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MORPHOLOGICAL CHANGES IN THE HEART DURING CHEMOTHERAPY IN WHITE OUTBREED RATS WITH BREAST CANCER

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Summary. Early diagnosis and timely detection of the cardiotoxic effects of anticancer drugs in the treatment of women with breast cancer (BC) are one of the tasks of the direction in medicine that has emerged in recent years - cardio-oncology [1]. Evaluation of pathomorphological changes of the myocardium in patients receiving chemotherapy for breast cancer allows us to speak about the cytotoxic effect on cardiomyocytes and is characterized by acute dystrophic, necrobiotic changes in cells, their death with subsequent replacement formation of connective tissue. The review is devoted to morphological changes in the heart during chemotherapy with drugs such as cisplatin and paclitaxel in white outbred rats with breast cancer.

Key words: chemotherapy, cisplatin, paclitaxel, morphology, heart.

МОРФОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ В СЕРДЦЕ ПРИ ХИМИОТЕРАПИИ У БЕЛЫХ БЕСПОРОДНЫХ КРЫС С РАКОМ МОЛОЧНОЙ ЖЕЛЕЗЫ

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Резюме. Ранняя диагностика и своевременное выявление кардиотоксических эффектов противоопухолевых препаратов при лечении женщин рака молочной железы (РМЖ) являются одними из задач сформировавшегося в последние годы направления в медицине – кардиоонкологии [1]. Оценка патоморфологических изменений миокарда у пациенток, получавших химиотерапию по поводу рака молочной железы, позволяет высказаться о цитотоксическом воздействии на кардиомиоциты и характеризуется острыми дистрофическими, некробиотическими изменениями клеток, их

гибелью с последующим заместительным формированием соединительной ткани. Обзор посвящен морфологическим изменениям в сердце при химиотерапии с такими препаратами как цисплатин и паклитакселом у белых беспородных крыс с раком молочной железы.

Ключевые слова: химиотерапия, цисплатин, паклитаксел, морфология, сердце.

KO'KRAK BEZI SARATONI BO'LGAN OQ ZOTSIZ KALAMUSHLARDA KIMOTERAPIYA FONIDA YUZAGA KELADIGAN YURAKDAGI MORFOLOGIK O'ZGARISHLAR

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Annotatsiya. Ko'krak bezi saratoni bilan og'rigan ayollarni davolashda saratonga qarshi dori vositalarining kardiotoxik ta'sirini erta tashxislash va o'z vaqtida aniqlash tibbiyotda so'nggi yillarda paydo bo'lgan kardio-onkologiya yo'nalishining vazifalaridan biridir [1]. Ko'krak bezi saratoni uchun kimyoterapiya olgan bemorlarda miokardning patomorfologik o'zgarishlarini baholash kardiomyositlarga sitotoksik ta'sir ko'rsatishi haqida gapirishga imkon beradi va hujayralardagi o'tkir distrofik, nekrobiotik o'zgarishlar, ularning o'limi bilan biriktiruvchi to'qimalarning keyingi almashinuvi shakllanishi bilan tavsiflanadi. Sharh ko'krak saratoni bilan og'rigan oq kalamushlarda sisplastin va paklitaksel kabi dorilar bilan kimyoterapiya paytida yurakdagi morfologik o'zgarishlarga bag'ishlangan.

Kalit so'zlar: kimyoterapiya, sisplastin, paklitaksel, morfologiya, yurak.

Relevance. In recent decades, in the developed countries of the world, advances have been made in the treatment of breast cancer (BC), both due to early detection of cancer and through the use of modern treatment methods (targeted and chemotherapy, radiation therapy and surgical treatment). In this regard, the time of relapse-free course of cancer and the life expectancy of patients have increased. However, a number of antitumor drugs used in the treatment of breast cancer are cardiotoxic [1].

Patients with malignancy are in a hypercoagulable state, and chemotherapy may increase the risk of venous or arterial thromboembolism [17, 18]. For example, the use of cisplatin was the cause of venous thromboembolism in 18% of patients; Most likely, the direct endothelium toxic effect and changes in the blood coagulation system are "responsible" for this side effect [Seliverstova D.V., Evsina O.V., 2016].

Antimicrotubule drugs include vinca alkaloids and taxanes (eg, paclitaxel and docetaxel). They block cell division by stabilizing microtubules. Paclitaxel is an extract of the rare Pacific yew tree. Poisoning from such extracts has previously resulted in VT, VF, and sudden death. Paclitaxel causes arrhythmia and bradycardia at doses approximately 10 times higher than therapeutic doses. In isolated perfused guinea pig hearts, paclitaxel caused conduction disturbances and decreased coronary blood flow as well as LV systolic pressure [14]. In the hearts of frogs and rabbits, taxanes slowed heart rate, caused atrioventricular (AV) block, and then asystole. In dogs, ECG changes progressed with QRS widening and ultimately followed by VF and death [5]. There are frequent cases of cardiovascular disease among patients using paclitaxel. These include frequent asymptomatic sinus bradycardia (29%) and first-degree AV block (25%). Later heart block and conduction disorders occur infrequently and are mostly asymptomatic [16].

