https://doi.org/10.23873/2074-0506-2024-16-2-219-229

Simultaneous visualization of changes in perfusion and myocardial function of a transplanted heart in emergency cardiology

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Abstract

Introduction. *In conditions of the Emergency Cardiology Department, a timely and differential diagnosis of myocardial pathology is especially important in the absence of visible focal changes and significant coronary artery stenosis. This group of patients includes recipients of a transplanted heart, when it is difficult to count on the high sensitivity of perfusion images alone. This can be explained by the diffuse, balanced distribution of ischemia.*

Objective. *To present the possibilities of perfusion myocardial single photon emission computed tomography synchronized with*

electrocardiography for a detailed assessment of the functional condition of both ventricles of the transplanted heart

Material and methods*. We have presented three clinical case reports of the patients with different pathology of the transplanted heart who referred themselves to the emergency cardiology clinic and underwent electrocardiography-synchronized perfusion myocardial single photon emission computed tomography for diagnostic purposes.*

Results. *In all the cases presented, the radionuclide study influenced making the diagnosis and changing the treatment tactics. In the first case, it was possible to identify focal myocardial changes, for which coronary angiography and percutaneous coronary intervention with thromboextraction were immediately performed. In the second case, the image analysis reflecting the function of the myocardium (polar maps of wall movement and systolic thickening) allowed us to note a low efficacy of treatment for the transplanted heart rejection. In the third clinical case, the initial single photon emission computed tomography suggested the inflammatory nature of changes in the myocardium, which was verified by the results of endomyocardial biopsy.*

Conclusion. *In the presented clinical cases, the urgently performed electrocardiography-synchronized perfusion myocardial single photon emission computed tomography made it possible to perform invasive interventions in time and thereby contribute to the recovery of the graft functional state and patient's condition improvement.*

Keywords: transplanted heart disease, myocardial perfusion single photon emission computed tomography, myocardial perfusion and function in transplanted hearts

Conflict of interest. The authors declare no conflict of interest

Financing The study was performed without external funding

For citation: Ostroumov EN, Migunova EV, Vovchenko EV, Nefedova GA, Spasskiy AA, Shemakin SYu, et al. Simultaneous visualization of changes in perfusion and myocardial function of a transplanted heart in emergency cardiology. *Transplantologiya. The Russian Journal of Transplantation.* 2024;16(2):219–229. (In Russ.). https://doi.org/10.23873/2074-0506-2024-16-2-219-229

AV, aortic valve
CA, circumflex artery
CB, circumflex branch
ECG, electrocardiogram / electrocardiogrpahy
EchoCG, echocardiography
ECS, electrical pacemaker
EDD, end diastolic dimension
EDV, end diastolic volume
EF, ejection fraction
EOS, electrical axis of the heart
ESD, end systolic dimension
ESV, end systolic volume
HR, heart rate
IVS, interventricular septum
LA, left atrium
LAD, left anterior descending artery
LCA, left coronary artery
LV, left ventricle
LVPWTh, left ventricle posterior wall thickness
MV, mitral valve
n/s, no specific findings
OMA, obtuse marginal artery
PCI, percutaneous coronary intervention
RA, right atrium
RBB, right His bundle branch
RCA, right coronary artery
RV, right ventricle
SPECT, single photon emission computed tomography
THCAD, transplanted heart coronary artery disease
TV, tricuspid valve

Introduction

The donor heart functioning after transplantation is inevitably influenced by both many pre-existing factors that affect the physiological

state of the transplanted organ (hypoxic damage to the graft in the donor's body, ischemic and low-temperature damage during preservation, specific features of the surgical technique for harvesting the donor heart, dependence on the transplantation method, etc.), and the impact on histocompatibility factors that can cause various graft dysfunctions (acute rejection, the transplanted heart coronary artery disease (THCAD, etc.)

Therefore, the main goal of all activities performed at each stage of heart transplantation is the timely diagnosis of possible dysfunctions of the transplanted heart and the restoration of adequate physiological interaction between the transplanted organ and the recipient's body, which determines the satisfactory functioning of the transplanted heart and, accordingly, the patient's life expectancy.

The diagnostic potential of perfusion single photon emission computed tomography (SPECT) for detecting, THCAD alone has shown varying sensitivity and specificity, ranging from 14–90% to 33–98% across patient populations and methods for detecting THCAD [1]. In this case, the authors analyzed, as a rule, only the distribution of perfusion in myocardium, while synchronization with electrocardiography (ECG) makes it possible to evaluate the myocardial function, as well. The potential of SPECT imaging to assess the myocardial perfusion for detecting the cardiac graft pathology has been currently most often studied by using stress tests. In this case, the authors analyze, as a rule, only the distribution of perfusion in the myocardium, comparing the study data at rest and after exercise [2, 3]. Meanwhile, for about a quarter of a century, the method of the perfusion SPECT synchronized with the ECG has been developed in cardiology, which allows both to assess changes in the left ventricle (LV) and right ventricle (RV) volumes, their ejection fraction (EF), diastolic function and ejection velocity parameters, and also to obtain images of motion, systolic thickening and the

asynchrony of the myocardium of both ventricles by segments and in digital values [4]. This is especially important during urgent repeated visits of patients to the emergency cardiology clinic.

