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## **STRUCTURAL CHANGES OF LOCAL TISSUES AFTER RADIATION THERAPY IN BREAST CANCER PATIENTS**

**Introduction.** The analysis of longterm researches of the pathological changes arising in soft tissues at patients with a breast cancer as a result of radical surgical treatment and adjuvant radiotherapy is carried out in work. The article shows that the standard approach to postoperative radiation therapy, which is based only on the prevalence of the primary tumor process is not always justified. Very often it leads to excessive radiation load on the patient's body and the development of local acute and chronic radiation reactions of the skin, subcutaneous tissue and other soft tissues. In this regard, the question of differentiated purpose of radiotherapy acquires special value first of all at patients with small primary prevalence of tumor process. The paper presents the results of studies to study changes in the anterior chest wall in patients with breast cancer. In relation to the conduct of adjuvant radiotherapy more often need to use the concept of personalized radiation therapy. Radical operation, postradiation early and late pathological changes in soft tissues, disturbance of microcirculation of lymph and blood, disturbance of innervation of vessels of an upper extremity, peripheral nerves in system of a cervical and plexus plexus, leads to intensive degenerative and dystrophic changes in soft tissues of the upper. and causes morphological changes in them and further progression of reflex neurovascular and neurodystrophic disorders. Based on the data of adverse effects of radiotherapy on the skin and surrounding tissues, as well as to reduce excessive radiation exposure to the patient's body, a differentiated approach to the appointment of adjuvant radiation therapy.

**Aim.** The objective is to study the structure of local acute and chronic radiation reactions of the skin, subcutaneous tissue and other soft tissues, after radical surgical treatment and radiation therapy in breast cancer patients.

**Materials and methods.** Examination of patients with malignant tumors of the mammary glands, who was treated with radiation therapy. The analysis of longterm researches of the pathological changes arising in soft tissues at patients with a breast cancer as a result of radical surgical treatment and adjuvant radiotherapy.

**Results and discussion.**

The need to bring IR to large volumes of tissue in the treatment of both primary and locally advanced forms of the disease, the problem of postradiation damage to healthy tissues is extremely relevant [1, 2]. Acute radiation reactions of the skin are one of the most common side effects of RT [3, 4, 5], which in turn is a risk of stress in some patients, and in some cases a factor limiting the full dose according to the treatment plan.

After receiving RT, 90 % of patients with breast cancer develop radiation epidermis. Therapeutic doses of radiation lead to persistent erythema of the skin, peeling, rash, pain and itching and the appearance of skin ulcers [3]. According to the results of the study, skin damage in 108 irradiated patients with breast cancer was found in 92 % of patients with erythema, 30 % of dry epidermis, 35 % of wet epidermis and 14 % of ulcers [3, 7].

The most common complication of radical surgery on the breast is secondary lymphatic edema of the upper extremity. Surgical interventions together with RT lead to violations of regional circulation of lymphatic and venous outflow distal to the irradiation zones (in the axillary region, upper extremity from the operation) and manifests itself in the form of lymphedema or recurrent inflammatory erythema [8, 9, 10]. The incidence of secondary lymphedema of the upper extremities in women after radical surgery for cancer in Western Europe ranges from 38 to 89 % and is considered as a consequence of axillary lymph dissection and (or) radiation irradiation of the axilla.

Lymphedema can be both a risk factor for erysipelas and severe complication of this infection. It is not always possible to determine which of them is primary and which is secondary. Very often persistent interstitial edema develops in patients with erysipelas on the background of functional insufficiency of lymphatic circulation, which occurs in subclinical or latent form. The often recurrent erythema arising against this background can lead to a lymphedema. The average incidence of erysipelas in secondary lymphedema is 34–56 %. At that time, the incidence of lymphedema in primary erysipelas is 10–15 % [9, 10, 11].

In the study of morphological changes in humans described vascular changes that develop within a few weeks after irradiation, causing narrowing and obliteration of capillaries, endothelial edema with foci of fibrosis and endothelial hyperplasia. Endothelial hyperplasia is also observed in large vessels, arteries and veins. Decreased capillaries cause tissue ischemia, which is also one of the causes of the development and progression of fibrosis. The accumulation of macrophages under the intima is described as a typical morphological picture of chronic radiation vasculitis, resembling the morphological features of atherosclerosis, in which macrophages are the main source of synthesis of fibrogenic cytokines [8, 12–14]. In the study of breast skin 1–5 years after irradiation in a total focal dose of 50 Gy for 25 fractions, the rate of type I and III collagen synthesis was doubled in the first years, as well as signs of collagen degradation.