Alkylating agents include chlorambucil, cyclophosphamide, busulfan, cisplatin and melphalan. They cause cross-linking of DNA strands, abnormal base pairing or DNA strand breaks and thus prevent cell division. They are typically used to treat slow-growing cancers. Cardiotoxicity of the drug cisplatin is most often associated with the development of rhythm disturbances - most often AF/AFL and paroxysmal supraventricular tachycardia. Severe sinus bradycardia was reported, including a patient with a heart rate of 35 beats/min, which recurred during each of six cycles of cisplatin therapy [15]. Intrapericardial and intrapleural administration of cisplatin in metastatic lesions led to AF in 12–32% of patients and non-paroxysmal supraventricular tachycardia in 8% of patients. The cause of all these cases is assumed to be direct irritation of the pericardium [13]. Cisplatin is clearly associated with acute thrombosis of the coronary arteries, and in some cases with thrombosis in multiple vascular beds [11-13]. Endothelial damage, thromboxane production, platelet activation and aggregation are the main mechanisms leading to coronary thrombosis [12]. The long-term risk of CAD and myocardial infarction (MI) is increased in patients receiving platinum-based drugs. [D.P. Dundua, A.V. Staferov, A.V. Sorokin, A.G. Kedrova, 2016].

According to Druzhinin A.E. et al. (2022) during autopsies of deceased breast cancer patients who had undergone chemotherapy treatment, general anemia of the parenchyma and vessels of internal organs was revealed. The heart had a cone shape, the average size of the organ was 10.6x11.5x5.4 cm, and the average weight was 339.38±12.08 g. In the control group, the size of the heart was 9.8x9.1x5.1 cm, the weight of the organ was 287.45±11.05 g. Along with the identified changes, there was

a significantly significant decrease in the thickness of the interventricular septum in the group of women with breast cancer by 16% ($p < 0.05$).

In the cavities of the heart and large vessels there were also mainly blood clots and a small amount of liquid blood. The heart muscle on the sections was flabby, dull, and red-brown in color. On transverse sections of the left ventricle, the subendocardial areas of the myocardium had a paler color. In the control group, there was liquid blood in the cavities of the heart and large vessels, the heart muscle on the sections was full-blooded, red-brown in color. In both study groups, the coronary arteries had atherosclerotic changes, predominantly corresponding to the stage of lipoidosis.

During a microscopic examination of myocardial sections in cases of death of patients with breast cancer, stromal edema and unevenly expressed blood filling of the vessels were observed, some of the arteries were spasmed, the veins were unevenly dilated and full of blood, and slugging of erythrocytes was noted in the vessels of the microvasculature. In a number of visual fields, a combination of fragmentation of muscle fibers and their wave-like deformation was revealed.

Microscopic examination of myocardial sections revealed variability in muscle fibers in 70% of cases. The nuclei of cardiomyocytes differed in polymorphism. In 30% of cases in the study group, small binucleate cardiomyocytes were observed. These cells had large heterochromic nuclei that were located close to each other. In individual cardiomyocytes, nuclear deformation was noted due to developing karyorrhexis. During microscopy in these cases, a change from a round or oval shape to a looped one was visually noted. When polarizing microscopy of myocardial sections of patients receiving chemotherapy for breast cancer, the formation of contractures of degrees I-II and III was observed. In individual fields of view, individual cardiomyocytes were in a state of myocytolysis and clumpy disintegration. When assessing the expression of matrix metalloproteinase (MMP-9) in myocardial sections from patients receiving chemotherapy for breast cancer, an increase in extracellular expression of the marker was noted. The detection in the myocardium in a third of cases of small binucleate cardiomyocytes, in which large heterochromic nuclei were located close to each other, indicates the preservation of the potential for intracellular regeneration of karyokinesis without cytokinesis.

Considering the trend towards an increase in the incidence of malignant neoplasms and an increase in the patient's life expectancy after chemotherapy treatment, the issue of parallel protection of the cardiovascular system both during treatment and in the future is relevant. Therefore, numerous studies are currently being carried out on the early

detection of heart damage and the identification of drugs that can protect against possible damaging effects. Assessment of pathomorphological changes in the myocardium in patients receiving chemotherapy for breast cancer allows us to speak about the cytotoxic effect on cardiomyocytes and is characterized by acute dystrophic, necrobiotic changes in cells, their death, followed by replacement formation of connective tissue.

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ХАРАКТЕРИСТИКА АНТРОПОМЕТРИЧЕСКИХ ПАРАМЕТРОВ ДЕТЕЙ 8-9 ЛЕТНЕГО ВОЗРАСТОВ СО СКОЛИОЗОМ

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Аннотация В исследовании были сопоставлены антропометрические параметры физического развития 180 детей 12 летнего возраста, из них 80 детей со сколиозом (40 мальчики и 40 девочки) и 100 здоровых детей (40 мальчики и 60 девочки). Во время исследований было выявлено, что из-за выраженной деформации позвоночного столба дети со сколиозом 8-9 летних возрастов ростом ниже, а также масса тела, параметры груди меньше чем у здоровых детей.

Ключевые слова: сколиоз, антропометрические параметры, окружность груди, дети .

SKOLIOZI BO'LGAN 10 YOSHLI BOLALAR ANTROPOMETRIK KO'RSATKICHLARINING TAHLILI

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Annotastiya Tadqiqotda 8-9 yoshli 180 ta bolaning jismoniy rivojlanishining antropometrik ko'rsatkichlari taqqoslandi, shulardan 80 nafari skoliozi bo'lgan bolalar (40 ta o'g'il bola va 40 ta qiz bola) va 100 nafari sog'lom bolalar (40 ta o'g'il bolalar va 60 ta qiz bolalar). Tadqiqot