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HEART TRANSPLANTATION AND COVID-19 IN THE EARLY POSTOPERATIVE PERIOD IN HYPERTROPHIC CARDIOMYOPATHY: A CLINICAL CASE

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Hypertrophic cardiomyopathy (HCM) is a disease that is usually unresponsive to conservative pathogenetic therapy. It does not have clearly developed surgical correction algorithms. Heart transplantation (HTx) is the sole therapeutic option when drug therapy is ineffective and surgical reduction of hypertrophic myocardium is not feasible. There are only sporadic reports in the literature about HTx for HCM. The novel coronavirus disease 2019 (COVID-19) pandemic has significantly affected the work of cardiac surgical units and, in particular, organ transplantation activities. This paper presents a clinical case of an HCM patient who underwent HTx, complicated by COVID-19 infection in the early postoperative period.

Keywords: hypertrophic cardiomyopathy, heart transplantation, COVID-19.

INTRODUCTION

HCM is a genetically determined myocardial disease characterized by severe left ventricular (LV) hypertrophy, less often by right ventricular hypertrophy, which cannot be explained exclusively by increased pressure load. It occurs in the absence of another cardiac or systemic disease, metabolic or multiorgan syndrome, associated with LV hypertrophy. More often, hypertrophy has asymmetric character due to thickened interventricular septum (IVS) [1].

HCM has an estimated prevalence of 1 in 500 to 1 in 200 people. One manifestation of the disease is sudden cardiac death (SCD), with an incidence of 1% per year [2–4].

HCM has been considered a "sarcomere disease" [5], caused by mutations in certain contractile protein genes. The morphological reflection of these processes is the development of cardiomyocyte disarray and hypertrophy, as well as interstitial fibrosis [6].

HCM pathophysiology is determined by a complex of interrelated factors, including obstruction syndrome, myocardial ischemia, diastolic LV dysfunction, presence of mitral regurgitation and arrhythmias. Obstruction is noted in certain left ventricular sections (left ventricular outflow tract (LVOT), middle section with papillary muscles and apical section). The main mechanism of obstruction is myocardial hypertrophy, which leads to LV cavity narrowing in different areas. In the LVOT, basal narrowing of hypertrophied IVS occurs; while the most frequent variant – hypertrophy of LV free wall, middle section of IVS and papillary muscles – occurs in middle sections of the LV, while apex hypertrophy occurs in the apical variant [7]. Another important mechanism in obstruction creation is considered to be systolic anterior motion (SAM) of the mitral valve. SAM is caused by the contact of anterior leaflet with the IVS in early systole as a result of accelerated blood flow through narrowed outflow tract, creating high-ejecting flow that pulls the mitral leaflet into LVOT [8].

To date, here are the existing HCM treatment methods: drug therapy, endovascular interventions and surgical methods of hypertrophic myocardial reduction. Conservative therapy includes drugs with negative inotropic action, aimed at reducing obstruction in LVOT (beta-blockers, verapamil, disopyramide) [9].

For patients with drug-refractory HCM, surgical treatment is decisive and is possible with the use of interventional methods of treatment (alcohol septal ablation) or with septal myoectomy under artificial circulation [10, 11]. The efficacy of the operation is quite high, with a decrease in pressure gradient in the LV cavity and, as a consequence, improvement in symptomatology and general condition of patients [12].

However, orthotopic heart transplantation (HTx) remains the only treatment modality for a small number

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of HCM patients who are not amenable to optimal drug therapy and are not candidates for conventional surgical treatment [13, 14].

This case report demonstrates the features of treatment of a patient with a transplanted donor heart and COVID-19 that developed in the early postoperative period.

CLINICAL CASE

Patient R., male, 35 years old, since 2018 started experiencing shortness of breath, chest tightness during minor physical exertion and associated the complaints with being overweight.

