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Modern methods of diagnosis and treatment of cardiotoxicity during chemotherapy in cancer patients

Author(s), MAMUROV OLIMJON ISLOMOVICH

Abstract:

Modern methods of diagnostics and treatment of oncological diseases, complications of anticancer therapy can often have an adverse effect on the cardiovascular system. As a result of the direct effect of radiation therapy, chemotherapy on the heart, damage to cardiomyocytes, endocardium and heart valves occurs, the development of myocardial dysfunction and / or heart failure, which is defined as cardiotoxicity. At the same time, determining the risk of cardiotoxicity is often a difficult task, which is due to the different susceptibility of patients to certain drugs, the appointment of combined antitumor therapy, as well as a combination with radiation therapy.

Keywords: diagnostics, treatment, oncology, diseases, therapy, chemotherapy, heart, endocardium, heart valves,

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About Author

Author(s):

MAMUROV OLIMJON ISLOMOVICH

Tashkent institute for advanced training of doctors,

Tashkent, Uzbekistan.

Cardiotoxicity is a term that includes various undesirable cardiovascular events associated with drug therapy for cancer patients. Cardiotoxicity can develop both during chemotherapy and at various times after its completion. Its manifestations are diverse, can proceed without symptoms and be registered only with instrumental examination, or be accompanied by a severe, sometimes life-threatening clinical picture. To systematize the wide range of cardiotoxic effects of chemotherapy, Ewer and Lippman introduced a valid classification based on the presence of structural abnormalities and the degree of functional reversibility of the myocardium. It is known that myocardial cells have limited regenerative capacity and are susceptible to constant or transient exposure to chemotherapeutic agents.

Type I cardiotoxicity is caused by the use of anthracycline antibiotics and is characterized by cumulative, dose-dependent, progressive myocardial damage, which can lead to the development of irreversible chronic congestive heart failure.

Acute cardiotoxicity, manifested in pericarditis-myocarditis syndrome in patients who had not previously had cardiac pathology, can develop at the time of administration or within 24-48 hours. It is characterized by the appearance of changes in electrocardiography and is manifested by an asymptomatic violation of repolarization on electrocardiography, a decrease in the voltage of the complex QRS, the development of sinus tachycardia, the appearance of ventricular and supraventricular extrasystoles, an increase in the QT interval, a decrease in myocardial contractility and a drop in blood pressure. The described changes on electrocardiography are considered reversible, often asymptomatic and regress within 1 month. after the end of chemotherapy.

Subacute cardiotoxicity is rare, but mainly manifests itself as toxic pericarditis and / or myocarditis a few weeks after the last anthracycline antibiotic.

Type II cardiotoxicity is not accompanied by the death of cardiomyocytes, and there are no noticeable structural changes in the myocardium. The risk of developing cardiac dysfunction is independent of dose; changes in the myocardium are reversible and when the drug is discontinued, they usually completely disappear, and rather quickly within 1-3 months. This type of cardiotoxicity is usually associated with the use of targeted drugs. Unlike classical cytostatics, whose action is based on disrupting the cell cycle, targeted therapy drugs target molecular targets, thereby blocking the earlier stages of carcinogenesis. Most targeted drugs do not have the ability to kill or severely damage tumor cells (cytotoxic effect), but only have an inhibitory effect on proliferation and / or stimulate the differentiation of tumor cells by turning off the mechanisms responsible for the formation of a malignant phenotype (cytostatic effect). In this regard, the main effect of their use is not a cure, but a long-term suppression of tumor growth or, at best, a decrease in the tumor mass.

Currently, more and more attention is paid to cardiotoxicity, which develops against the background of antitumor treatment. Achievements of modern oncology are associated with the use of effective combinations of chemotherapeutic drugs and radiation therapy, at the same time, some of the commonly used drugs, as well as radiation therapy in some patients, lead to the development of various complications. With an increase in the life expectancy of patients and the duration of their observation, the number of late complications of anticancer treatment also increases. Some hematological cancers at a certain stage can be completely curable (for example, Hodgkin's lymphoma), with many other

cancers, long-term remissions are achieved (for example, with breast cancer). A situation arises when, with successful treatment of the underlying disease, there is a likelihood of complications of this treatment, including fatalities, both during its implementation and in completely different periods after its termination.

While the main "classic" causes of chronic heart failure (CHF) are ischemic heart disease (postinfarction cardiosclerosis, chronic postinfarction aneurysm), arterial hypertension and their combination, cardiomyopathies (CMF, most often dilated) and myocarditis, increasingly in various recommendations for the diagnosis and treatment of heart failure (HF), it is said about the toxic and radiation effects on the myocardium as its etiological factor.

Anthracycline cardiotoxicity.

