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CHANGES IN THE MYOCARD DURING CHEMOTHERAPY WITH INTRAVENOUS BLEOMYCIN IN TESTIC CANCER: A CLINICAL CASE

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Abstract

The study was aimed to assess the impact of bleomycine on the myocard.

The clinical case is presented by the male patient I. (DOB: 1978), receiveing bleomycine for testic cancer. The ultrasound echocardioscopic tests were out on the Imagic Agile (USA) apparatus. Scintigraphy with the early (30 min) and delayed uptake of Tc99 by the myocardium (3 hours) were assessed as well. MRI of the heart was conducted on Siemens Avanto 1.5T MRI scanner. Philips intellispace Portal 9.0 Cardiac Analyzis package was used for the assessment of functional parameters.

Subclinical changes in the myocardium were detected after the administration of bleomycine. Thus its cardiotoxicity could be underestimated.

All human studies were conducted in compliance with the rules of the Helsinki Declaration of the World Medical Association "Ethical principles of medical research with human participation as an object of study". Informed consent was obtained from all participants.

Keywords: *bleomycine, cardiotoxicity, clinical monitoring, clinical case*

Introduction

Extensive use of various chemotherapy regimens in the treatment of patients with Hodgkin's lymphoma, testicular and ovarian, skin, lung, thyroid cancer; malignant lymphomas (non-Hodgkin's tumors); reticulosarcoma; cancer of the penis and female external genital organs, cervical cancer makes it possible to increase the life expectancy of patients, improve their life quality, thereby improving the prognosis. In most schemes with the above-described oncological pathology, the drug bleomycin is used [1].

Bleomycin is an anti-tumor antibiotic, which is an A2-fraction isolated from a culture of *Streptomyces verticillus*. Among the known side effects of bleomycin, in the first place, there is a toxic effect on lung tissue with the development of pulmonary fibrosis, pleurisy with pain syndrome, increasing respiratory failure; rarely - toxic effects on blood vessels, including cerebral arteritis, stroke, myocardial infarction, thrombotic microangiopathy, Raynaud's syndrome. At the same time, not much is known about the toxic effect on the myocardium, especially with intravenous administration of the drug, and the dynamics of the cumulative effect of the drug has not been studied. Determination of functional morphological changes by EchoS allows early detection of systolic and diastolic dysfunction of the left and right ventricles, violations of the volume and size of the right and left heart [8].

The study was aimed to assess the impact of bleomycine on the myocard.

Methods

The clinical case is presented by the male patient I. (DOB: 1978), receiveing bleomycine for testic cancer. The ultrasound echocardioscopic tests were out on the Imagic Agile (USA) apparatus. Scintigraphy with the early (30 min) and delayed uptake of Tc99 by the myocardium (3 hours) were assessed as well. MRI of the heart was conducted on Siemens Avanto 1.5T MRI scanner. Philips intellispace Portal 9.0 Cardiac Analyzes package was used for the assessment of functional parameters.

Results

We observed patient Igor V., born in 1978, who underwent chemotherapy with bleomycin. Upon receipt of a complaint about the underlying disease, there were no complaints from the cardiovascular system, with an objective examination - blood pressure 120/70 mm Hg, heart rate 70 per 1 min., no peripheral edemas. ECG, echocardiography within normal limits. After the surgical treatment, the patient was prescribed a course of chemotherapy according to the BEP scheme (bleomycin 30mg on day 1,3,5, cisplatin on days 1-5, etoposide 200mg on days 1-5. Before the first course of chemotherapy, the patient underwent an ECG, echocardiography. Monitoring of cardiotoxicity, before the second and third courses of chemotherapy was performed as well. According to the ECG, changes in intervals and teeth were not observed in dynamics. In dynamic observation of Echocardiography data (before the second and third courses of chemotherapy), there was a decrease in the rate of contraction of the walls of the left ventricle (total and septal according to tissue Doppler data), a decrease in the left ventricular ejection fraction, an increase in the Tei, IVRT, DecTime index from the primary parameters.

In connection with the above changes, to clarify the degree of cardiotoxicity, and taking into account the discrepancy in the parameters obtained with echocardioscopy and indicators obtained with MRI the patient was scheduled for cardiac MRI and Tc99 scintiography (MIBI). Evaluation of the right ventricular ejection fraction was calculated in relation to the area of the right ventricle during systole to the area of the right ventricle during diastole (FAC - Fractional Area Change). The right ventricular ejection fraction should normally be more than 44%.