In 2019, while at work, he felt chest compression and lost consciousness. The ambulance crew recorded an ECG with rhythm disturbance and ischemic changes (atrial flutter rhythm, ST elevation to 1–2 mm in leads I, aVL, and V3–4, and ST depression to 2 mm in leads II, III, and aVF). After care (heparin 4000 units intravenously, clopidogrel 300 mg orally, acetylsalicylic acid 250 mg orally), the patient was taken to the hospital with acute coronary syndrome (ACS). Coronary angiogram (CAG) revealed no application points for percutaneous coronary intervention (PCI) – thrombotic occlusion was visualized in the distal third of the circumflex artery with the diameter of the artery in this section being less than 1.5 mm; the other arteries were without organic lesions). Spontaneous thrombolysis probably occurred.

Further examination of the patient in the current hospitalization resulted in the final diagnosis of HCM with LV outflow tract obstruction. Genetic testing to confirm the diagnosis was not performed. The diagnosis was made by specific results of instrumental diagnostic methods characteristic of HCM, as well as by excluding pathological conditions that could lead to LV hypertrophy (primary and secondary arterial hypertension, aortic stenosis).

EchoCG showed marked LV myocardial hypertrophy with predominant IVS thickening (3.8 cm) with LVOT obstruction (maximum pressure gradient, 19.4 mmHg MPG at rest, 40 mmHg MPG in Valsalva maneuver). Left ventricular end-diastolic diameter (LVEDD) – 72, left ventricular ejection fraction (LVEF) – 57%. LV enlargement. SAM of the mitral valve. Grade 1 mitral regurgitation (MR).

Myocardial perfusion scintigraphy showed scintigraphic signs of HCM with predominant IVS lesion. Regional contractility parameters: moderate septal hypokinesis. No signs of postinfarction cardiosclerosis (PICS) were detected.

Contrast-enhanced cardiac MRI showed asymmetric pronounced left ventricular myocardial hypertrophy with predominant thickening of the basal and middle IVS segments, left ventricular middle lower segment, with LVOT obstruction signs (Fig. 1).

In addition, to confirm the diagnosis, a morphological examination of the myocardium was performed as shown in Fig. 2. The patient was prescribed drug therapy with beta-1 blockers (bisoprolol 5 mg per day).

