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Department of Internal Diseases No. 4

Methodological guidelines for conducting practical classes with students of the 6th year of the Faculty of Medicine on the topic "Introduction to cardioncology"

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Guidelines for conducting practical classes

with students of the 6th year of the Faculty of Medicine on the topic:

"Introduction to cardioncology"

The purpose of the lesson: to study the general principles of cardioncology development, to identify changes in the cardiovascular system when using potentially cardiotoxic drugs in oncological patients.with special attention to subclinical signs and symptoms of damage to the cardiovascular system

Motivation for the relevance of the topic:

Currently, oncological diseases are one of the main causes of mortality, second only to cardiovascular diseases. At the same time, modern antitumor therapy, including chemotherapy, radiation therapy, targeted therapy, allows cancer patients to save their lives and social adaptation for decades. However, the use of antitumor therapy is limited due to their side effects, in some cases severe cardiotoxic effects and complications (coronary heart disease, systolic or diastolic

Cardiotoxic drugs used in oncology:

* 1 Anthracycline antibiotics (doxorubicin, epirubicin).

• 2 Alkylating drugs (cyclophosphamide)

• 3 Platinum drugs (cisplatin).

• 4 Pyrimidines (capecetabine, fluorouracil)

• 5 Antimicrotubulin agents (paxlitaxel)

• 6 Targeted drugs (trastuzumab)

• 7 Vascular endothelial growth factor inhibitors (VEGF inhibitors)

and so on…

Mandatory routine examination of the oncopatient includes ECG, EchoCG. Consultation with a cardiologist

Additional examination: Daily monitoring of the Holter ECG. Daily monitoring of blood pressure. Treadmill test. CAG. MRI/CT of the heart and blood vessels (with contrast if necessary). MSCT of the heart, CHPEHOKG. Laboratory cardiomarkers

Cardiotoxic effect of chemo- and targeted drugs

Toxicity in chemotherapy is associated with the mechanism of action of drugs, doses, method of administration and the main risk factors, such as cardiovascular diseases, genetic predisposition, age, etc. Toxic effects may occur immediately or many years after treatment. Concomitant chemotherapy and radiation therapy can mutually potentiate the toxic effect.

Irreversible cytotoxicity or interaction with functional aspects of cardiac cells, primarily non-cytotoxic, can lead to ventricular dysfunction. Various combinations of chemotherapeutic drugs can lead to arrhythmia, arterial hypertension, venous and arterial thromboembolism, ischemia and myocardial infarction.

Clinical signs and symptoms, electrocardiographic changes, instrumental visualization of the heart (mainly left ventricular ejection fraction [LVEF] and assessment of contractility), increased levels of troponin and natriuretic peptide may occur during chichemo and radiation therapy.

There are several strategies for preventing and treating the toxicity of various chemotherapeutic drugs. All of them are based on accurate patient selection, short- and long-term monitoring, as well as treatment methods that can prevent and delay cardiac dysfunction

Possible cardiovascular complications of chemotherapy and/or radiation therapy:

* coronary heart disease (CHD);

* myocardial dysfunction and heart failure (HF);

* valvular pathology;

* arrhythmias — acquired shortened QT syndrome, atrial fibrillation and atrioventricular(AV) blocks;

* arterial hypertension;

* thromboembolic disease;

* peripheral vascular diseases and stroke;

* pulmonary hypertension;

* pericarditis.

Many of these states can develop together and cause a summation effect. Each individual adverse reaction should be evaluated and fully analyzed in order to avoid the progression of the whole picture and maintain the optimal result for each patient taken.

Coronary heart disease (CHD)

Preliminary diagnosis of coronary artery disease in order to correctly choose a treatment regimen for a patient with ZNO requires a thorough clinical assessment based on age, gender, anamnesis and diagnostic tests for ischemia. Pyrimidine analogues may have a high risk and require careful monitoring with constant electrocardiograms (ECGs) throughout the duration of observation. If ischemia is detected, it is necessary to temporarily suspend chemotherapy if there are no alternative methods of treatment.

Radiation therapy can also be the cause of the development of coronary heart disease. Sudden death or progressive angina can be a manifestation of the disease. Patients with progressive coronary artery disease are recommended to undergo long - term follow - up with the help of tests for induction of ischemia even several years after the end of therapy with ZNO .

Myocardial dysfunction and heart failure

Myocardial dysfunction can be caused by cell necrosis (type I toxicity), due to the toxic effect of a chemotherapeutic drug, which leads to permanent damage to the heart or cell dysfunction, mainly by biological drugs (type II toxicity).

Risk factors for cardiotoxicity in anthracycline therapy are: 1) cumulative dose, 2) female, 3) age > 65 years or < 18 years, 4) renal insufficiency, 5) pre-existing heart diseases, 6) arterial hypertension, 7) genetic factors, 8) concomitant or previous radiotherapy involving the heart and / or concomitant or chemotherapeutic therapy with the introduction of alkylating agents and especially immunotherapy and targeted therapy.

