INVESTIGATION OF MORPHOLOGICAL CHANGES IN PATIENTS WITH UTERINE CANCER BY THE IMMUNOHISTOCHEMICAL METHOD BCL 2 AND P53

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Abstract. *In this study, morphological changes in patients with uterine cancer were studied by immunohistochemical analysis. The study included 60 patients treated at the Tashkent Regional Branch of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology from 2018 to 2022. By the method of immunohistochemical examination, Bcl 2 and p53 antigens were studied. The obtained results showed that the lower the differential level of malignant tumors, the higher their aggressive course, growth into neighboring organs, and the rate of metastasis.*

Keywords*: Uterine cancer, immunohistochemical analysis, Bcl 2 and p53, tumor morphology, tissue expression.*

BCL-2 VA P53 IMMUNOGISTOKIMYOVIY USULI YORDAMIDA BACHADON SARATONI BILAN OG‘RIGAN BEMORLARDA MORFOLOGIK O‘ZGARISHLARNI O‘RGANISH

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Annotatsiya. *Ushbu tadqiqotda bachadon saratoni bilan og‘rigan bemorlarda morfologik o‘zgarishlar immunogistokimyoviy tahlil orqali o‘rganildi. Tadqiqotga 2018–2022 yillar davomida Respublika ixtisoslashtirilgan onkologiya va radiologiya ilmiy-amaliy tibbiyot markazining Toshkent viloyati bo‘limida davolangan 60 nafar bemor kiritildi. Immunogistokimyoviy tekshiruv usuli yordamida Bcl-2 va p53 antigenlari o‘rganildi. Olingan natijalar shuni ko‘rsatdiki, o‘smalarning differensiallashuv darajasi qanchalik past bo‘lsa, ularning agressiv kechishi, qo‘shni organlarga o‘sib kirishi va metastaz berish ko‘rsatkichi shunchalik yuqori bo‘ladi.*

Kalit so‘zlar*: bachadon saratoni, immunogistokimyoviy tahlil, Bcl-2 va p53, o‘sma morfologiyasi, to‘qima ekspressiyasi*

ИССЛЕДОВАНИЕ МОРФОЛОГИЧЕСКИХ ИЗМЕНЕНИЙ У БОЛЬНЫХ РАКОМ МАТКИ МЕТОДОМ ИММУНОГИСТОХИМИИ BCL-2 И P53

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Аннотация. *В данном исследовании изучены морфологические изменения у больных раком матки методом иммуногистохимического анализа. В исследование были включены 60 пациенток, проходивших лечение в Ташкентском областном филиале Республиканского специализированного научно-практического медицинского центра онкологии и радиологии в период с 2018 по 2022 годы. Методом иммуногистохимического исследования изучены антигены Bcl-2 и p53. Полученные результаты показали, что чем ниже степень дифференцировки злокачественных опухолей, тем выше их агрессивность, инвазия в соседние органы и скорость метастазирования.*

Ключевые слова: *рак матки, иммуногистохимический анализ, Bcl-2, p53, морфология опухоли, экспрессия тканей.*

Relevance of the problem: Eendometrial cancer (ES) ranks first in the structure of gynecological oncological pathology; The growth rate of ESR cases is significantly higher in women than in other malignant neoplasms of the reproductive system [2, 12, 35].

According to long-term forecasts, at the beginning of the 21st century, endometrial cancer will occupy the first place in the structure of the female population's morbidity in many developed countries of the world, as in the USA [1, 5, 28].

According to the general data of the International Federation of Obstetricians and Gynecologists, 5-year survival for uterine cancer is possible only in 67.7% of patients, while 22.4% of patients die from the development of the tumor process [6, 9, 22].

A characteristic feature of endometrial cancer is that it is asymptomatic for a long time and in most patients against the background of hyperestrogenism, as well as against the background of a whole complex of complex endocrine-metabolic disorders, in particular, pathology of the ovulation process, lipid metabolism disorders, carbohydrates, lipid metabolism disorders, a hormone-dependent variant of the tumor (60-90%). 7, 10].

According to a number of authors, the first, estrogen-dependent, pathway of development in endometrial cancer occurs slowly, is characterized by a favorable clinical course and sensitivity to hormonal therapy. The second variant of oncogenesis is associated with mutations in suppressor genes and is characterized by a more aggressive course, as well as a lack of sensitivity to hormonal therapy [8, 12].

This requires the selection of patients with a poor prognosis for more aggressive treatment and monitoring. However, the biological behavior of endometrial tumors remains unpredictable even for patients with the same degree of tumor progression [13, 14, 36].