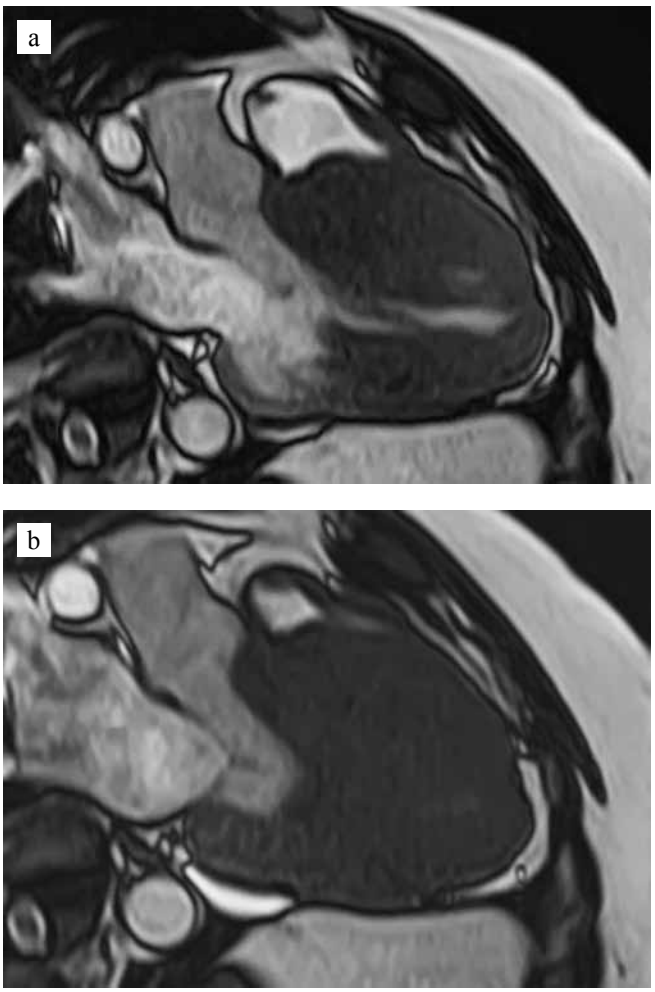

Fig. 1. Contrast-enhanced cardiac MRI. a, diastole; b, systole

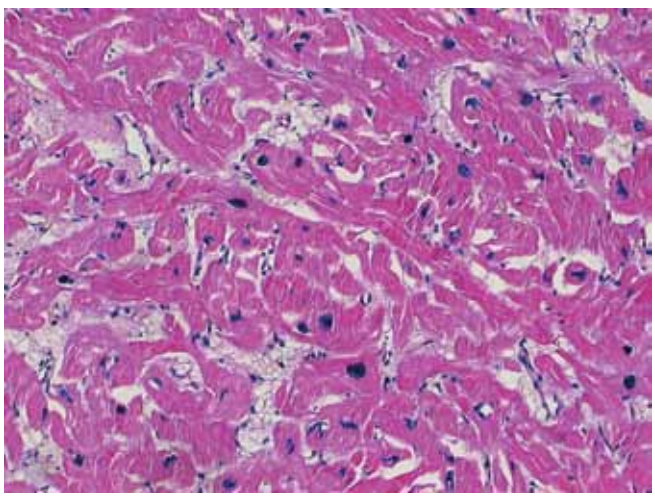

Fig. 2. Morphological analysis of the myocardium. Myocardial disarray: chaotic multidirectional course of muscle fibers, pronounced hypertrophy of some cardiomyocytes combined with atrophy of others, intermuscular fibrosis and stromal lipomatosis. H&E staining, 200× magnification

The patient was then referred to Bakulev National Medical Research Center of Cardiovascular Surgery for examination. Here, surgical correction via septal myoectomy was considered inappropriate due to the extreme thickness of the IVS. The patient was discharged with recommendations for orthotopic HTx. Given the risk of sudden arrhythmic death, a dual-chamber implantable cardioverter-defibrillator (ICD) was implanted. The SCD stratification on the HCM Risk-SCD scale was more than 6%, which was the indication for ICD implantation. The scale considers parameters such as family history of SCD, syncope, unstable ventricular tachycardia, maximum LV wall thickness, age, LV diameter and LVOT pressure gradient.

In October 2020, due to the emergence of a heart donor, the patient was admitted to the cardiac surgical unit for HTx with complaints of severe weakness, shortness of breath when walking up to 100 m, and retrosternal pain during physical exercise.

Upon admission, the patient's condition was moderate, he was fully conscious, body temperature 36.7 °C. Respiratory rate 16 per minute, breathing independently, SpO_2 99%. Blood pressure 138/74 mm Hg, heart rate 64 per minute, pacemaker rhythm (ICD), no pulse deficit. A PCR test for COVID-19 was performed (21/10/20) – SARS-CoV-2 RNA was not detected.

According to echocardiography, at the moment of admission, pronounced asymmetric LV myocardial hypertrophy with predominant IVS thickening (39 mm) and LVOT obstruction with 21 mmHg MPG at rest, 40 mmHg MPG in Valsalva maneuver. LVEDD 70. LVEF 55%. Enlargement of both atria. Minor mitral and aortic regurgitation.

On the day of admission (October 21, 2020), the patient underwent orthotopic HTx under artificial circulation and pharmacological cold cardioplegia.

HTx was performed using a bicaval technique. After median sternotomy and longitudinal dissection of the pericardium, the body was heparinized. A heart-lung machine was connected according to the scheme: aorta – superior vena cava (SVC) – inferior vena cava (IVC). The vena cava was squeezed and a transverse clamp was applied to the aorta. The aorta and the pulmonary artery were crossed above the commissures of the semilunar valves, the vena cava at the level of their confluence with the right atrium. A platform with the mouths of the pulmonary veins was made from the left atrium. The patient's heart was extracted, and the donor heart implanted. Implantation started with left atrial anastomosis. Then, anastomosis of the IVC and SVC was performed. The implantation was completed by forming aortic and pulmonary artery anastomoses. The operation was completed by preventing air embolism, removing the clamp, decannulating the heart-lung machine, installing drains, electrodes and layer-by-layer wound suturing.

