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RADIATION PATHOMORPHOSIS IN A POSTMENOPAUSAL WOMAN AFTER THERAPY OF A MALIGNANT NEOPLASM OF THE BREAST

Tamila Abubakarovna Temikhanova[1], Khanbagi Muradovna Isupanova[2], Jamila Albertovna Abdulmezhidova[1], Mansur Movsarovich Niniev[2], Mahmutmerzayeva Zarema Suleymayevna[3], Kamila Sirazhutdinovna Kazimurzaeva[4*]

1. ***Department of Therapy, Pediatric Faculty of the Chechen State University named after A.A. Kadyrov, Grozny, Republic of Chechnya, Russia***
2. ***Department of Therapy, Medical Faculty of Saratov State Medical University named after V. I. Razumovsky, Saratov, Russia***
3. ***Department of Therapy, Medical Faculty of First Moscow State Medical University named after I.M. Sechenov, Moscow, Russia***
4. ***Department of Therapy, Pediatric Faculty of Rostov State Medical University, Rostov-on-Don, Russia.***

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ABSTRACT

About 20% of women after radiation therapy for the presence of malignant neoplasm of the pelvic organs have signs of radiation dysplasia of the mucous membrane of the cervix, in rare cases, the occurrence of these changes in the epithelium of the cervix can be observed in women after treatment of malignant tumors of other organs. This article describes a clinical case of a woman admitted to the Diagnostic Center. The patient had adenomyosis and malignant neoplasm of the left breast with 3 courses of neoadjuvant chemotherapy. The patient's complaints, symptoms of diseases, as well as the results of the conducted studies confirm the presence of radiation dysplasia in her. It is known that changes in cells caused by the treatment of malignant processes are associated with a violation of the synthesis of nucleic acids, inactivation of enzyme systems, chromatin coagulation, mitosis disruption, and transition to amitotic division and denaturation of proteins of the nucleus and cytoplasm, the same thing happens in cells under the influence of ionizing radiation and chemotherapeutic drugs.

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Introduction

Changes in the morphology of epithelial cells after exposure to ionizing radiation and chemotherapeutic agents may occur a few days after the start of therapy and persist throughout life. They are described in the literature as radiation pathomorphosis or radiation dysplasia [1, 2]. About 20% of women after radiation therapy for the presence of malignant neoplasm of the pelvic organs have signs of radiation dysplasia of the cervical mucosa, in rare cases, the occurrence of these changes in the cervical epithelium can be observed in women after treatment of malignant tumors of other organs [3, 4].

Changes after radiation therapy are noted both in tumor cells and in normal cells. According to the law of Bergonié and Tribondeau, the lesions mostly occur in young cells and cells at the premitotic and mitotic stages of development [5, 6]. Exposure to ionizing radiation leads to disruption of DNA synthesis, the ability to normal division, inactivation of enzyme systems, denaturation of proteins of the nucleus and cytoplasm [7].

Corresponding Author: Kamila Sirazhutdinovna Kazimurzaeva; Department of Therapy, Pediatric Faculty of Rostov State Medical University, Rostov-on-Don, Russia. E-mail: bucky99@ya.ru.

The purpose of this work was to consider the case of radiation dysplasia in the example of a postmenopausal woman after radiation therapy for the presence of a malignant neoplasm of the left breast.

Clinical Case

A 63-year-old woman turned to the clinical diagnostic center of the city of Stavropol (Russia) for the consultation of an obstetrician-gynecologist with complaints of itching and burning in the area of the external genitals and pulling abdominal pains for three months.

The patient has a history of adenomyosis and malignant neoplasm of the left breast with 3 courses of neoadjuvant chemotherapy. Previously, the patient underwent a cervical cancer screening program, which includes a molecular biological diagnosis of HPV with low, medium, and high oncogenic risk and microscopic examination of scrapings of the cervix and cervical canal, the results were negative.

According to the gynecological examination, the external genitalia of the patient is formed correctly, the vagina is in a state of deep atrophy with the omission of the anterior wall, the cervix is not eroded, or undeformed, length is 2.5 cm, the uterus is mobile, traction is painless, appendages are painless.

In order to diagnose the patient, an ultrasound of the pelvic organs, general blood and urine tests were prescribed, gynecological material was taken (vaginal secretions, scraping from the cervical canal for atypical cells, scraping for molecular biological studies of bacterial vaginosis and HPV).

According to the results of ultrasound – signs of adenomyosis, a general urine test – without pathology, a general blood test – insignificant leukocytosis (12,1x10 ^9 / l), a decrease in the number of red blood cells (3.3 x10 ^9 / l) and hemoglobin (117 g / l). Molecular biological diagnostics of bacterial vaginosis and HPV gave negative results.

Results and Discussion

The study of vaginal secretions showed the presence of an insignificant amount of mucus, mixed microflora, leukocytes 14-20-22 in the field of vision, squamous epithelial cells of different layers (intermediate: 1-1-2 in the field of vision, parabasal: 2-1-2 in the field of vision and basal: 1-1-3 in the field of vision).