In this regard, recently, great importance has been attached to immunohistochemical markers for predicting the clinical course and outcome of various neoplasms. A number of studies have proven that some molecular markers are independent prognostic indicators [6, 9, 34, 37].

Bcl 2 - Suppresses apoptosis in multicellular systems, including lymphohematopoietic and neuronal cells. It regulates cell death by controlling the permeability of the mitochondrial membrane. Preventing the release of cytochrome c from mitochondria inhibits phosphatases by binding an apoptosis-activating factor.

p53- The antigen for these antibodies is the w p53 protein, which controls the course of cellular cycle processes, as well as the presence of damage in the genome, which can lead to the further development of pathology. w p53-dependent apoptosis is a powerful selector, preventing the accumulation of mutations, and if they have already appeared, w p53-dependent apoptosis allows the destruction of such potentially dangerous cells for the organism. Mutations have been found in 50% of all types of cancer cases. This gene encodes a transcription factor that controls the entry of cells into the cell cycle. Many intracellular systems that monitor the "health" of the cell send signals about "malfunctions" to the w r53 protein. With its help, the cell decides whether to divide or not. If a cell is irreparably damaged, the w p53 protein triggers a chain of events that lead to cell "suicide," otherwise called apoptosis. Cells that lack or don't function properly with w p53 are unable to control such self-regulation and continue to divide even when it's dangerous for the body. Like all tumor suppressants, w p53 controls the normal course of the cell cycle. w p53 is a transcription factor that regulates the cell cycle, this reagent acts as an inhibitor of the formation of malignant tumors. The w p53 gene is an anti-oncogenic agent.

Material and method:

Highly differentiated adenocarcinoma: In highly differentiated adenocarcinoma of the uterine body, a mild positive reaction was observed in 10 (50%) patients with a p53 indicator. A moderate positive reaction was observed in 6 patients (30%) and a high positive reaction in 4 patients (20%). Depending on the prevalence and intensity of the immunohistochemical reaction, the eyepiece and objective 10-40 objects were examined in the field of view depending on the percentage of stained cells, and the lack of expression or staining of less than 10% of cells was assessed systematically - 0 points, from 10 to 30% - 1 point, from 30 to 60 50% - 2 points, from 60 to 100% - 3 points. The expression of Bcl2 manifested itself in the form of brown staining of the cytoplasm of epithelial cells of varying intensity.

Table 1.

In uterine carcinoma with highly differentiated adenocarcinoma p53 level of proliferative activity of the reagent (No 20)

No	Level	Patients (No. 20)
1.	Low activity <30%	10 (50%)
2.	30-60% moderate activity	6 (30%)
3.	>60% high proliferative activity	4 (20%)

Diagram of the obtained results No20

Bcl 2 including suppresses apoptosis in lymphohematopoietic and neuronal cells. It regulates cell death by controlling the permeability of the mitochondrial membrane. Preventing the release of cytochrome c from the mitochondria inhibits phosphatases by binding an apoptosis-activating factor. In the study, a positive reaction to the tumor marker Bcl2 was observed in 9 (45%) of 20 patients with differentiated uterine corpuscular adenocarcinoma G-1 with a mild positive reaction. A moderate positive reaction was observed in 7 patients (35%), and a high positive reaction was observed in 4 (20%). By microscopic appearance: endometrial glands with hyperplasia and polymorphism and foci of pathological mitosis. Loose fibrous connective tissue between polymorphosed tumor cells and with signs of invasion into myometrium. The membranes of tumor cells undergoing polymorphism are stained dark brown.

Table 2.

Uterine body cancer with highly differentiated adenocarcinoma Bcl -2 level of proliferative activity of the reagent (No. 20)

No	Level	Patients (No. 20)
1.	Low activity <30%	9 (45%)
2.	30-60% moderate activity	7 (35%)
3.	>60% high proliferative activity	4 (20%)

The obtained results show that the low degree of Bcl 2 differentiation of cancer facilitates its and treatment possibilities. However, the high proliferative activity of Bcl 2 indicates a high degree of metastasis in patients with subsequent tumor recurrence.

Moderately differentiated adenocarcinoma:

In the study, a positive reaction to the tumor marker p53 was observed in 7 (35%) of 20 patients with a mild positive reaction. A moderate positive reaction was observed in 8 patients (40%) and a high positive reaction in 5 patients (25%).

Table 3.

Uterine body cancer in moderately differentiated adenocarcinoma p53 proliferative activity level of the reagent (No. 20)

No	Level	Patients (No. 20)
1.	Low activity <30%	7 (35%)
2.	30-60% moderate activity	8 (40%)
3.	>60% high proliferative activity	5 (25%)

By microscopic appearance: endometrial glands with hyperplasia and polymorphism and foci of pathological mitosis. Loose fibrous connective tissue between polymorphosed tumor cells and with signs of invasion into myometrium. The tumor cells, undergoing polymorphism, are stained dark brown.