Early detection of ventricular dysfunction should be carried out by evaluating LVL before and periodically during chemotherapy. Two-dimensional (2D) and three-dimensional (3D) echocardiography and assessment of myocardial contraction, as well as other imaging methods and biomarkers can be used. It is recommended to use the same method with good quality, possibly by the same operator, during the entire observation period to avoid variability of results between tests.

If the LVL is within the normal range before the course, then a re-evaluation should be carried out every four cycles of chemotherapy. LVLF less than 50% and a decrease in LVLF by more than 10%, but not below the lower limits, is a manifestation of current It is a manifestation of toxicity and requires repeated short-term evaluation during and shortly after chemotherapy. A decrease in LVL of less than 10% below the lower limit of the norm indicates the need to start ACE-Is(or ARB) therapy+beta-adrenoblocker to prevent further LV dysfunction. The same drugs are recommended for asymptomatic LV dysfunction or symptomatic heart failure .

Valvular pathology

The most common cause of coronary heart disease in cancer patients is radiation therapy (up to 10% of treated patients) with fibrosis and calcification of the aortic root, aortic valve flaps, mitral valve rings, as well as the base and middle part of the mitral valve flaps. 2D and 3D echocardiography are the methods of choice for determining further treatment tactics for such patients.

Many complications of radiation therapy (mediastinal fibrosis, impaired wound healing and related coronary artery disease, myocarditis and pericarditis) can complicate open surgical interventions, if necessary. In such cases, transcatheter valve implantation may be the method of choice for the treatment of aortic stenosis, while CABG using the intra-thoracic artery may be technically impossible.

Arrhythmias

An ECG in 12 standard leads with the determination of the QT interval is required in all patients before chemotherapy and radiation therapy as a basic diagnosis.

Repeated ECGs should be performed mainly in patients with a history of QT interval shortening, organic heart disease and other factors, affecting QT. QT > 500 msec. Is the threshold for stopping treatment. Also, the increase in QT is > 60 msec. Or the appearance of arrhythmias requires discontinuation of therapy. It is recommended to avoid conditions (hypokalemia, extreme bradycardia and other prolonging QT drugs) that potentially cause an atypical form of torsades de pointes.

An important problem is the occurrence of atrial fibrillation, (mainly after ibrutinib therapy) difficult to correct. In addition, there are concomitant problems of thromboembolism prevention, with the use of new oral anticoagulants (POAC).

Some chemotherapeutic drugs and radiation therapy have a toxic effect on the conduction system of the heart with the occurrence of bradyarrhythmias requiring temporary or permanent interruption or modification of therapy and/or implantation of a pacemaker.

Arterial hypertension

Careful monitoring of blood pressure before starting chemotherapy is mandatory. Periodic monitoring of blood pressure (BP) should be carried out in every patient who has undergone chemotherapy. Treatment of hypertension should be carried out in accordance with current recommendations. To avoid cardiovascular complications, early and aggressive antihypertensive treatment is mandatory. ACE inhibitors and dihydropyridine-calcium channel blockers are preferred agents, while the use of non-dihydropyridine channel blockers should be avoided due to possible adverse drug interactions. If blood pressure is not corrected, therapy should be intensified. In case of failure, VEGF inhibitors should be reduced or discontinued. After blood pressure stabilizes , the use of VEGF can be resumed .

Thromboembolic disease

Risk factors for the development of venous thromboembolism associated with ZNO are:1) primary cancer (pancreas, brain, stomach, kidney, lung, lymphoma, myeloma), 2) histological type of tumor (especially adenocarcinoma), 3) the presence of metastatic foci and 4) late stage of ZNO.

The factors associated with the patient are: 1) old age, 2) female, 3) African race, 4) concomitant diseases - infection, chronic kidney disease, pulmonary diseases, thrombotic diseases, obesity, 5) venous thromboembolism or hereditary thrombophilia and 6) a state of inactivity.

The factors associated with treatment are: 1) volumetric surgery, 2) prolonged bed rest, 3) chemotherapy with antiangiogenic drugs, 4) hormone therapy, 5) a history of blood transfusion, 6) installed central venous catheters.

Thromboprophylaxis is performed in all patients hospitalized for cancer, although recent meta-analyses have not been able to identify ways to increase the effectiveness or reduce the risk of this therapy. Low molecular weight heparin (NMH) can cause thrombocytopenia, which does not disappear with the use of a vitamin K antagonist. Recently, the use of POAC seems safe and effective for the prevention of thromboembolism in cancer patients.

Peripheral vascular diseases and stroke

Even in the absence of risk factors for the development of cardiovascular diseases, severe peripheral artery disease can be observed in 30% of patients treated with many chemotherapy drugs (nilotinib, ponatinibil and tyrosine kinase inhibitors BCR-ABL used in chronic myeloid leukemia). Peripheral artery damage may occur in the first months of therapy or after several years. In addition, the use of chemotherapy can provoke the occurrence of Raynaud's syndrome and and it is of the ischemic type. The risk of stroke at least doubles after radiation therapy for mediastinal, cervical or brain cancer. Intracranial aneurysms are also detected after radiation therapy. Similar changes can also occur in the aorta .