In this article we present three clinical cases reports to share our practical experience in the Nuclear Medicine Diagnostic Department.

Case Report No. 1

Patient Yu., 65 years old, was admitted with complaints of general weakness, shortness of breath on exertion, and cough with sputum. From the medical history it was known that 2.5 years ago he underwent orthotopic heart transplantation and a pacemaker implantation. The postoperative period was uneventful, and the patient was followed-up on an outpatient basis. On admission, a number of studies were urgently performed: ECG, echocardiography (EchoCG) and myocardial perfusion SPECT.

At performing an ECG, the rhythm of an electrical pacemaker (PAC) was recorded with stimulation of the ventricles with a heart rate (HR) of 90 beats/min. With the pacemaker functioning, it is difficult to judge ischemic damage to the myocardium. Generally, ST segment assessment is difficult due to ventricular pacing.

When performing EchoCG, the following data were obtained:

Aorta 3.0 см. Left atrium (LA) 4.2 cm. RV 2.3cm. LV using the "S-L" formula: end-diastolic dimension (EDD)is 5.2 cm; end systolic dimension (ESD) is 3.6 cm; end-diastolic volume (EDV) 133 ml, end-systolic volume (ESV) 76 mm, EF 43%, stroke volume (SV) 57 ml. The thickness of the anterior wall of the RV is 1.1 cm, the right atrium (RA) is 5.8×4.3 cm. The interventricular septum thickness (IVSTh) is 1.5 cm. The posterior wall thickness is 1.4 cm.

Local contractility of the LV: dyskinesia of the IVS, hypokinesis of the LV apex segments. Aortic valve (AV): thickened, grade 0-1

regurgitation, mitral valve (MV): walls are thickened, grade 0-1 regurgitation. Tricuspid valve (TV): without specific findings (n/s), grade 0-1 regurgitation. Pulmonary artery pressure: 32 (syst.) mm Hg.

SPECT data synchronized with ECG were compared with the results of the previous investigation performed in the early post-transplantation period (Fig. 1). The figure shows (sequentially from left to right) the maps of perfusion distribution, wall motion, systolic thickening, and phase images. Top row (A): after transplantation, bottom row (B): upon re-admission. The arrows indicate (from left to right) the perfusion defect that has appeared in the anterior wall, the expansion of the hypoakinesis zone in the anteroseptal region. The greatest changes were detected in the LV anterior wall manifested in a decrease in systolic thickening and the appearance of a pathological asynchrony focus.

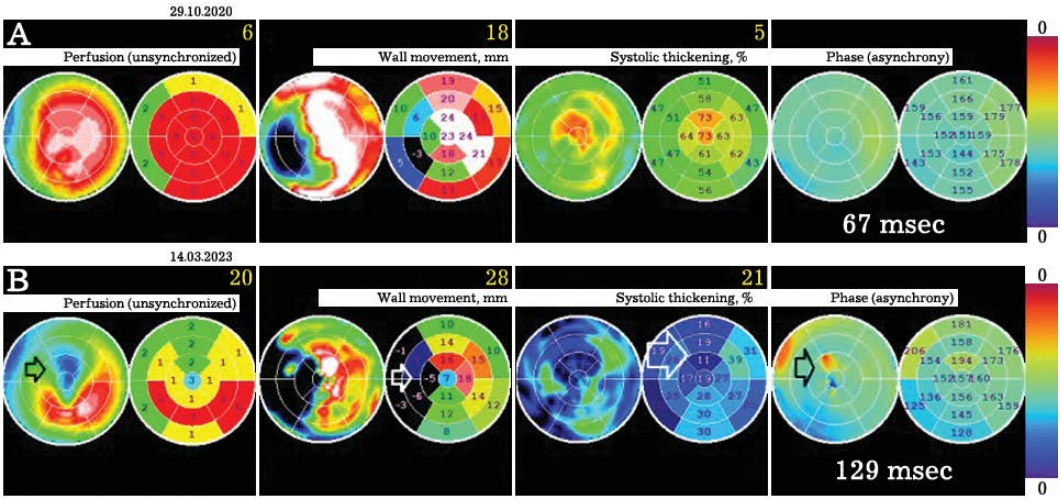

Fig. 1A-B. The results of perfusion myocardial SPECT performed on the 15th day after transplantation (A) and 29 months later (B)

When comparing the study results, the attention was paid to the increase in EDV from 100 to 150 ml, as well as the appearance of a zone of deep decrease in perfusion, akinesia and compact pathological

asynchrony in the anterior wall, which are the scintigraphic signs of the anterior wall ischemia.

