IDENTIFICATION OF BLOOD-BASED PROGNOSTIC PREDICTORS FOR IDENTIFYING CANCER PATIENTS AT INCREASED RISK OF RADIATION THERAPY COMPLICATIONS

E.A. Domina, Y.V. Dumansky, L.I. Makovetska, V.M. Mikhailenko, A.A. Glavin, V.V. Sarnatska

R.E. Kavetsky Institute of Experimental Pathology, Oncology, and Radiobiology, National Academy of Sciences of Ukraine, Kyiv, Ukraine

Introduction. Radiation therapy is one of the leading methods for treating gynecological oncological diseases; however, its use is accompanied by the risk of radiation-induced complications in normal tissues and critical pelvic organs. Despite significant progress in modern radiation oncology, the increased sensitivity of non-malignant cells to radiation largely determines the development of radiation-induced side effects, which can significantly reduce treatment efficacy and impair patients' quality of life.

The aim of this study is to identify a set of prognostic blood markers for the early identification of gynecologic cancer patients at increased risk of radiation therapy complications.

Materials and methods. Study materials: peripheral blood samples from patients with cervical cancer and endometrial cancer. The study utilized a combination of biochemical, cytogenetic, and cytological research methods. The concentration of malondialdehyde (MDA) in blood plasma was determined as an indicator of the intensity of lipid peroxidation processes and the development of oxidative stress. Cytogenetic analysis was performed on peripheral blood T-lymphocyte cultures in accordance with the IAEA's international recommendations (2011), assessing the frequency and spectrum of chromosomal aberrations. Apoptosis levels were determined by flow cytometry using Annexin V FI TC.

Results. It was found that even before the start of radiation therapy, gynecological cancer patients exhibited a significant increase in plasma MDA levels compared to healthy controls. This indicates an intensification of lipid peroxidation processes and a disruption of the redox balance in the patients' bodies. Test irradiation in vitro is accompanied by a dose-dependent increase in MDA levels, confirming the relationship between oxidative stress and individual radiosensitivity of cells.

Cytogenetic studies demonstrated a significant increase in the frequency of chromosomal aberrations in the blood lymphocytes of patients. Chromatid-type aberrations predominated in the spectrum of cytogenetic abnormalities, and dicentric and ring chromosomes were also recorded, which are markers of radiation-induced genomic instability. The detected changes indicate that even before the start of therapeutic irradiation, non-malignant cells of cancer patients are characterized by signs of genetic instability and increased sensitivity to the effects of ionizing radiation.

At the same time, a significant increase in the level of early T-lymphocyte apoptosis was observed in patients with cervical cancer compared to the control group. The observed prolongation of apoptotic processes following radiation therapy may be one of the mechanisms underlying the development of late radiation complications.

Conclusions. Based on radiobiological studies, a new strategy has been developed to identify cancer patients at high risk of developing radiation complications in non-malignant cells adjacent to the tumor even before the start of therapeutic irradiation:

- Laboratory testing of gynecologic oncology patients using a combination of biochemical, cytogenetic, and cytological tests will provide the most well-founded assessment of the risk of radiation therapy-related complications prior to treatment initiation and will contribute to increasing its effectiveness as well as improving the quality of life of treated patients;
- Screening of gynecologic oncology patients prior to the start of radiation therapy to assess the increased risk of radiation-related complications may be limited to a biochemical test—determination of MDA levels in blood plasma—as it is less costly and time-consuming;
- However, if the patient's medical history includes information regarding occupational radiation exposure, residence in radiation-contaminated areas following the Chernobyl disaster, or other exposure to radiation sources, it is recommended to perform a comprehensive examination using cytogenetic and cytological predictors. This will provide the most comprehensive assessment of the individual risk of radiation-related complications in patients exposed to radiation.

Such a strategy for planning radiation therapy for patients will help increase its effectiveness and improve their quality of life.