Microscopic examination of the cervical canal scraping using the traditional method (Romanovsky-Giemsa staining) revealed mucus strands with accumulations of leukocytes up to 30 in the field of view, squamous epithelial cells of different layers and glandular epithelial cells with reactive changes, some squamous epithelial cells showed signs of pronounced hyperplasia and minor hyperchromia, shifted nuclear-cytoplasmic ratio **(Figure 1)**, there were multinucleated squamous epithelial cells and scanty mixed microflora **(Figure 2)**.

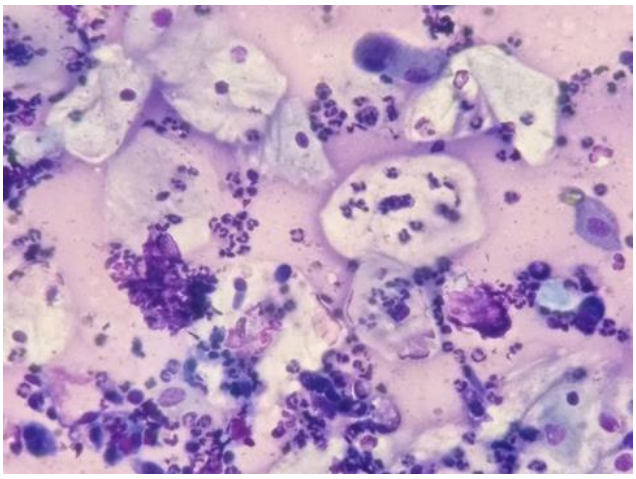

Figure 1. On the background of mucus: pronounced leukocyte infiltration with partial degeneration of leukocytes, mixed microflora, reactively altered squamous epithelial cells, some of which have signs of hyperplasia and hyperchromia (increase x400)

The presence of multinucleated cells of the squamous epithelium and mixed microflora was noted **(Figure 2)**.

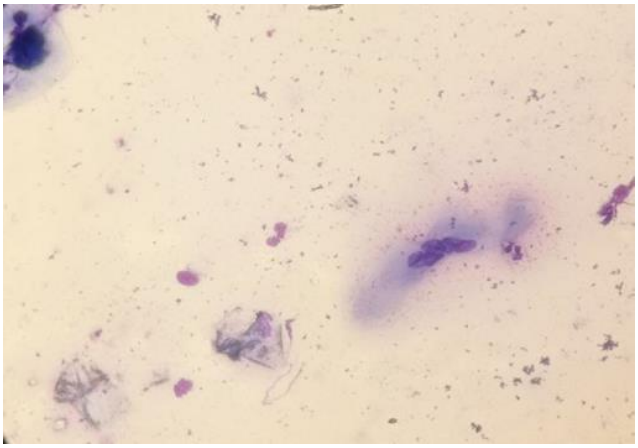

Figure 2. A multinucleated cell of the squamous epithelium

The changes found may belong to the post-radiation transformation of cells. Such a cytological picture may be mistakenly regarded as pathological dysplasia, which has a significant impact on the tactics of the patient's treatment [8]. According to the recommendations of the Association of Clinical Cytologists of Russia, when examining cytological material from the cervical canal or cervix, it is necessary to analyze the microscopic picture according to the signs reflected in **Table 1**.

Table 1. Cytological signs of changes in pathological and radiation dysplasia

	Dysplasia	**Acute radiation changes**	**Long-term radiation changes**
Background of the drug	With mild dysplasia without concomitant infections – clean, with severe dysplasia – dirty, "tumor" diathesis	More often dirty with leukocyte infiltration	More often dirty with severe leukocyte infiltration
Cytoplasm	With mild dysplasia – "mature", with severe – "immature"	Enhanced vacuolization	Vacuolization of the cytoplasm is less pronounced; the cells are sharply elongated
The core	Dyskariosis	Increase of nuclei as a result of edema, vacuolization of nuclei, erased chromatin structure	Karyorexis / Karyolysis
Nuclear-cytoplasmic relationship	Shifted towards the core	More often shifted towards the core	"Balloon-like" cells can be shifted towards
General view of cells	The cells are arranged in layers, with weak dysplasia – two-core cells	Multinucleated cells, enlarged in size	the nucleus
Other signs	The phenomenon of para- and hyperkeratosis	The appearance of "ray giants"	The appearance of giant foreign body-type cells with degenerative changes in the nuclei, the appearance of fibroblasts

Conclusion

The prognostic value of radiation dysplasia has not been reliably studied to date. The phenomenon of post-radiation pathomorphosis can be used to evaluate the effectiveness of the destruction of malignant cells. It is known that changes in cells caused by the treatment of malignant processes are associated with a violation of the synthesis of nucleic acids, inactivation of enzyme systems, chromatin coagulation, mitosis disruption, and transition to amitotic division and denaturation of proteins of the nucleus and cytoplasm, the same thing happens in cells under the influence of ionizing radiation and chemotherapeutic drugs. However, in the case of radiation and chemotherapeutic atypia in organs whose cells have not been subjected to tumor transformation, it is more likely to be adaptive.

Thus, it is necessary to conduct a detailed comparative analysis of cytological preparations, the patient's anamnesis, and related studies to issue a conclusion. Unfortunately, in some cases, it is quite difficult to give a correct cytological conclusion due to the lack of correct filling of the referral, collection of anamnesis, or unsatisfactory quality of the cytological preparation, which can lead to hypo- or overdiagnosis.

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