The postoperative period from October 21, 2020 to November 8, 2020 was uneventful. The patient was fully conscious on day 1 after surgery. He was extubated on day 2. Breathing was spontaneous (unassisted) and adequate. Hemodynamics was stable, cardiotonic support was disconnected on day 6. On day 7, the patient was transferred from the intensive care unit to the general ward of the cardiac surgery department.

On day 19 (November 9, 2020), the patient's temperature increased to 38.0 °C; he had general weakness, increased sweating, chills, slight shortness of breath, cough with little sputum, he could still taste and smell. It should be noted that further slight increase in temperature to subfebrile values (37.0–37.7 °C) was associated with the treatment with immunosuppressive drugs (tacrolimus, mycophenolic acid), whose use was necessary according to the management protocol for patients after solid organ transplantation. His condition was satisfactory, he was fully conscious. Respiratory rate was 16 per minute, breathing was unassisted, SpO_2 99%. Blood pressure 120/74 mm Hg, heart rate 82 per minute, sinus rhythm.

Due to the spread of COVID-19, a swab was taken from the nose and throat for PCR to exclude COVID-19 infection. The result turned out positive. A chest CT scan was performed (November 11, 2020), which revealed infiltrative hypoventricular changes in the lower lobes on both sides, focal changes in the lungs, with a high probability corresponding to viral pneumonia, CT-2.

After the patient had tested positive to COVID-19, a case conference of physicians was held, which resulted to a decision to add the following to the management protocol for patients after solid organ transplantation: anticovid convalescent plasma (4 times 200 mL each), monoclonal antibodies against human IL-6 receptor (olokizumab 0.4 mL once, tocilizumab 400 mg once).

Based on the results of clinical and instrumental data, a telemedical consultation was conducted with leading specialists in the management of patients after HTx from Shumakov National Medical Research Center of Transplantology and Artificial Organs. It was recommended to reduce immunosuppressive therapy (withdrawal of mycophenolic acid preparations, reduction of methylprednisolone dose), to continue tacrolimus therapy, add broad spectrum antibiotics (azithromycin/ceftaroline/levofloxacin) and to start low molecular weight heparins (enoxaparin sodium). All recommendations were implemented.

In the laboratory data, the concentration of C-reactive protein increased during the first days of the disease and then decreased. Other inflammatory markers (leukocytes, sedimentation rate) were within the reference values (Fig. 3).

The patient was dynamically followed up for changes in the lungs by chest CT scan. In the lungs, on both sides, we detected ground-glass type lung tissue thickening

zones, which increased as the disease progressed from small foci to diffuse nature. The degree of lung lesions progressed from CT-2 to CT-4. In addition, consolidation zones in the lower lobes of both lungs persisted for a long time (Fig. 4).

On day 23 (November 13, 2020), there was a decrease in oxygen saturation (SpO_2 88%). The patient was transferred to humidified oxygen with 95% SpO_2 saturation. The dynamics of changes in SpO_2 is shown in Fig. 5.

