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STUDY OF THE EXPRESSION OF IMMUNOHISTOCHEMICAL (KI-67) (BCL-2) MARKERS OF CHANGES IN LIVER CELLS AS A RESULT OF BREAST CANCER

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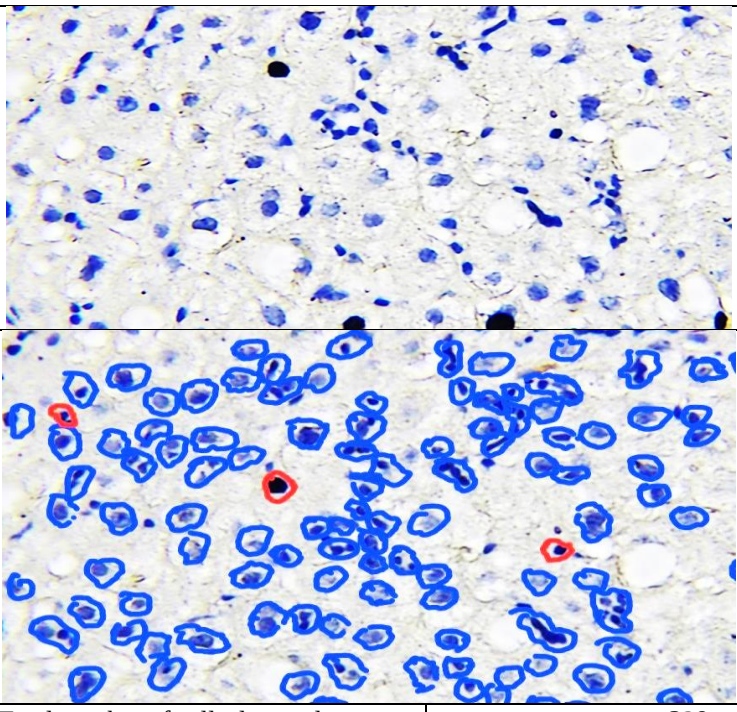
Abstract: In the experiment, liver complications in breast cancer (BC) were studied using immunohistochemistry.The Ki-67 antigen is a protein located in the nuclear material of the tumor cell, and it is necessary for cell proliferation. Detection of the Ki-67 antigen indicates tumor cells in the mitotic phase of the cell cycle. This allows us to understand how active and rapid tumor cell division is, and therefore assess the tumor's growth rate, the risk of metastasis, therapeutic strategies, potential responses to treatment, and the prognosis of the disease. Histological and immunohistochemical examination of the tumor tissue enables us to first obtain a morphological description of the process, and then determine its proliferative activity—the rate and speed of cell division. This provides a clear and objective assessment of the tumor's degree of malignancy and its prognosis for further development.

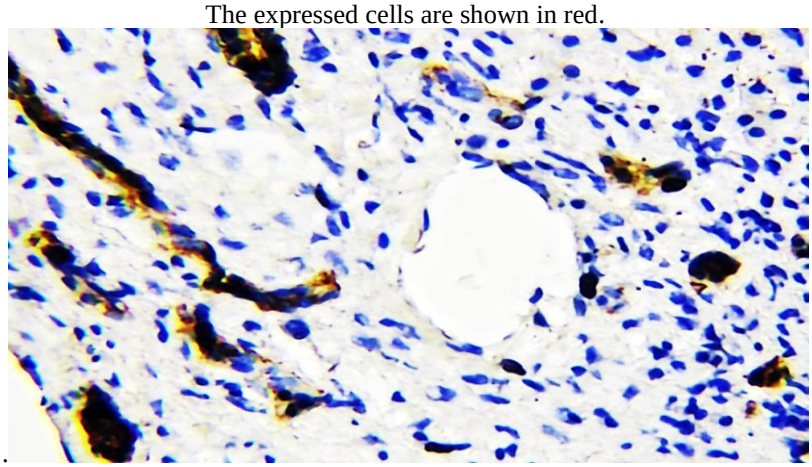
Keyword: Ki-67, QuPath.

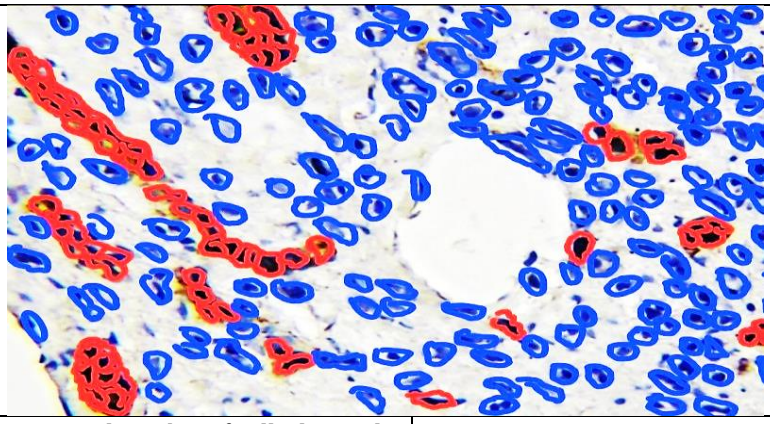


Total number of cells detected	329
Positive expression	5

Negative cells	334
Positive expression	1,45%
Positive expression	1043270 px^2

Figure 4.1. The Ki-67 marker shows low expression (1.45%) in liver tissue of rats in the 2-3 group of the experiment. The image was stained using the DAB chromogen method and magnified 400 times. Scanned using QuPath-0.4.0.ink software, and the expression level was determined.
The expressed cells are shown in red.