To date, a large number of cases of cardiac complications have been described that develop against the background of the administration of anthracycline antibiotics, which is associated with their high antitumor activity, as well as with their widespread use in various schemes of chemotherapeutic treatment. For a long time, there was a hypothesis that the cause of anthracycline cardiomyopathy (ACM) is the formation of an excess of reactive oxygen species (reactive oxygenic formations, ROS) due to the exchange of electrons between the quinone part of anthracycline and oxygen molecules and other electron donors present in cells. Anthracyclines also form complexes with iron, which undergo redox reactions that result in oxygen radicals. And although in vitro studies confirmed an increase in the amount of ROS in cardiomyocytes after the use of anthracycline antibiotics, neither the use of antioxidants nor iron chelators prevented the development of ACMP.

Recently, topoisomerase 2b has been shown to be a key mediator of anthracyclines-induced cardiotoxicity. Topoisomerase of the second type unwinds DNA strands during its replication, transcription, or recombination. In humans, there are 2 types of type 2 isomerase: topoisomerase 2a (Top2a) and topoisomerase 2b (Top 2b). It is believed that Top2a is found predominantly in proliferating cells, is involved in DNA replication, and is the main molecular target of anthracycline antitumor activity. In contrast, Top2b is found in resting cells, including cardiomyocytes. Unfortunately, she is also exposed to anthracycline antibiotics.

Primary prevention of anthracycline cardiotoxicity is based on two strategies:

1. Reducing potential cardiotoxicity: the use of long-term infusion of drugs, the use of liposomal forms, the use of less toxic derivatives (for example, epirubicin or idarubicin).

2. The use of cardioprotective agents: dexrazoxane, beta-blockers, ACE inhibitors, angiotensin II receptor blockers during polychemotherapy.

The prevention of the development of cardiovascular complications during therapy with anthracycline antibiotics is primarily associated with compliance with the recommended doses and duration of infusion. As mentioned above, the cardiotoxicity of doxorubicin is directly related to its total dose, the same can be said about adriamycin: the risk of developing ACMP when administered at a cumulative dose of 550 mg / m2 is 7%; with an increase in the total dose, this risk increases linearly, reaching 50 % (!) at its level of 1000 mg / m2.

The liposomal form of doxorubicin with altered pharmacokinetics, but retained high antitumor activity, is also an attempt to reduce the cardiotoxicity of anthracyclines. This form penetrates more easily into tumor tissues than into healthy ones, including the heart.

However, the high cost of liposomal forms of doxorubicin limits its use. Their use is approved by the FDA for ovarian cancer, HIV-associated Kaposi's sarcoma, multiple myeloma with ineffectiveness of previous therapy.

Currently, only dexrazoxane (ICRF-187, cardioxan) has been approved as a cardioprotective drug that prevents the effects of anthracyclines on the myocardium. This drug is an iron chelating agent. The products of its hydrolysis are capable of chelating free and bound intracellular iron in the myocardium, which leads to a decrease in the amount of iron ions that can form complexes with anthracyclines, thereby reducing the formation of free radicals during redox transformations of anthracycline antibiotics. As shown recently, dextrazoxane changes the configuration of topoisomerase 2 by closing the ATP-binding sites, thus preventing the attachment of anthracycline to it and the formation of the

Top2-anthracycline complex. It also reduces the toxic effects of anthracyclines. The protective effect of dexrazoxane has been proven in many studies.

One study also demonstrated the possibility of reducing the antitumor efficacy of anthracyclines with concomitant use of dexrazoxane, which was then refuted by many other studies. Another undesirable, not fully proven effect of dexrazoxane was the potential risk of secondary malignant diseases. Thus, in one study, it was shown that its addition to the standard therapy of Hodgkin's lymphoma in 8 children after four years led to the occurrence of acute myeloid leukemia or myelodysplastic syndrome (in 6 children), thyroid cancer (in one child), osteosarcoma (1 case). However, two other large studies of the use of dexrazoxane in adolescents and children with acute lymphoblastic leukemia treated with anthracyclines refute this possibility.

For the timely detection of signs of cardiotoxic damage to the cardiovascular system and the appointment of the necessary therapy for patients with malignant diseases, an extended examination and joint observation by oncologists and cardiologists are recommended. The examination of patients must be carried out without fail before the upcoming treatment, during its implementation and for many years after its completion - taking into account the complications developing in the long-term period, the dynamic observation of these patients should actually be lifelong.

Literature

Golubtsov O.Yu., Tyrenko V.V., Lyutov V.V., Maslyakov V.V., Makiev R.G. CARDIOVASCULAR COMPLICATIONS OF ANTITUMOR THERAPY // Modern problems of science and education. - 2017. - No. 2 .;

Source: Gendlin G.E., Emelina E.I., Nikitin I.G., Vasyuk Yu.A. A modern view of the cardiotoxicity of chemotherapy for oncological diseases, including anthracycline antibiotics // RKZh. 2017. No. 3 (143).

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