Before coronary angiography, the pacemaker was turned off and the ECG showed sinus rhythm with a heart rate of 65 beats/min with the signs of a complete left bundle anterior branch block and ST segment elevation in V3-V6, indicating focal changes in the myocardium in the apex area, along the anterior, anteroseptal, and lateral LV walls.

Given the results of the studies, the patient urgently underwent coronary angiography, which revealed a multiple vessel damage: the trunk of the left coronary artery (LCA) was typically located, without significant changes. Anterior interventricular branch (LAD): occlusion in the proximal third without restoring the blood flow in the distal channel. CA: stenosis in the proximal third from the orifice up to 90% with transition to the orifice of the obtuse marginal artery (OMA) up to 75%. There were no significant changes in the right coronary artery (RCA) (Fig. 2 A).

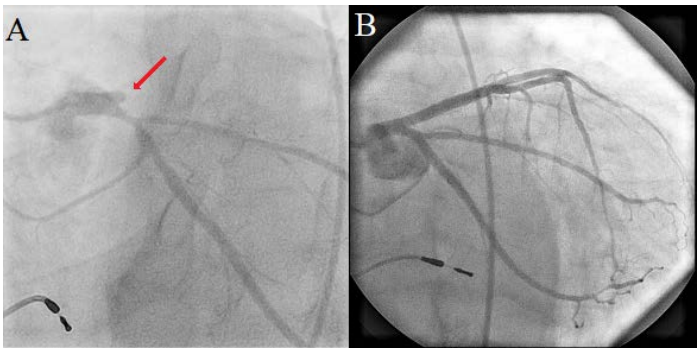

Fig. 2. Selective coronary angiogram of the left coronary artery before (A) and after (B) restoration of blood flow.

Percutaneous intervention and manual thrombus aspiration were performed simultaneously at the LAD ostium and proximal part with stenting the LAD, OMA and circumflex branch (Fig. 2B).

According to the histological examination results, the pronounced activation and proliferation of the endothelium was revealed in the vessels of the microvasculature (Fig. 3A) with occasional complete obliteration of the lumens; there were polynuclear leukocytes in the lumen of individual sinusoids and arterioles (Fig. 3 B). There is a rare infiltration of leukocytes in the interstitium.

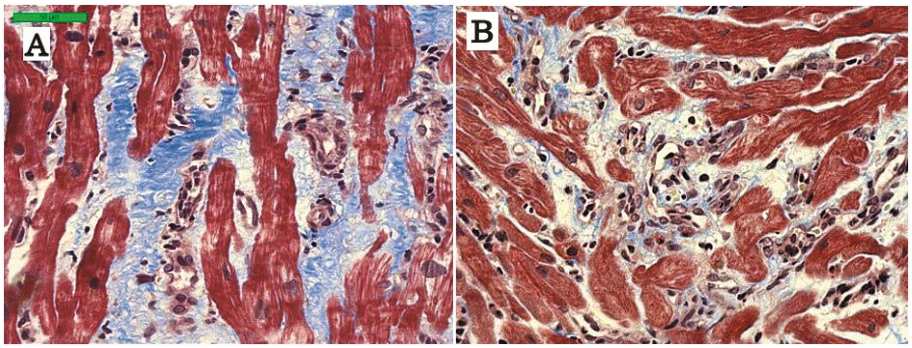

Fig. 3. A-B. Histological section of the myocardium in patient Yu. In all fragments, there is diffuse focal interstitial sclerosis, pronounced cardiomyocyte dystrophy. Interstitial edema. Staining with hematoxylin and eosin, ×400

At polymerase chain reactions for virus Epstein–Barr RNA, there were identified 8 copies/$1*10^5$ cells

Thus, according to the results of pathology and immunohistochemistry assays, a chronic rejection of the transplanted heart was revealed in combination with acute viral myocarditis.

Case Report No. 2

Patient Sh., 61 years old, was admitted with complaints of shortness of breath on minimal exertion. It was known that 3.5 years ago he underwent an orthotopic heart transplant. On examination, the general condition is moderately severe. Breathing is vesicular, respiratory rate at

rest is 17/min, there are no rales. On auscultation, heart sounds are muffled, no murmurs are heard. The heart beat is regular, heart rate is 97 beats/min, no pulse deficit is detected. Blood pressure (BP) is 100/70 mmHg. The ECG shows sinus rhythm, heart rate 79 beats/min. The electrical axis of the heart (EAH) is deviated to the left. Complete right bundle branch block (QRS=152 ms), low QRS voltage in standard limb leads, negative T wave in V1-V5.