In the study, a positive reaction to the tumor marker Bcl2 was observed in 6 (30%) of 20 patients with a mild positive reaction, mainly with differentiation of uterine corpuscular adenocarcinoma G-2. A moderate positive reaction was observed in 7 patients (35%), and a high positive reaction was observed in 7 (35%). By microscopic appearance: endometrial glands with hyperplasia and polymorphism and foci of pathological mitosis. Loose fibrous connective tissue between polymorphosed tumor cells and with signs of invasion into myometrium. The membranes of tumor cells undergoing polymorphism are stained dark brown.

Table 4.

Uterine body cancer with moderately differentiated adenocarcinoma Bcl -2 level of proliferative activity of the reagent (No. 20)

No	Level	Patients (No. 20)
1.	Low activity <30%	6 (30%)
2.	30-60% moderate activity	7 (35%)
3.	>60% high proliferative activity	7 (35%)

The obtained results show that a low degree of Bcl2 differentiation of the cancer facilitates its treatment. However, the high proliferative activity of Bcl 2 indicates a high degree of metastasis in patients with subsequent tumor recurrence.

Low-differentiated adenocarcinoma: In the study, a positive reaction to the tumor marker p53 was observed in 5 (25%) of 20 patients with a mild positive reaction. A moderate positive reaction was observed in 6 patients (30%) and a high positive reaction in 9 patients (45%).

Table 5.

In low-differentiated adenokarycinoma with uterine carcinoma p53 proliferative activity level of the reagent (No. 20)

No	Level	Patients (No. 20)
1.	Low activity <30%	5 (25%)
2.	30-60% moderate activity	6 (30%)
3.	>60% high proliferative activity	9 (45%)

In the study, a positive reaction to the tumor marker Bclmainly in the G-3 differentiation of uterine corpuscular adenocarcinoma was observed in 5 (25%) of 20 patients with a mild positive reaction. A moderate positive reaction was observed in 7 patients (35%), and a high positive reaction was observed in 8 (40%). By microscopic appearance: endometrial glands with hyperplasia and polymorphism and foci of pathological mitosis.

Table 6.

Bcl-2 in low-differentiated adenocarcinoma with uterine body cancer level of proliferative activity of the reagent (No. 20)

No	Level	Patients (No. 20)
1.	Low activity <30%	5 (25%)
2.	30-60% moderate activity	7 (35%)
3.	>60% high proliferative activity	8 (80%)

Conclusion.

Immunohistochemical research is conducted to analyze various processes. **Highly differentiated adenocarcinoma**: In the study, a positive reaction to the tumor marker p53 was observed in 10 (50%) of 20 patients with a mild positive reaction. A moderate positive reaction was observed in 6 patients (30%) and a high positive reaction in 4 patients (20%). In the study, a positive reaction to the tumor marker Bcl2 was observed in 9 (45%) of 20 patients with differentiated uterine corpuscular adenocarcinoma G-1 with a mild positive reaction. A moderate positive reaction was observed in 7 patients (35%), and a high positive reaction was observed in 4 (20%).

Moderately differentiated adenocarcinoma: In the study, a positive reaction to the tumor marker p53 was observed in 7 (35%) of 20 patients with a mild positive reaction. A moderate positive reaction was observed in 8 patients (40%) and a high positive reaction in 5 patients (25%). In the study, a positive reaction to the tumor marker Bcl2 was observed in 6 (30%) of 20 patients with G-2 differentiation of uterine corpuscular adenocarcinoma with a mild positive reaction. A moderate positive reaction was observed in 7 patients (35%), and a high positive reaction was observed in 7 (35%). The obtained results show that the low degree of Bcl 2 differentiation of cancer facilitates its treatment. However, the high proliferative activity of Bcl 2 indicates a high degree of metastasis in patients with subsequent tumor recurrence.

Low-differentiated adenocarcinoma: In the study, a positive reaction to the tumor marker p53 was observed in 5 (25%) of 20 patients with a mild positive reaction. A moderate positive reaction was observed in 6 patients (30%) and a high positive reaction in 9 patients (45%). In the study, a positive reaction to the tumor marker Bcl2 was observed in 5 (25%) of 20 patients with a mild positive reaction, mainly with differentiation of uterine corpuscular adenocarcinoma G-3. A moderate positive reaction was observed in 7 patients (35%), and a high positive reaction was observed in 8 (40%). The obtained results showed that the lower the differential level of malignant tumors, the higher their aggressive progression, proliferation into neighboring organs, and the rate of metastasis.

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