Pericarditis

Some chemotherapeutic drugs (mainly anthracyclines) can lead to acute pericarditis, however, this is not typical after radiation therapy is usually associated with pericardial or mediastinal tumors. Acute pericarditis with typical chest pain, fever, ST-T changes and large effusions, even leading to tamponade, can develop 2-145 months after chest radiation therapy, with an absolute cumulative frequency of 2-5%. Echocardiography is the main diagnostic method. Treatment of effusion pericarditis consists of the appointment of nonsteroidal anti-inflammatory drugs and colchicine. Pericardiocentesis may be required with significant volumes of fluid .

Exudative pericarditis

In patients with ZNO, pleural effusion usually occurs due to the underlying disease, heart failure, infections or other causes. Some cancer medications (for example, dasatinib and imatinib) can cause fluid retention or reversible pleural effusion.

Autonomic dysfunction

Damage to the conduction system of the heart can be observed after radiation therapy to the chest area and is manifested by sympathovagal imbalance and sinus tachycardia, heart rate variability and a decrease in the thresholdexcitability. A higher pain threshold or minor ischemia may develop in patients who are in remission after specific treatment.

Pulmonary hypertension

Precapillary pulmonary hypertension is a rare complication of some anticancer drugs. This condition is often reversible after discontinuation of the drug or replacement with another drug. Recently, cyclophosphamide and other alkylating agents have been considered as the cause of the development of severe pulmonary veno-occlusive hypertension, which is poorly amenable to pharmacological therapy.

Standard echocardiographic evaluation, including the search for signs of right ventricular overload, should be performed in each patient on program chemotherapy, which can cause pulmonary hypertension (dasatinib). Patients with initial elevated pulmonary artery pressure need a cardiological assessment of their etiology, especially in the case of LV dysfunction or chronic thromboembolic pulmonary hypertension, as this may affect the strategy of cancer treatment.

One of the solutions to improve the effectiveness of treatment of such a severe group of patients is the creation of specialized cardioncological teams built on the principle of multidisciplinary

Tasks of the cardioncological team:

1) Before the treatment of a malignant neoplasm

Prevention of cardiovascular complications in patients who are planned for antitumor therapy, with an assessment of the cardiovascular risk profile and physical examination in order to detect cardiovascular diseases, hypertension and dysfunction. Such a diagnosis can help in choosing the appropriate therapy is mandatory for cancer with a good prognosis, when cured patients have a favorable prognosis for the duration and quality of life. Accordingly, it is necessary to determine the optimal frequency of monitoring and evaluate the interaction of

antitumor drugs with previously prescribed cardiological drugs, as well as the features of the use of drugs such as antiplatelet agents and anticoagulants.Interdisciplinary interaction of an oncologist and a cardiologist to ensure the most effective treatment of ZNO with minimal impact on the cardiovascular system.

2) During the treatment of a malignant neoplasm.

Early detection and treatment with careful monitoring of symptoms/signs of cardiovascular complications in order to differentiate the symptoms associated with ZNO from other cardiac symptoms. The dilemma is the balance between In continuation and discontinuation of anticancer therapy, and whether cancer or cardiovascular disease is the main threat to patients.

3) After a course of treatment of a malignant neoplasm

Control of late cardiovascular events in patients after a course of chemotherapy and radiation therapy. However, this is the most difficult function to implement in practice, since the harmful effects of both systemic chemotherapy and radiation therapy can manifest themselves years and decades later.

Cardioncology is a relatively new and promising area at the intersection of cardiology and oncology. Its relevance is due to the large number of comorbid patients combining oncological and cardiovascular diseases. The existing system of oncological care in the Russian Federation allows you to organize monitoring of cardiovascular complications of the treatment of the underlying disease, even in the long term, through systematic follow-up in primary oncology booths working in all major municipalities of the region of the Russian Federation. The organization of the cardioncological service allows solving complex clinical cases. Taking into account the cardiotoxicity of many antitumor drugs, earlier detection of cardiovascular risk factors makes it possible to choose the optimal and safest treatment regimen. Consultation with a cardiologist is necessary before and for a long time after receiving antitumor therapy.

Security questions.

1. Cardiovascular complications of antitumor therapy: diagnosis, prevention, treatment, cardiological monitoring on the background of chemotherapy.

2 General information on cardiotoxicity of antitumor drugs

3 Cardiomyopathy and heart failure associated with chemotherapy

4 Coronary complications of chemotherapy

5 Cardiac arrhythmias associated with chemotherapy

6 Arterial hypertension associated with chemotherapy

7 Cardiac complications of radiation therapy

8 Approaches to comorbid cardiovascular pathology in an oncological patient.

9 Atrial fibrillation/flutter in an oncological patient, prevention of thromboembolic complications"

10.Ischemic heart disease in an oncological patient

11 Pulmonary embolism and/or venous thrombosis in an oncological patient: prevention and treatment

12. Pericarditis in cancer patients

13 Monitoring of cardiac complications in the long-term period after the end of antitumor