According to MRI data, there was a decrease in the right ventricular ejection fraction, stroke volume, and cardiac output - in patient V. it was 33%. The accumulation of MIBI by the left ventricular myocardium after 30 and 180 minutes is normally 30 ± 4 U. According to the scintigraphy data, the passive absorption of MIBI by the myocardium in the patient was 52 U (Fig. 1).

Thus, the functional disorders of the heart revealed by the EchoCS, MRI of the heart and myocardial scintigraphy in the patient confirm the data obtained us earlier under experimental conditions [7] and suggest the toxic effect of the drug bleomycin both on the left ventricle and on the

right ventricle, and damage to the right ventricle occurs primarily, which may be due to the direct toxic effect of the drug when administered intravenously.

Right ventricular dysfunction plays an important role in morbidity and mortality in people with cardiopulmonary disease. It is believed that structural, functional and geometric changes in the right heart can determine the severity of manifestations of chronic heart failure in patients with ischemic heart disease and other diseases. Decompensation of the right ventricle can manifest itself as a decrease in global and local contractility, a change in geometric parameters [9]. It is also known that chronic left ventricular failure can develop rather slowly over many years. But at the stage of decompensation of the right ventricle, it becomes refractory to therapy and portends an extremely unfavorable prognosis [10].

Conclusions

1. In this clinical case, for the first time, functional changes in the right ventricle were revealed during intravenous administration of bleomycin (in dynamics).

2. A decrease in the left ventricular ejection fraction, a decrease in myocardial velocities in the zone of syncintial branching, the formation of early diastolic dysfunction, a violation of the echo density of the myocardium in the septal, posterior-basal parts of the myocardium, the formation of hypokinesis zones in this area are evidence of the cardiotoxic effect of bleomycin with a pronounced cumulative effect.

3. The cardiotoxic effect of bleomycin (with a total dose of bleomycin 270 mg (SOD Bl 270 mg)) has no subjective (patient complaints, rhythm disturbances, decreased exercise tolerance and objective manifestations (changes in hemodynamics, edema of the lower extremities, changes in the size of the heart, changes in the ECG) changes on the part of biochemical blood tests, general blood count).

4. Repeated administration of bleomycin has a cumulative cardiotoxic effect leading to changes in the myocardium and endothelial dysfunction clinically not manifested in the early stages and detected by instrumental methods.

5. In myocardium Tc99, changes were noted indicating the toxicity of bleomycin to the myocardium (a decrease in the ejection fraction of the left and right ventricles, stroke volume of the right ventricle, a decrease in the minute systolic ejection, an increase in the accumulation of the radioisotope Tc99 by the myocardium and the dynamics of its excretion). icina180mg) the cardiotoxic effect of bleomycin is confirmed by echocardiography.

6. Side toxic effects of the drug require further research and consideration of measures for the prevention and treatment of cardio- and endothelial toxicity in a patients taking chemotherapy regimens with Bleomycin.

7. Early detection of right ventricular dysfunction makes it possible to prevent the development of left ventricular systolic dysfunction and the formation of chronic heart failure in the early stages.

Acknowledgments

The authors declare that there are no conflicts of interest.

References

1. Vatutin NT, Ketting EV, Kalinkina NV etc. Histopathological changes of a rat myocardium at chronic influence of anthracycline antibiotics. / Proceedings of the III National Congress of Rheumatologists of Ukraine. - Dnipropetrovsk, October 23-26, 2001 // Ukr. rheumatol. magazine. 2001. - Appendix. - P. 54. (6) (in Ukrainian)
2. Keting E.V., Kalinkina N.V. Histopathological changes in rat myocardium under acute exposure to anthracycline antibiotics // III Ukrainian Conference of Young Scientists, dedicated to the memory of Academician VV Frolkis. Abstracts (January 28, 2002, Kyiv). – P. 86. (10) (in Russian)
3. V.B. Simonenko, S.A. Boytsov, A.A. Glukhov Apoptosis and myocardial pathology // Clinical Medicine № 8 — 2000. — P. 12-16. (in Russian)
4. Guidelines for the chemotherapy of tumor diseases, edited by N.I. Translator. // "Practical Medicine". - Moscow 2013. — P. 435- 436. (in Russian)
5. Meinardi MT, van der Graaf WT, van Veldhuisen DJ, et al. Detection of anthracycline-induced