On day 29 (November 19, 2020), a repeated telemedicine consultation with Shumakov National Medical

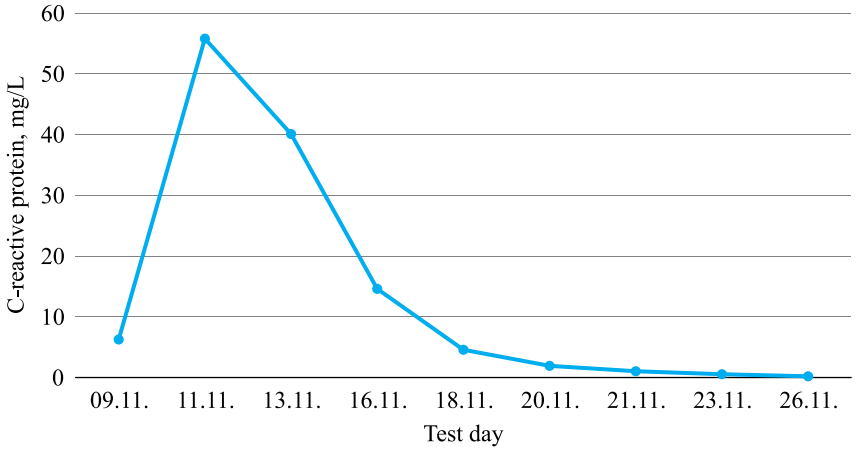

Fig. 3. Changes in C-reactive protein

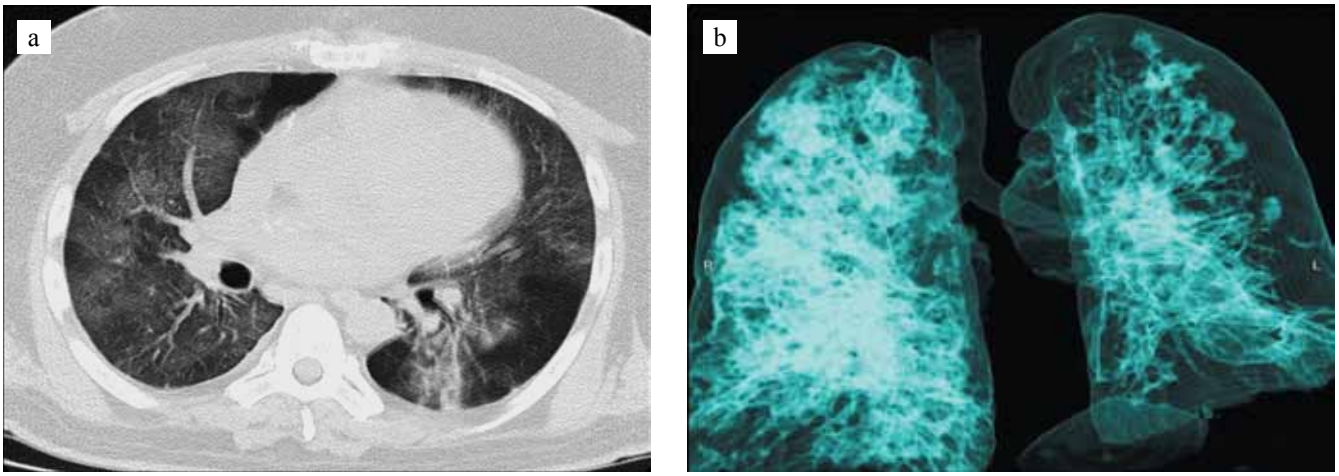

Fig. 4. a, Axial chest CT image (18/11/20); b, Chest CT image in pulmonary view (18/11/20)

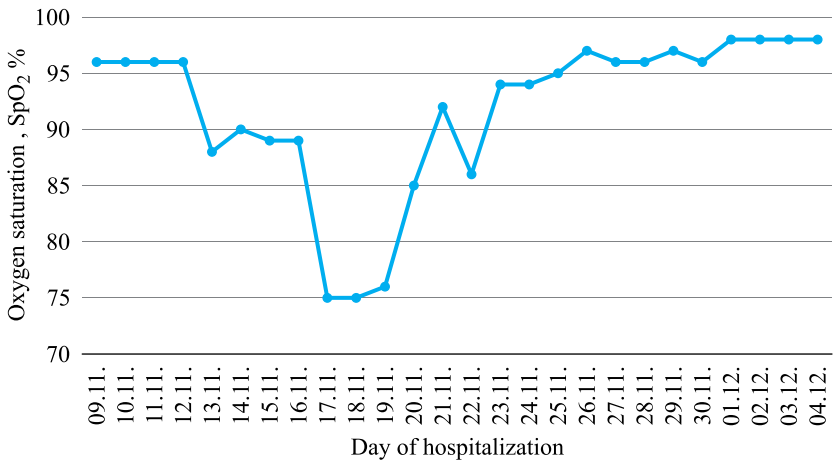

Fig. 5. Changes in oxygen saturation (SpO_2, %)

Research Center of Transplantology and Artificial Organs was conducted. It was recommended to continue therapy in the same volume.