Total number of cells detected	523
Positive cells	103
Negative cells	420
Positive expression	20,2%
Positive expression	1045250 px^2

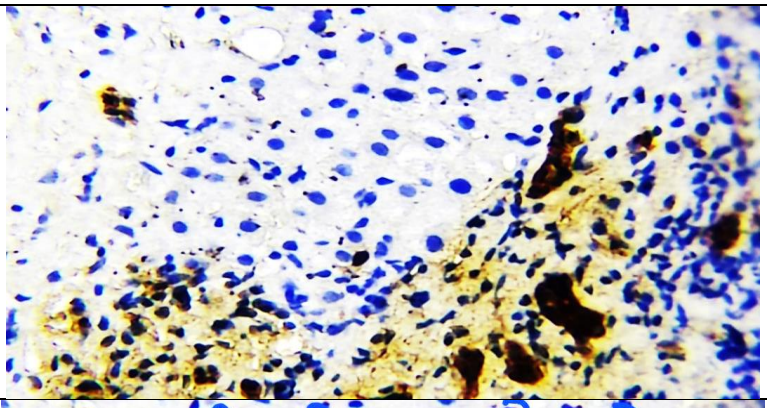
4.2 In the liver tissue of rats from the 4-5 group of the experiment, the Ki-67 marker shows moderate expression (21.2%). The tissue was stained using the DAB chromogen method, and the image was magnified 400 times. It was scanned using QuPath-0.4.0.ink software, and the expression level was determined. The expressed cells are shown in red.

For performing immunohistochemical analysis, biopsy samples from various parts of the liver were prepared from the experimental animals. A total of 15 paraffin blocks were selected. Tissue sections were cut at a thickness of 2-4 microns using a microtome, placed on slides, and covered with a poly-L-lysine-coated cover glass. The tissues were processed using the avidin-biotin immunoperoxidase method for dehydration and defatting the paraffin. After deparaffinization, dehydration and demasking were performed, and then the tissue samples were stained with antibodies using the Ventana Benchmark XT automated system (Roche, Switzerland). The study involved the Ki-67 and Bcl2 antibodies for staining, and the

obtained micrographs (QuPath-0.4.0, NanoZoomer Digital Pathology Image) show the cells with positive expression in high numbers.

The level of Ki-67 (proliferation index) and the expression of Ki-67 and Bcl2 were evaluated in percentage terms. The markers' expression levels were assessed quantitatively as relative percentages and classified as mild, moderate, or strong expression. The scoring system for these markers was as follows:

- 0 (no staining)
- 1+ (<20% of cells stained lightly)
- 2+ (20-60% of cells moderately stained)
- 3+ (>60% of cells strongly stained).

