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CYTOMORPHOLOGICAL CHARACTERISTICS OF MCF7-DOX BREAST ADENOCARCINOMA CULTURE CELLS AFTER THE INFLUENCE OF PHOTOBIOMODULATION IN COMBINATION WITH LOW DOSES OF DOXORUBICIN

Sergii Konovalenko
Junior Researcher
ORCID 0000-0001-9212-9255
Lesia Naleskina
PhD, Professor
ORCID 0000-0002-8623-4419
Department of Monitoring of Tumor Process and Therapy Design
RE Kavetsky Institute of Experimental Pathology,Oncology and Radiobiology,
National Academy of Sciences of Ukraine
Ukraine, Kyiv, 03022, str. Vasylkivska, 45

Abstract. *The evaluation of morphological characteristics in micropreparations testifies to the antitumor effectiveness of the combined effect of infrared laser irradiation and doxorubicin. It is noteworthy that the cytotoxic effects of chemotherapy in combination with photobiomodulation were observed when using different doses of doxorubicin: 2 μg/ml and 0.5 μg/ml. The results of the study allow us to consider the use of low doses of doxorubicin in combination with photobiomodulation as a promising method of cytotoxic effect on tumor cells.*

Key words: *Breast cancer, photobiomodulation, doxorubicin*

Introduction. The pronounced heterogeneity of breast cancer (BC) and the selection of subtypes of this disease, based on clinical-morphological, molecular-genetic, epidemiological and other approaches, as well as noticeable differences in risk factors, allow us to say that the issue of treatment of patients with BC has not been finally resolved.[1] It should also be noted that one of the main tasks of developing new approaches to treatment in oncology is to reduce toxicity for healthy tissues while maintaining the effectiveness of malignant neoplasms treatment.

On the path to improving treatment methods in oncology, one of the decisive roles is played by the progress of modern laser medicine, which has led to the emergence of fundamentally new technologies that are gradually being introduced into clinical practice. The effectiveness of tumor treatment using laser technology has been confirmed in many preclinical and clinical studies [2-6]. The study of lasers effects on biological objects, in particular as part of the improvement of therapeutic

approaches to the treatment of oncological diseases, continues to be the focus of attention of researchers around the world [7-9].

Objective. To study the cytomorphological characteristics of MCF7DOX breast adenocarcinoma cells after exposure to photobiomodulation in combination with low doses of doxorubicin.

Results. According to light microscopy, in the control group where there was no photobiomodulation and doxorubicin, the cells showed active growth and were located in a continuous layer, with the formation of anastomoses, layering, centers of structures like symplasts. In the group with photobiomodulation and without the addition of doxorubicin cells in some separate areas grew in the form of a mesh structure with thinning and the formation of niches.

