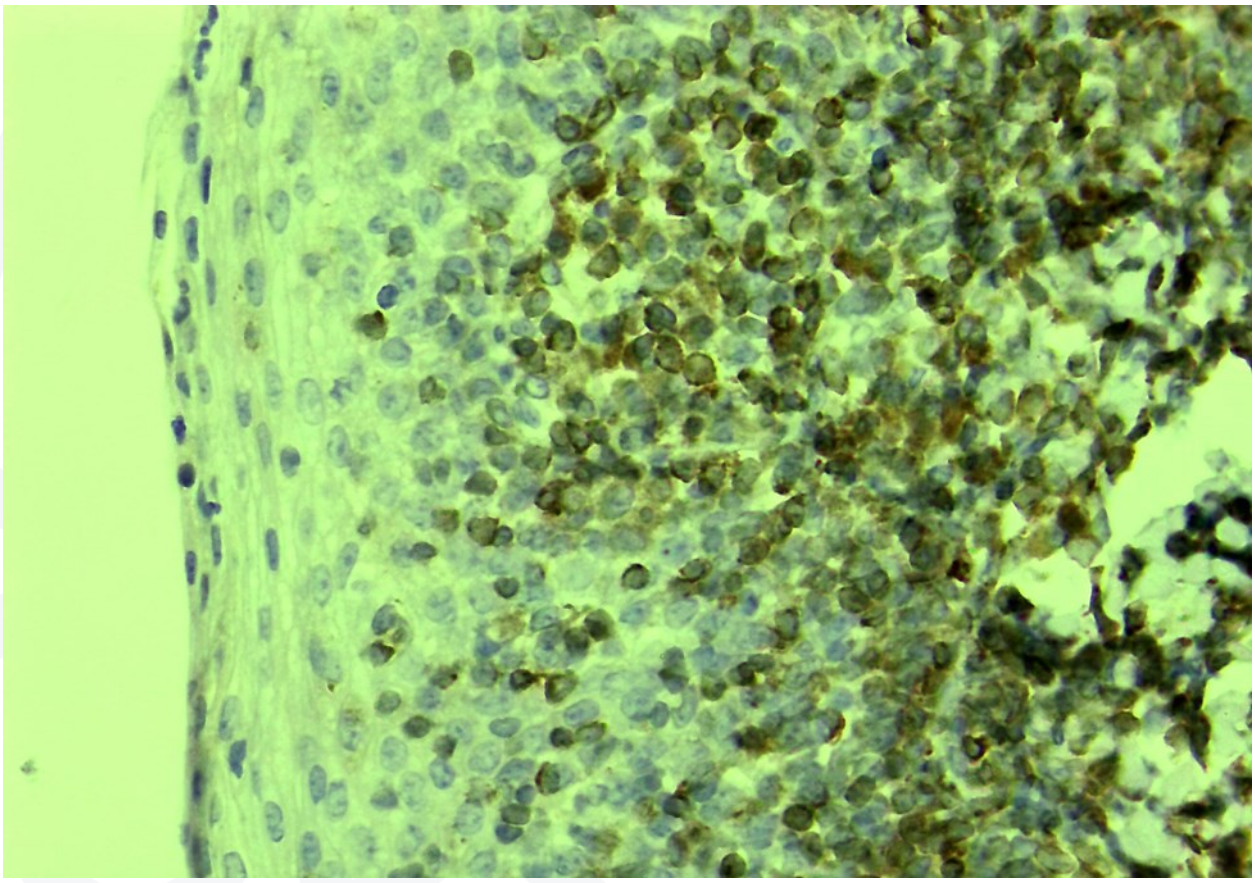

Figure 5. Bladder, grade III papilloma, Bcl-2 is expressed in most cells of the basal and intermediate layers. Coloring: immunohistochemistry. Floor: 10x40.

The difference between stage III papilloma of the mucous membrane of the bladder from the previous stages is that proliferative activity and the process of metaplasia is developed in almost all basal and intermediate rows of the epithelium. Another

distinctive feature of this period is the chronic inflammatory infiltrate in the subepithelial connective tissue plate, proliferation of vascular wall cells and positive expression of Bcl-2 protein in them. It was noticed that the immunohistochemical study also differed from previous periods. During this period of the disease, it is observed that the Bcl-2 protein is expressed in brown color inside the cytoplasm and in the outer cytolemma, sticking to the nuclei of epithelial cells. It is noteworthy that during this period it is confirmed that it is expressed only in the nuclear membrane of some cells of the intermediate layers, and in other cells only in the outer cytolemma.

Conclusions

Immunohistochemical examination of bladder papilloma, i.e. determining in which layers of the integumentary multilayer variable epithelium the antiapoptotic protein Bcl-2 is expressed, is an important factor in the diagnosis of this disease.

In the control group without any diseases in the bladder, the Bcl-2 protein is expressed only at a low level in the basal layer, which indicates that apoptosis activity persists in them. In the initial I-period of papilloma development, when a metaplastic process occurs in a changing epithelium, the expression of Bcl-2 protein in cells of the basal layer of the epithelium with developed acanthosis indicates the activation of an anti-apoptotic gene. It was found that at stage II of papilloma, all cells of the epithelial layers are metaplastic and arranged vertically, the Bcl-2 protein is expressed at a relatively higher level in the cells of their basal and intermediate layers. At stage III of papilloma, proliferative activity and metaplasia develop in cells of all epithelial layers, inflammation is noted in the private plate, Bcl-2 protein is expressed at a high level in all epithelial cells.

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