When performing transthoracic EchoCG, moderate changes were revealed in AV, MV, and TV, the valve leaflets being hardened, regurgitation of the 1st degree. *Midsystolic pressure gradient was 5 mm Hg. LA 30 mm, volume 40 ml; LV: EDD 3.9 cm, EDV 65 ml, EF 61%, ESD 2.6 cm, EDV 25 ml. RA volume 36 ml, RV volume 2.7 cm. Estimated systolic pressure in the RV 27 was mmHg. The IVS thickness was 1.05 cm, the left ventricle posterior wall thickness (LVPWTh) was 1.0 cm. Heart cavities were not dilated. LV global and regional systolic functions were preserved, LV EF was 61% (Simpson). Diastolic function is not impaired. Regurgitation of grade I on AV, grade I on MV, grade I on TV. The mean pulmonary artery pressure was 27 mm Hg. The LV myocardium local contractility was not impaired.*

Myocardial perfusion SPECT visualizes a non-enlarged LV myocardium with a diffused decrease in the diaphragmatic wall perfusion, a zone of moderate hypokinesis in the anterior apical sections extending to the IVS and the diaphragmatic wall (Fig. 4A). Diastolic dysfunction was of the restriction type. LV EF = 80% (Fig. 5).

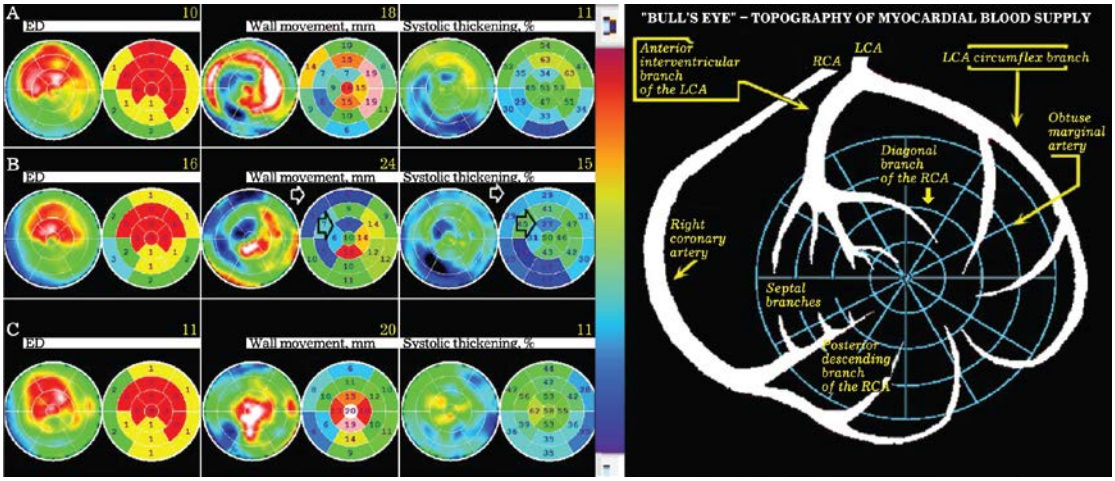

Fig. 4 A-C. Polar maps of patient Sh. Left ventricular myocardium before treatment (A), after treatment (B), after stenting (C).

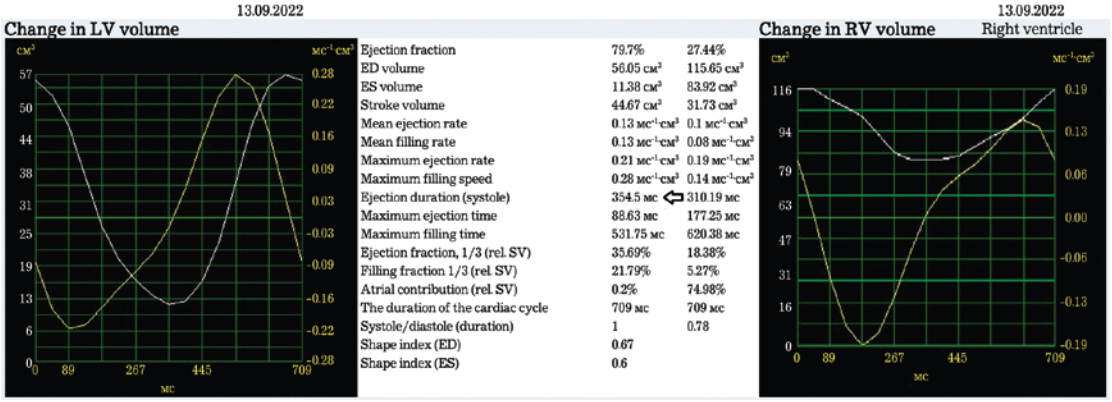

Fig. 5. Volumetric and temporal parameters of ventriculogram in patient Sh.

RV was not enlarged. Diastolic dysfunction was of elasticity disorder type. Intraventricular pathological asynchrony was up to 250 ms. Mitochondrial function is impaired mainly in the area of the apex and anterior wall (the percentage of washout Tc99m-MIBI in 4 hours) making 38% and 33%, respectively, the acceptable EC level is ≤23%). RV EF = 28%. Interventricular asynchrony = 44 ms. The right ventricle was the first to reach the terminal systole.