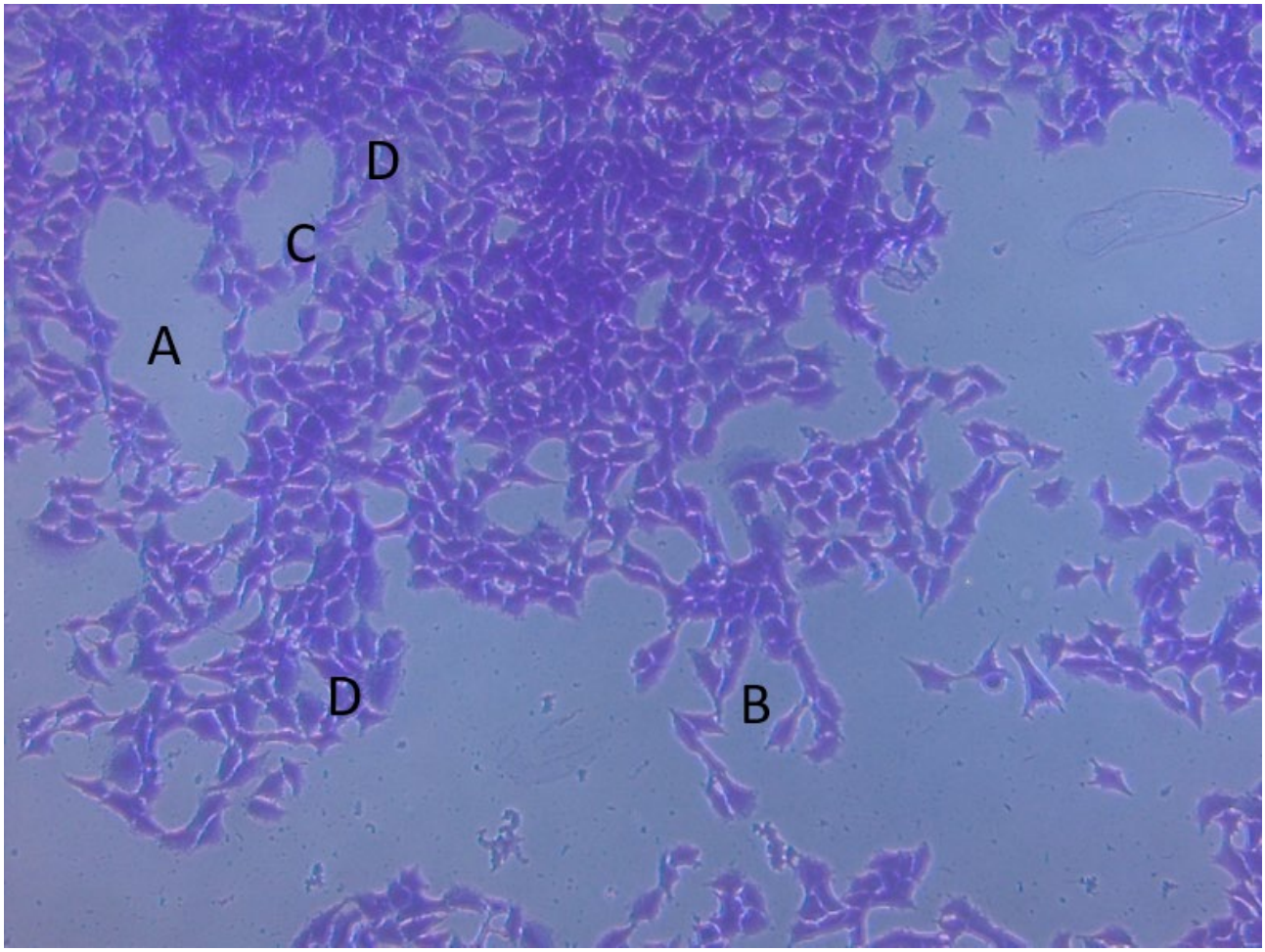

Figure 1 Micrograph of MCF7-DOX cells: photobiomodulation + 2.0 µg doxorubicin. *Loss of connections between growing tumor cells with the formation of large cavity structures (A); groups of cells and individual cells (B); individual cells with ruptured membranes and stratified cytoplasm (C), giant cells with large nuclei (D) are observed.*

In the group without photobiomodulation and with the addition of doxorubicin, we observed fields of solid growth of tumor cells with the formation of anastomoses and separate areas of thinning. But in general, according to light microscopy, MCF-7 DOX cells in the control groups and in the groups after the application of only laser or only doxorubicin showed active growth.