During treatment, the patient was stable, temperature was within the normal range with episodes of return to subfebrile numbers, minor shortness of breath persisted, oxygen saturation rose to normal units, hemodynamics was stable (BP 125/75, pulse 75, sinus rhythm).

A second swab was taken from the nose and throat for PCR test to check for COVID-19: no SARS-CoV-2 RNA was detected.

Chest CT scan (December 2, 2020) before the patient's discharge showed positive dynamics, pathological changes in the resolution stage.

Echocardiography (December 4, 2020) before the patient's discharge showed no zones of impaired local myocardial contractility in the left ventricle. EF 56%. Cardiac chambers were not dilated. Moderate pulmonary hypertension (pulmonary artery systolic pressure 44 mm Hg). Minor mitral and tricuspid regurgitation.

Myocardial transplant biopsy (December 2, 2020) conducted before discharge showed mild cellular rejection without signs of humoral crisis (Fig. 6).

The patient was discharged with improved condition. Body temperature and oxygen saturations were normal, there were no complaints.

At present, a year later, the patient is in satisfactory condition.

DISCUSSION AND CONCLUSION

The COVID-19 pandemic has presented an unprecedented challenge to the global health and public health system. The epidemiologic situation has led to limitations in access to routine surgical care, as well as limitations in the ability to perform solid organ transplantation procedures due to the regrouping of hospital resources.

This, in turn, leads to the so-called secondary effects in the form of delayed patient care, including patients with heart failure of various etiologies. Therefore, the adaptation of high-tech surgery centers to work under the current epidemiological situation is an extremely important task.

The given clinical case allows us to conclude that HTx can be successfully performed in patients with hypertrophic obstructive cardiomyopathy when other methods of radical correction cannot be applied due to clinical and anatomical features. The COVID-19 infection is a disease with a significant risk of fatal complications, especially in patients with organ transplants and immunosuppressive therapy. However, even in the early postoperative period, timely and multidisciplinary management of this complex category of patients allows to achieve a good clinical outcome.

The authors declare no conflict of interest.

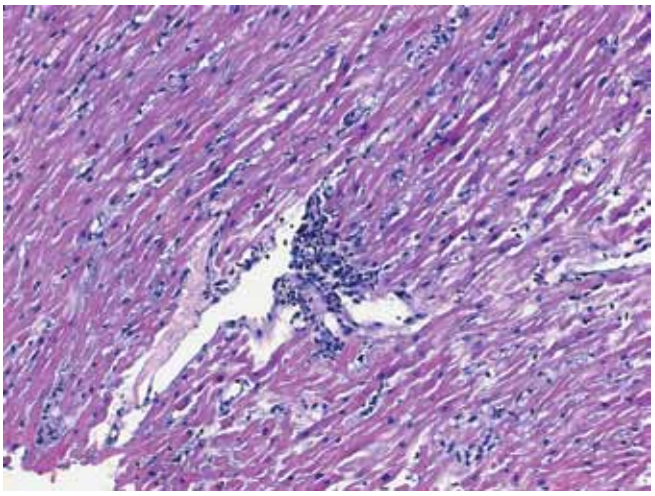

Fig. 6. Morphological examination of myocardial transplant. Myocardial transplant has a mild cellular rejection without signs of humoral crisis, RI pAMR0: a single focal perivascular lymphocytic infiltrate without cardiomyocyte damage in the interstitium. H&E staining, 200× magnification

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