The selective coronary angiography demonstrated the coronary blood supply from the right coronary artery. The LCA trunk is ordinary

developed, unchanged. LAD is 75% stenotic in the middle third. Diagonal artery has 1 occlusion in the middle third, DA has 2 ostial stenosis 75%. CB is of uneven contours, without hemodynamically significant stenoses. OMA has uneven contours, without hemodynamically significant stenoses. RCA is of uneven contours, without hemodynamically significant stenoses (Fig. 6).

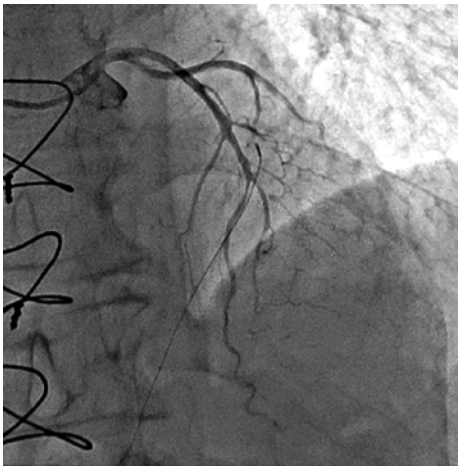

Fig. 6. Selective coronary angiogram of the left coronary artery of patient Sh.

In this case, we can talk about the stenosis significance for the blood supply zone, as well as consider the prospects of percutaneous coronary intervention (PCI).

Taking into account the data of the studies performed, the anti-inflammatory therapy with Solumedrol at a dose of 1000 mg for 3 days was prescribed, as well as the immunomodulation therapy (human immunoglobulin 100 ml for 2 days), and the detoxification (plasmapheresis). To assess the treatment effect, a 6-minute walk test was performed, which showed the result of 180 m.

To assess the dynamics of parameters in the course of treatment, the radionuclide study was performed again. A trend toward the improvement in LV and RV diastolic function was revealed. At the same

time, the appearance of dissociated zones of hypokinesis was noted in the anterior, diaphragmatic, and lateral walls of the LV (indicated by arrows in Fig. 4B). The contractile function of both ventricles is satisfactory: LV EF = 76%; RV EF = 42%.

Fig. 4 shows sequentially from left to right the maps of the perfusion distribution, wall motions, systolic thickening and the diagram of the blood supply to the myocardium on the right in the figure.

No significant focal abnormalities in myocardial perfusion were detected. There were signs of ongoing diffuse process in the myocardium, of possible rejection.

The analysis of the data obtained suggested that there were stenotic changes in the LAD middle third; and repeated coronary angiography was performed which confirmed the presence of 75% stenosis in the middle third (indicated by the arrow in Fig. 7).

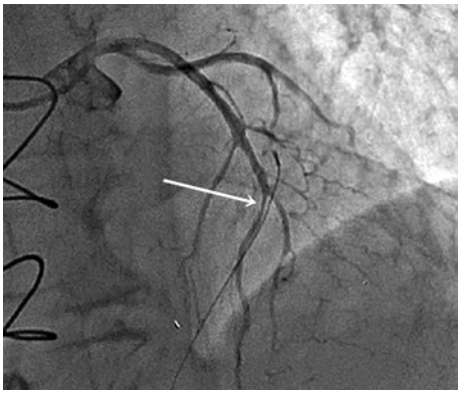

Fig. 7. Coronarogram of patient Sh.

At PCI, the balloon angioplasty was performed in the LAD middle third at a pressure of up to 12 atm and a stent was implanted in the LAD middle third at a pressure of 10 atm. On control angiograms, the stent is fully extended, there is no dissection at the intervention site, antegrade blood flow is TIMI 3.

On the 4th day after stent placement, in order to assess the intervention efficacy, a repeat myocardial perfusion SPECT was performed, which showed the disappearance of hypokinesis foci in the LV anterior wall (Fig. 4C). To confirm the positive dynamics, a 6-minute walk test was repeated, which results increased from 180 to 540 meters.

Histological examination of subendocardial myocardium specimens revealed mild sclerosis signs with a few lymphocytes in the pericapillary spaces in the absence of degenerative changes in cardiomyocytes (Fig. 8 A–C).