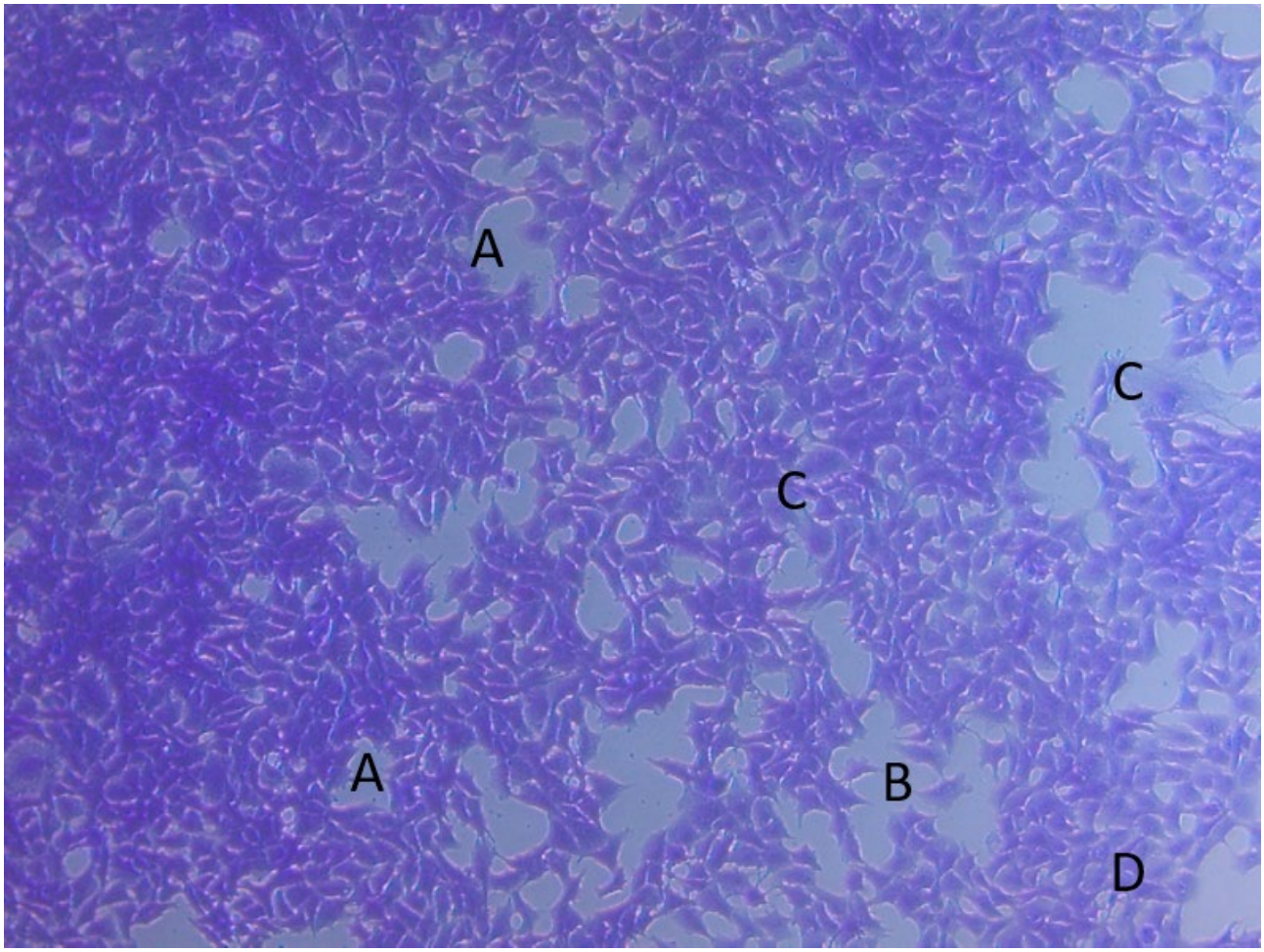

Figure 2 Micrograph of MCF7-DOX cells: photobiomodulation + 0.5 µg doxorubicin. *Areas of rarefaction, alternating with continuous areas of growth of tumor cells (A); formation of cavities and separation of individual groups of cells and single cells (B); giant cells (C); deformed cells with damaged membranes (D).*

Instead, the infrared laser in combination with doxorubicin caused the rupture of solidly growing tumor cells with the formation of cavities and the separation of isolated groups of cells and single cells and the loss of connections between tumor cells with the formation of large cavity structures in which groups of cells and individual cells were defined. Microscopically, cells with ruptured membranes and stratified cytoplasm (necrosis, apoptosis) were detected, the appearance of giant tumor cells with large nuclei was observed.

It is noteworthy that we observed such changes both after photobiomodulation with a doxorubicin concentration of 2.0 μg/ml and with a concentration of 0.5 μg/ml. (Fig. 1, 2)

The results of this study, taking into account the assessment of the morphological characteristics of cells in micropreparations, testify to the antitumor effectiveness of the combined effect of photobiomodulation and doxorubicin. The fact that the cytotoxic effect on cells was recorded by us at low doses of the chemotherapeutic agent (both at 2.0 μg/ml and at 0.5 μg/ml) suggests that the synergistic effect of infrared laser radiation and doxorubicin can create foundations for reducing the toxicity of chemotherapy while maintaining its effectiveness.

Conclusion

An infrared laser in combination with doxorubicin, probably due to its effect on mitochondria and modulation of the release of ROS, creates conditions for tumor cells to undergo apoptosis, which is confirmed by cytomorphological data of light microscopy.

The results of the study allow us to consider the use of low doses of doxorubicin in combination with photobiomodulation as a promising method of cytotoxic effect on tumor cells. And in a strategic perspective - as a way to reduce the toxic effects of chemotherapy by reducing doxorubicin doses while maintaining antitumor effectiveness.

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Academic Supervisor

Academician of the National Academy of Sciences of Ukraine,

Doctor of Medical Sciences, Professor

Vasyl Chekhun