cardiotoxicity. // Cancer Treat Rev 1999; 25: 237-47
6. Altena R, Perik PJ, van Veldhuisen DJ, de Vries EG, Gietema JA. Cardiovascular toxicity caused by cancer treatment: strategies for early detection. Lancet Oncol. 2009 Apr;10(4):391-9. doi: 10.1016/S1470-2045(09)70042-7. PMID: 19341970.
7. "Method for detecting cardiotoxic properties of the drug bleomycin in an experiment" Patent for utility model UA 103638. Bestanchuk OM, Godovan VV, Zakharova VP, Kashchenko OA, Narbutova TE (in Ukrainian)
8. Lytkina V.S., Matyushin V., Kuzhel D.A. Modern approaches to assessing the function of the right ventricle // Siberian Medical Review, 2014,2. – P. 52- 57. (in Russian)
9. I. V. Koksheneva Dysfunction of the myocardium of the right ventricle: structural and functional features and clinical significance in patients with ischemic heart disease of cardiac surgery profile: author. dis. ... Doctor of Medical Sciences. — M., 2007.-47 p. (in Russian)
10. Rydnn L., Remme W.J. Treatment of congestive heart failure; has the tirrie come for decreased complexity?//Eur.Heart J. — 1999 — Vol.20. — P.867-871.

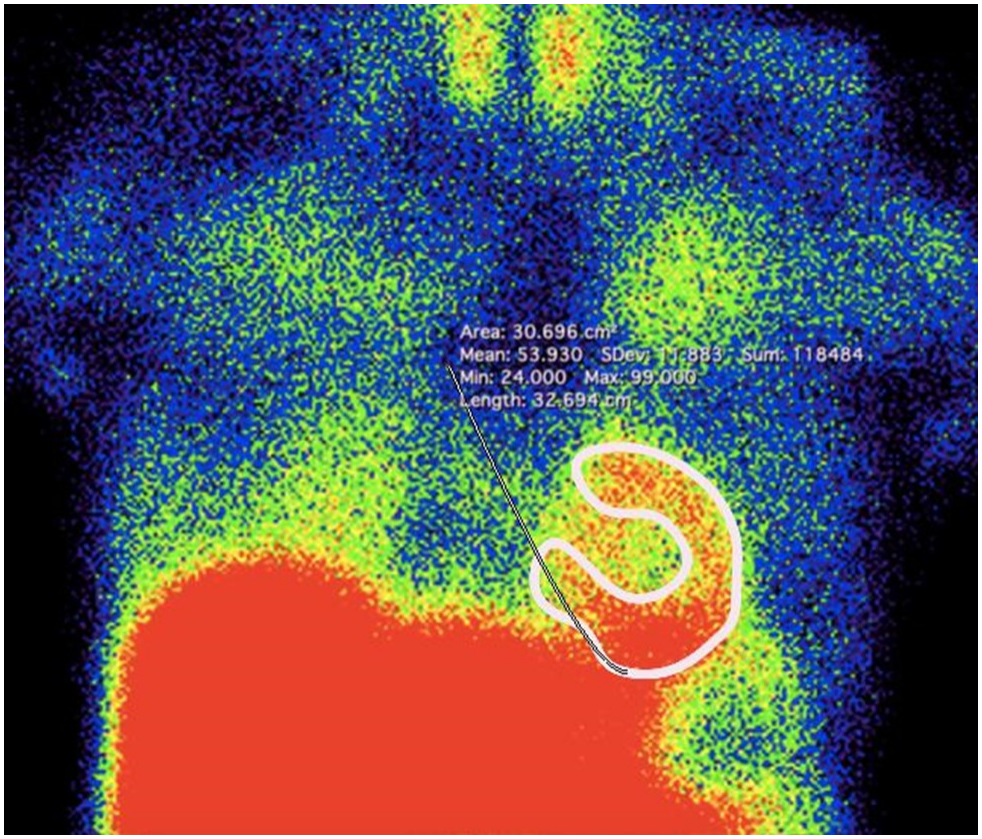

Figure 1. Scintigraphy of heart