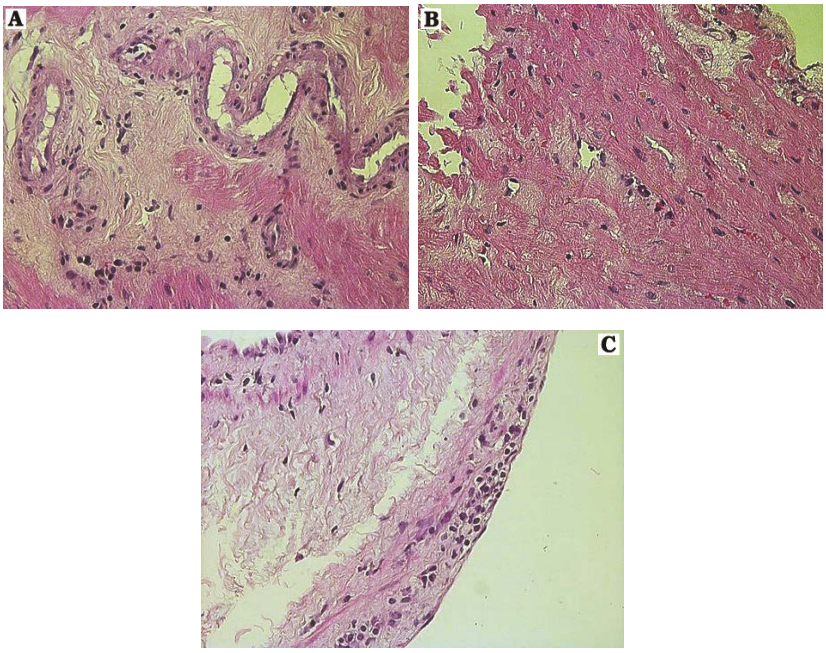

Fig. 8. Histological section of the myocardium. A–B. Perivascular and intermuscular sclerosis, single lymphocytes and their small clusters. C. Severe subendocardial sclerosis and lymphocyte clusters. Staining with hematoxylin and eosin, ×400

Case Report No. 3

Patient F., 49 years old, was admitted with complaints of decreased physical activity and weakness. From the medical history it was known

that 8 months ago he underwent orthotopic heart transplantation. During observation, progressive heart failure was noted. Receives immunosuppressive, antiviral, antimicrobial, anti-platelet, glucocorticoid therapy, statin therapy (*tacrolimus 4 mg × 2 times a day, mycophenolic acid 720 mg × 2 times a day, metypred 4 mg × 1 time a day, Biseptol 480 mg × 1 time a day, acyclovir 450 mg × 1 time a day, acecardol 100 mg × 1 time a day, rosuvostatin 20 mg in the evening*). The condition at admission was moderate. On examination, breathing is coarse, breath sounds being evenly transmitted over all parts of the lungs. There is no wheezing, respiratory rate is 16/min. On auscultation, heart sounds are muffled, no additional murmurs are heard. The heart rhythm is regular, the heart rate is 102 beats/min, there is no pulse deficit. Blood pressure 160/100 mm Hg. The results of a 6-minute walk test are 300 m. The ECG records sinus rhythm, EAH deviation to the left, and ECG signs of LV hypertrophy. Negative T wave in leads V2-V6.

When performing transthoracic echocardiography: *Aorta is 4.0 cm, ascending limb was 3.4 cm, Aortic valve is 3-leaf valve, opening amplitude is 18 mm, no regurgitation was detected. LA is 4.6 cm, LA volume is 110 ml, LV EDV is 105 ml, ESV is 42 ml, EF is 60%, IVS thickness in diastole is 1.3 cm, LVPWTh in diastole is 1.1 cm. RV is 2.6 cm. RV local contractility is unimpaired. The RV free wall thickness is 0.4 cm. TV: leaflets are without specific findings, grade I regurgitation, regurgitation gradient is 20 mm Hg, pulmonary artery diameter is 23 mm, pulmonary artery systolic pressure (PASP) is 25 mm Hg. The inferior vena cava is 25 mm, collapse on inspiration is less than 50%. The LV myocardium local contractility is unimpaired.*

Moderate hypertrophy of the LV myocardium was revealed. Marked dilatation of the left atrium cavity, mitral and tricuspid

regurgitation of grade I. Type 1 LV diastolic dysfunction without the LV systolic function impairment.

A myocardial perfusion SPECT showed an acute slowdown of ejection from the LV; and the ejection duration began to prevail over the LV filling duration. Extensive zones of hypoakinesis appeared in the anterior wall, spreading to the lateral wall, as well as in the diaphragmatic wall. The zones of hypoakinesis topographically coincide with the foci of maximum perfusion (Fig. 9). There was a downward trend in the myocardial contractility index (LV EF is 70%). In the RV, ESV increased significantly; as a result, RV EF decreased to 31% (initially is 55%); and intraventricular pathological asynchrony appeared (up to 177 ms in 8 segments). In addition, interventricular asynchrony of 12 ms appeared, the first one was on the right.

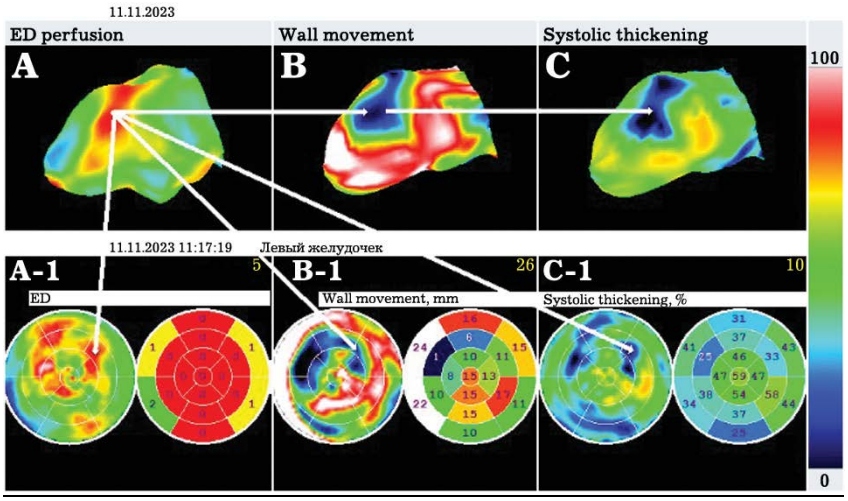

Fig. 9. A-C. Polar maps of patient F.