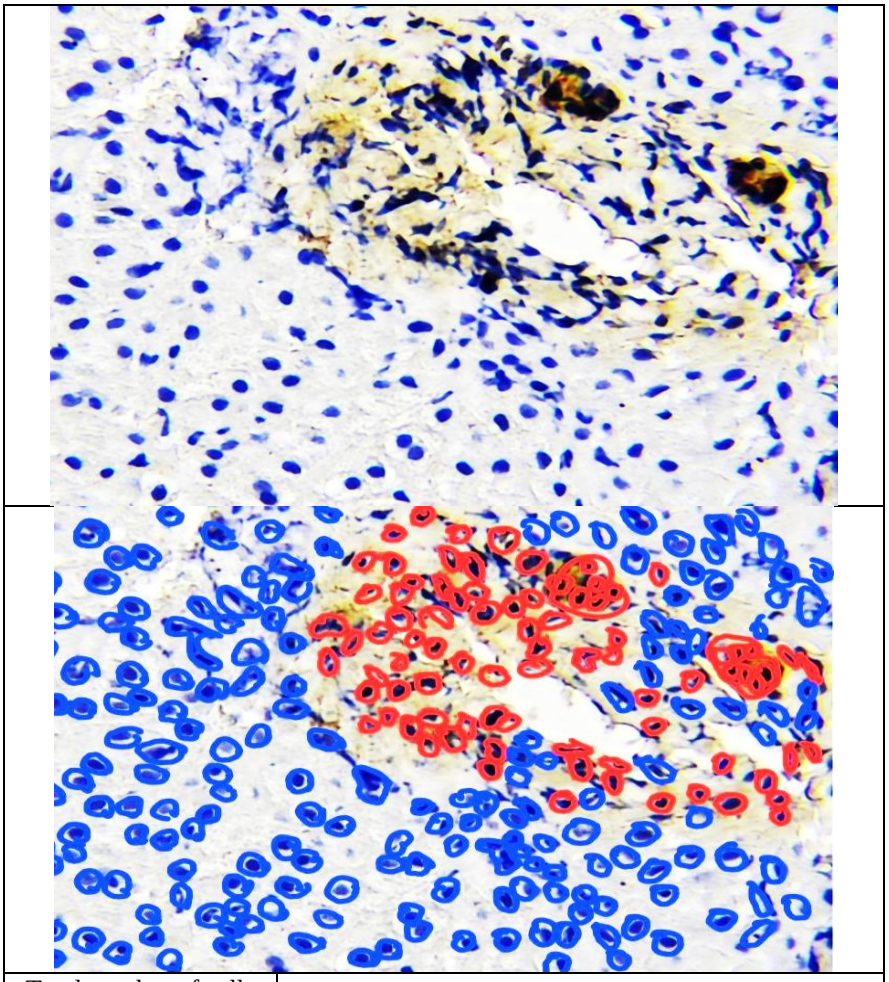


Total number of cells detected	519
Positive cells	170
Negative cells	349
Positive expression	33,03 %
Positive expression	1037079 px^2

4. Medium level expression of Ki-67 marker (34.03%) was observed in the liver tissue of 3 non-breed rats fed groundwater with high chemical transport. Dab is created by the chromogenic method. Image magnified 400 times. In QuPath-0.4.0.ink, scanning and expression levels are defined. Expressed cells are in red".

Bcl-2 family proteins are regulators of apoptosis, one of the most studied types of programmed cell death. This family of proteins is expressed by pro- and antiapoptotic members. Anti-apoptotic proteins of the Bcl-2 family are often used by tumor cells as a mechanism of resistance to death, they play an important role both in the process of oncological diseases and in the resistance of malignant cells to therapeutic effects. Therefore, these proteins are targeted as antitumor therapies. A thorough study of the interactions between

Bcl-2 proteins that underlie the regulation of the initiation of apoptosis has made it possible to make an important breakthrough in the development of highly selective inhibitors of individual antiapoptotic members of the family. In this study, conducted in albino rats, we used the Bcl-2 marker to study the process of apoptosis in liver tissues as a result of the effects of chemotherapy..



Total number of cells detected	527
Positive cells	117
Negative cells	410
Positive expression	22,2%
Positive expression	1045250 px^2

Figure 4.7. The liver tissue of experimental animals of groups 11-12 showed a moderate level of expression of the Bcl-2 marker (22.2%). Stained using the Dab chromogenic method. Image magnified 400 times. Scanned and the level of expression was determined using the QuPath-0.4.0.ink program. Expressed cells are colored red."

Conclusion

Ki-67 antigen plays a key role in the process of cell division and is an important marker for assessing the proliferative activity of tumor cells. The results of the study show that the expression level of Ki-67 antigen changes in the liver of experimental groups as a result of chemotherapy. Thymalin and especially pomegranate seed oil cause a positive shift in the existing changes in the liver.

Proteins belonging to the Bcl-2 family play an important role as regulators of apoptosis. Pro- and anti-apoptotic members of this family form anti-death mechanisms of tumor cells, which is of great importance in oncological diseases and resistance to therapeutic effects. Our study aimed to study the process of apoptosis in liver tissues using the Bcl-2 marker.

The conducted studies open new opportunities for the development of inhibitors of individual anti-apoptotic members of the Bcl-2 family, which will help improve oncological therapy. The following levels of Ki-67 and Bcl-2 expression were noted in liver samples of experimental rats exposed to various chemotherapy:

Ki-67 - 1.5%, Bcl-2 - 3.3% (low); Ki-67 - 21.2%, Bcl-2 - 22.2-24.25% (medium); and 34.03% for Ki-67 (high) Thymalin and pomegranate seed oil resulted in 7.45% expression of Ki-67 antigen and 3.8% expression of Bcl-2 (low) in liver tissues.

These immunohistochemical changes lead to increased proliferation of high-dose chemotherapeutic drugs, which reduces the risk of metastasis and has a good effect on the prognosis of the disease. The study shows that breast cancer promotes the increase of Ki-67 and Bcl-2 antigens in liver tissues, which indicates the proliferative activity of tumor cells and a decrease in the apoptosis process. In particular, when we used chemotherapy in the liver of the experimental group of animals, it reached 34.03%, which indicates the risk of tumor development and metastasis. Also, when we used thymalin and pomegranate seed oil, the level of Ki-67 expression decreased to 7.45% and 3.8% (low). This indicates the potential benefit of these substances in reducing the proliferative activity of tumor cells and, therefore, reducing the risk of tumor development. Thus, treatment with pomegranate seed oil leads to correction and reduction of liver complications of breast cancer. Therefore, it may be an effective method for reducing the risks for tumor prevention.

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