The metabolism of the main protein of collagen skin under the conditions of IR can be judged by the amount of its marker amino acid hydroxyproline in organs and tissues. Changes in the level of hydroxyproline in the serum of patients may be an indicator of collagen metabolism in a critical organ for this pathology, especially in cases of PT in irradiated skin.

After the course of RT there is a significant increase in the content of all serum fractions of hydroxyproline by 25–45 % relative to normal ( $p < 0.06$ ). This is dominated by an increase in the amount of bound hydroxyproline by 35.6–45.6 % compared to patients who were before RT. The fraction of free hydroxyproline also significantly increases not only relative to normal values, but also relative to free hydroxyproline in the postoperative period. An increase in the content of free hydroxyproline demonstrates the destruction of connective tissue in the irradiation zone, and almost 1.5-fold increase in the concentration of bound and total hydroxyproline may indicate the activation of collagen formation processes with the development of fibrosis [15]. Uncontrolled activation of collagen synthesis and accumulation in irradiated skin and adjacent tissues can lead to its fibrotization, and later to the development of radial skin fibrosis, which is often an undesirable separate consequence of radiation [8, 12, 15].

Patients receiving RT are at risk of developing secondary malignancies of the skin. The increased risk of skin cancer can last a lifetime, depending on the dose and increasing during the patient's life [6, 16]. In most cases, squamous cell carcinoma develops in the area of the ulcer, often highly differentiated, less often moderately differentiated [17, 18].

Stewart-Treves syndrome (FW Stewart, American pathologist; N. Treves, American surgeon) was first described in 1948, characterized by the development of angiosarcoma on the background of prolonged limb lymphedema, most often due to radical mastectomy, especially in combination with radiation therapy [19, 20]. The disease is characterized by high malignancy, aggressive course with metastasis to the lungs and liver, sometimes to the adrenal glands, ovaries and other organs, 5-year survival is from 10 to 18 % [21].

Significant surgical interventions and radiation therapy in the treatment of breast cancer lead to a violation of the parameters of arterial and venous blood flow of the upper extremity [22–24].

Changes in the volumetric blood flow (Vid) of the upper extremity, namely an increase in arterial blood flow in patients who have undergone radical surgery for breast cancer should be associated directly with surgical trauma, which results in the intersection of a large number of small nerve fibers, leading to loss of sympathetic-vasoconstrictor control [25, 26]. This leads to a change in the vascular component with changes in the vascular wall of the arteries, reducing its vasoconstrictor and elastic properties, which is reflected in the change of the peripheral resistance index (RI), pulsation index (PI) [22].

After radical surgical treatment and RT in 67–90 % of cases, extravasal stenoses of the axillary-subclavian segment of the vein, of varying degree and length (length) are detected. At the same time, more than 40 % of patients have a significant narrowing of the vein (50–75 %) and occlusion [24, 27, 28]. Despite the fact that extravasal stenoses of this segment of the vein are quite common, hemodynamically significant they are, according to various authors, from 24.2 % to 62 % of cases. Such data discrepancies are considered to be related to the use of different methods of venous blood flow study – phlebomanometry, phlebography, ultrasound Doppler phlebography [28, 29, 30]. Extravasal stenoses are associated with the development of scarring around the vascular-nervous bundle and in 13.7 % they are associated with cicatricial degeneration of vessels that have been bandaged and crossed, as well as with the development around ligatures that were imposed during radical surgery, coarse connective tissue.

Within 12 months after surgery and RT, almost all patients (99.42 %) invariably form and then progressively develop anterior ladder muscle syndrome, which provides stable compression of the neurovascular bundle of the upper extremity. Clinical manifestations of scalenus syndrome on the side of radical treatment were detected in 65.45 % [29, 31, 32].

### **Conclusions.**

We believe that ART is not indicated in patients after IE and lymph node dissection of I–II level and systemic therapy in cases of small tumor size (T1–2) and in the absence or presence of 1–3 affected by tumor cells lymph nodes (N0–1), which affected by the Chernobyl accident and live in contaminated areas or have a history of radiation. With adequately performed axillary lymph dissection, there is no reason to perform ART on the axillary region, due to the low risk of regional recurrence, but there is a high probability of possible complications after irradiation. In patients with a complete pathomorphological response after neoadjuvant chemotherapy with stage I or II at the time of diagnosis, in this category of patients we believe – ART is not indicated.

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