In Fig. 9, the top row shows three-dimensional images of the myocardial perfusion distribution in diastole (A), wall motion (B), and systolic wall thickening (C). In the bottom row there are images in the form of polar maps (bull's eye) with a quantitative assessment of the parameters (A-1, B-1, and C-1, respectively). It can be seen that the zones

of maximum perfusion in the images in diastole topographically coincide with the zones of akinesis. When examined after 4 hours, diffuse accelerated clearance is noted, most pronounced in the area of the anterior wall and septum (the percentage of washout of Tc99m-MIBI in 4 hours is 38% and 36%, respectively). Also, matches were found in the maps of wall motion and systolic thickening (indicated by arrows). The results of the study indicate inflammatory diffuse changes in the myocardium of both ventricles, the nature of which requires clarification - rejection? Myocarditis?

The reference study for answering this question is an intravital pathological and anatomical study of biopsy (surgical) material, which results revealed the signs of acute cellular rejection 1B-3A within the obtained material.

Considering the data obtained, the patient was given an intensive treatment including anti-inflammatory, immunosuppressive and metabolic therapy; and a control radionuclide study of the LV was performed.

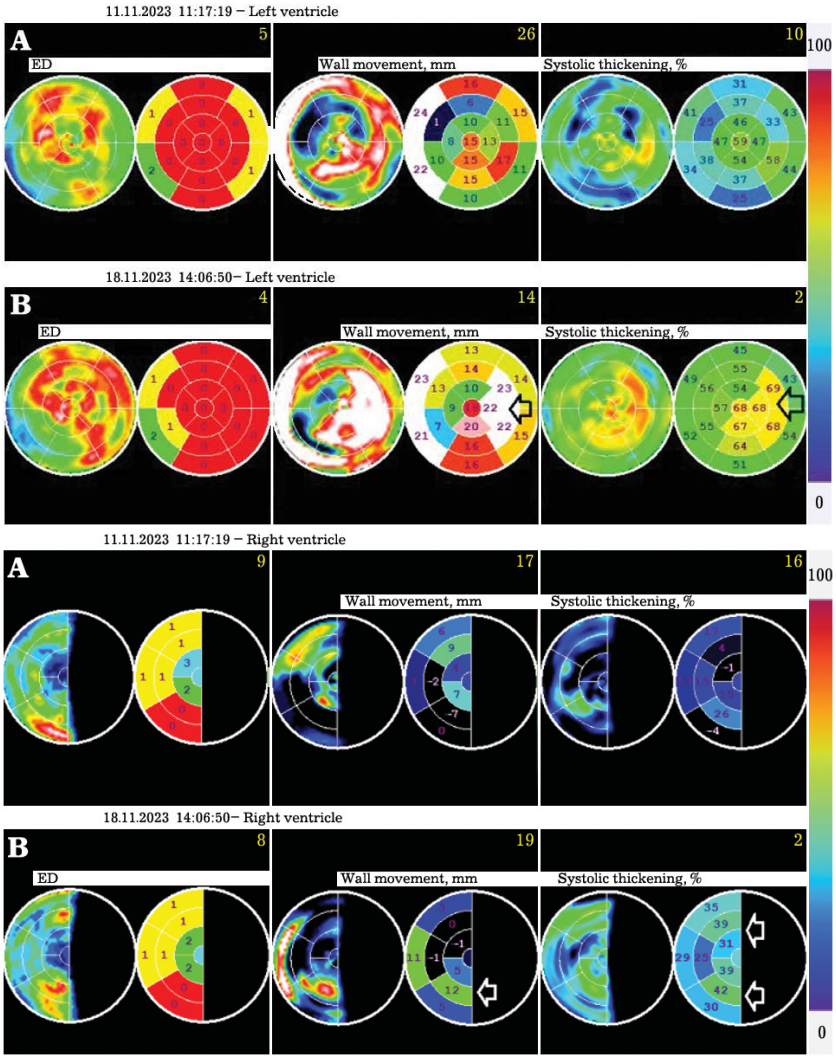

Fig. 10. Polar maps: end-diastolic, wall movements, and systolic thickening of the left and right ventricles of patient F. before (A) and after (B) treatment.

