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A clinical case

Management of Patients Following Heart Transplantation: Experience of the Heart Center in Astana

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Abstract

This clinical case describes a patient who was diagnosed with mitral valve prolapse in childhood. Subsequently, the patient was diagnosed with dilated cardiomyopathy with progressive reduction of ejection fraction down to 20%. In 2014, an implantable cardioverter-defibrillator (ICD) was placed.

Over time, the patient's condition worsened due to the progression of chronic heart failure symptoms and the lack of significant effect from conservative therapy. Based on the decision of a medical board, in February 2015, a left ventricular assist device (LVAD) — the HeartMate III — was implanted as a bridge to heart transplantation. The early postoperative period was complicated by right ventricular failure.

In July 2017, after 2.5 years on mechanical circulatory support, the patient underwent orthotopic bicaval heart transplantation under conditions of cardiopulmonary bypass and hypothermia. The early postoperative period was complicated by acute renal failure,

requiring prolonged hemodialysis sessions, as well as an episode of acute humoral (and cellular) transplant rejection.

After a course of pulse therapy with methylprednisolone (1 g for 3 days), the patient's condition improved. Lifelong immunosuppressive therapy was initiated, including tacrolimus (Prograf), methylprednisolone, and mycophenolic acid (Myfortic), along with prophylactic therapy with valganciclovir (Valcyte) for six months post-transplant, followed by a switch to acyclovir. In addition, supportive therapy was prescribed, including antiplatelet, lipid-lowering, and gastroprotective agents.

At present, the patient is on continuous therapy with acetylsalicylic acid (Thrombo ASS), a β-blocker (bisoprolol), and combined lipid-lowering therapy (Rosulip Plus).

Keywords: dilated cardiomyopathy, chronic heart failure, heart transplantation, postoperative period, immunosuppressive therapy.

1. Introduction

The number of patients with cardiovascular diseases (CVDs) continues to increase exponentially each year. In the natural course of most cardiovascular conditions, the progression often leads to a decline in the heart's pumping function, resulting in the development of chronic heart failure (CHF) [1,2].

In recent years, significant advances have been achieved in the pharmacological treatment of CHF. Nevertheless, surgical intervention-specifically, orthotopic heart transplantation-has proven effective in managing advanced stages of cardiac diseases with poor prognoses [3]. According to recent data, the average functional lifespan of a transplanted heart may reach five, and in some cases, even ten years [3]. In 2020 alone, approximately 4,000 heart transplant surgeries were performed worldwide, and this number continues to grow [2]. In Kazakhstan, 100 such transplantations have been carried out over the past 10 years [4].

The primary indications for heart transplantation include severe circulatory failure due to dilated cardiomyopathy or ischemic heart disease. While a meticulous patient selection process is employed, only a fraction of those in need ultimately gain access to this form of treatment [3].

These patients are considered high-risk for a variety of conditions-chiefly cardiovascular and infectious diseases-which often compels them to seek medical attention from specialists in multiple disciplines. Therefore, healthcare professionals must possess adequate knowledge about the post-transplant condition to determine the optimal management strategy for such patients [5].

In the present report, we describe a case of a patient who underwent orthotopic heart transplantation for dilated cardiomyopathy. We also highlight the most common post-transplant complications that healthcare providers-particularly those in outpatient and primary care settings, including general practitioners and internists-should be aware of.

2. Methods

This case report illustrates the comprehensive patient journey with dilated cardiomyopathy (DCM) and heart transplantation.

The study was conducted in strict accordance with the principles outlined in the Helsinki Declaration. Prior to commencement, the study received approval from the Local Bioethics Committee of the Corporate Foundation "University Medical Center," protocol #3 dated 14/07/2023. Informal consent was taken from the patient before analyzing data.

3. Case report

Patient T., a 30-year-old male, first presented to the local outpatient clinic during childhood, where he was diagnosed with mitral valve prolapse. He was followed up regularly. According to his medical history, beginning in December 2014, he developed dyspnea with minimal physical exertion and in the supine position. Further evaluation led to a diagnosis of dilated cardiomyopathy (DCM).

In 2014, the patient was rehospitalized twice due to decompensated heart failure. In December 2015, he was admitted to the National Research Cardiac Surgery Center (NRCSC), where he underwent evaluation under the chronic heart failure (CHF) program. Given the short clinical history, low left ventricular ejection fraction (20%), and the presence of polymorphic ventricular extrasystoles in a bigeminy pattern, a joint decision with the electrophysiology team was made to implant an implantable cardioverter-defibrillator (ICD).

The ICD implantation procedure was complicated by sustained ventricular tachycardia, requiring cardiopulmonary resuscitation. The patient was rehospitalized in January 2015. Despite optimal medical therapy for CHF, the patient exhibited progressive clinical deterioration. Due to worsening heart failure symptoms and a lack of response to conservative treatment, a multidisciplinary team decision was made to proceed with implantation of a HeartMate III left ventricular assist device (LVAD) in February 2015, as a bridge to heart transplantation. The early postoperative period was complicated by right ventricular failure.

Following LVAD implantation, the patient reported significant improvement in well-being, including reduced dyspnea and improved functional status. In February 2017, he was readmitted for right heart catheterization, which revealed: pulmonary artery pressure (PA) of 17/8–11 mmHg and pulmonary vascular resistance (PVR) of 1.2 Wood Units. The patient was subsequently listed for heart transplantation.