According to the results, there was seen an improvement in the myocardial regional function of both cardiac ventricles (Fig. 10 A-B), a decrease in interventricular asynchrony; when examined after 4 hours, a decrease in the percentage of washout of Tc99m-MIBI in 4 hours to 23–33% and an improvement in the myocardium ejection parameters of both ventricles. The bottom row shows the similar images after treatment (Fig. 10 B). The arrows indicate the area of a complete motion recovery

and of systolic thickening in the LV lateral wall, and the restored systolic thickening of the myocardium of the right ventricle.

The positive dynamics were confirmed by the results of pathologist's examination of biopsy (surgical) material. Histological examination revealed diffuse and focal lymphoplasmacytic infiltration, stromal sclerosis of varying severity, signs of circulatory disorders in the form of paresis and capillary congestion.

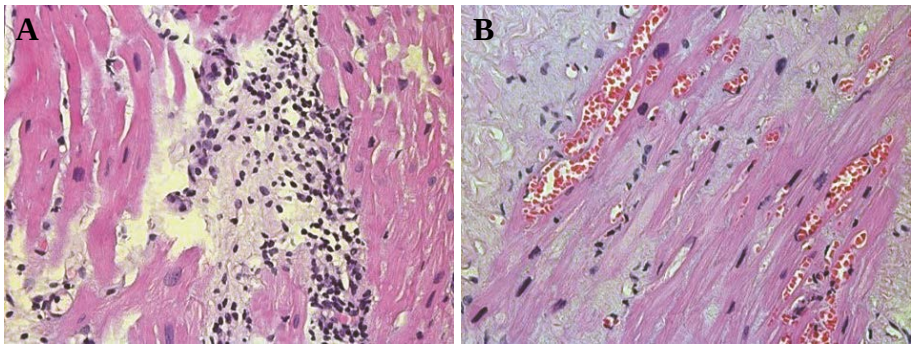

Fig. 11. Histological section of the myocardium. A. Diffuse and focal, mainly perivascular, lymphoplasmocytic infiltration. B. Pronounced sclerosis of the stroma, hypertrophy of cardiomyocytes, capillary paresis and erythrostasis. Staining with hematoxylin and eosin, X400

The observed positive dynamics in the ECG consisted of a decreased T wave in leads V4-V6 and the results of the 6-minute walk test, which increased significantly from 300 m to 421 m (Fig. 11).

Discussion

In an Emergency Cardiology Department, it is especially important to have an idea of the radionuclide method feasibility in diagnosing rare complications after heart transplantation such as acute myocardial infarction, the development of stenoses in the graft coronary arteries, and graft rejection. Of course, the diagnosis of acute focal changes in the

myocardium, myocardial infarction in the transplanted heart, and in one's native heart, remains the priority of scintigraphy [5].

In the first clinical case, the patient reported no pain upon presentation, only malaise. The clinical examination of the patient revealed no signs of acute heart failure. The results of electrocardiography and echocardiography indicate no focal changes in the myocardium. The myocardial perfusion SPECT results were decisive and important in making the diagnosis; after its images analysis the coronary angiography and PCI with thromboextraction were immediately performed.

In the second clinical case, the analyzed results of the coronary angiography did not show the need for PCI. The therapeutic treatment for rejection turned out to be ineffective. And only SPECT revealed the progression of focal pathology in the myocardium, which was the reason for repeated expert evaluation of angiograms and undertaking PCI. The results allowed both improving the myocardial function, and also restoring the patient's functional abilities, as confirmed by the results of the 6-minute walk test. Of greatest importance in this patient were the images reflecting the myocardial function: the polar maps of wall motion and systolic thickening.

In the third clinical example, the initial SPECT suggested the inflammatory nature of myocardial changes, which were verified by the results of endomyocardial biopsy. A repeated gated SPECT after therapeutic treatment showed an evident restoration of the general and regional functions of the myocardium of both heart ventricles. In that case, the comparison of polar maps of perfusion and function was important. In conclusion, we should emphasize that SPECT synchronized with ECG allows the assessment of both perfusion distribution, and also the myocardial function. In case of absent focal changes, and moreover, without availability of making the stress tests, it is difficult to rely on the

high sensitivity of perfusion images alone in detecting myocardial pathology of the transplanted heart [6]. A transplanted heart is characterized by a diffuse, balanced distribution of ischemia in Coronary Artery Disease of the Transplanted Heart (BCAPS), which often does not depend on the area and volume of changes in myocardial perfusion [7]. In these cases, a global, uniform decrease in perfusion may be missed, leading to false-negative results.

Conclusion

In the presented case reports, urgent implementation of perfusion single-photon emission computed tomography of the myocardium synchronized with electrocardiography made it possible to perform invasive interventions in a timely manner and thereby contribute to the restoration of graft function and the improvement of patient’s condition.

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24%, study concept, conducting research, collection of material, literature analysis

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The article was received on March 14, 2024;
Approved after reviewing March 25, 2024;
Accepted for publication March 27, 2024