In July 2017, after 2.5 years on mechanical circulatory support, the patient underwent orthotopic bicaval heart transplantation under cardiopulmonary bypass and hypothermia. The early postoperative period was complicated by acute kidney injury, requiring prolonged hemodialysis, as well as acute cellular and humoral rejection of the cardiac allograft. After administration of pulse therapy with methylprednisolone (1 g daily for 3 days), the patient's condition improved.

Lifelong immunosuppressive therapy was initiated, including tacrolimus (Prograf), methylprednisolone, and mycophenolic acid (Myfortic), alongside prophylactic therapy with valganciclovir (Valcyte) for 6 months post-transplant, followed by acyclovir. Concomitant therapy included antiplatelet agents, lipid-lowering drugs, and gastroprotective medications.

Prior to the patient's discharge to their home region, an official letter was sent to the local outpatient clinic and the regional health authority. The letter indicated that the patient, following a heart transplantation, must be placed under medical observation. It also requested assistance in ensuring that the patient is provided with life-saving immunosuppressive medications under the state-guaranteed package of free medical services. If necessary, arrangements could be made to send a physician for short-term training on the management of this patient population.

Regular monthly outpatient follow-up for life was recommended, along with annual hospitalizations for comprehensive evaluation, including clinical and biochemical blood tests, echocardiography, endomyocardial biopsy (EMB), and coronary angiography with intravascular ultrasound every 1–2 years.

In 2018, the patient underwent coronary angiography (CAG) at the National Research Cardiac Surgery Center (NRCSC), with the following findings:

- LM: unchanged;

- LAD: irregular contours, extended stenosis up to 40% in the mid-third, and tandem 50% stenosis at the junction of the mid and distal thirds;
- Intermediate artery (AI): well-developed, with 50% stenosis in the mid portion;
- Circumflex artery (CFX): irregular contours;
- Obtuse marginal branch (OM): irregular contours;
- Right coronary artery (RCA), posterior descending artery (PDA), and posterior lateral branch (PLB): no hemodynamically significant stenosis.

An EMB revealed no signs of rejection. The findings were interpreted as cardiac allograft vasculopathy (CAV). The patient was discharged in satisfactory condition with reinforced immunosuppressive and lipid-lowering therapy.

In 2019, the patient was hospitalized at NRCSC due to an intestinal infection. Neither CAG nor EMB were performed at that time.

During a scheduled hospitalization in 2020, the patient was clinically stable, echocardiography findings were within normal limits, and EMB showed no evidence of rejection.

In 2022, the patient was re-hospitalized at NRCSC. CAG findings were as follows:

- Coronary blood supply type: right-dominant;
- LM: unchanged;
- LAD: irregular contours, 60% lumen narrowing;
- Circumflex artery (CX): diffuse changes along its entire length;
- Intermediate artery (AI): 80% stenosis in the proximal third;
- OM: diffuse changes throughout;
- RCA: irregular contours with 55% stenosis in the terminal segment;
- PLB: irregular contours;
- PDA: small-diameter artery with prolonged 65% narrowing from the ostium.

Following a multidisciplinary team consultation in July 2022 (five years post-transplant), surgical intervention was performed: resternotomy, mammary-coronary bypass to the LAD, and autovenous aortocoronary bypass with composite anastomosis, under cardiopulmonary bypass using parallel perfusion.

An EMB performed in July 2022 showed no signs of rejection. The patient was discharged in satisfactory condition on medical therapy, including clopidogrel (Plavix), acetylsalicylic acid (Thrombo ASS), bisoprolol (Concor), and a statin (Rosulip Plus).

In July 2023, the patient underwent a scheduled hospitalization at NRCSC. CAG showed no hemodynamically significant lesions, and all grafts were functioning. Echocardiography revealed a global longitudinal strain (GLS) of –23.9% and a left ventricular ejection fraction (LVEF) of 61.31%. No laboratory evidence of transplant rejection was detected.

As of the most recent examination at the Heart Center in March 2024, the patient's condition was satisfactory. Tissue turgor was preserved, and no edema was observed. Vesicular breath sounds were heard throughout all lung fields. Cardiac borders were enlarged to the left by 1 cm. The pulse was rhythmic, of satisfactory volume and tension, with a heart rate of 78 beats per minute. Blood pressure was 120/80 mmHg. On percussion, the liver was not enlarged; on palpation, its edge was soft and non-tender.

To assess the patient T.'s psycho-emotional state, a consultation with a psychotherapist was offered [6], which revealed no signs of anxiety or depression.

In addition to the previously mentioned therapy, the patient is currently on continuous treatment with acetylsalicylic acid (Thrombo ASS), a beta-blocker (bisoprolol), and combination lipid-lowering therapy (Rosulip Plus).

4. Discussion

The clinical interest of this case lies in the fact that over a period of more than five years, the patient, while on immunosuppressive therapy, developed clinical signs of cardiac allograft vasculopathy (CAV). Importantly, the ischemic heart disease remained asymptomatic due to cardiac denervation and was only detected through

routine annual follow-up. This case thereby demonstrates the necessity for dedicated attention to this patient population and reinforces the need for annual evaluations, including invasive procedures.

Dilated cardiomyopathy (DCM) is a disease that affects the myocardium and is characterized by significant enlargement of the heart chambers, reduced systolic function of both the left and right ventricles, and diastolic dysfunction. The annual incidence of newly diagnosed DCM is 5–8 cases per 100,000 population. The disease most commonly presents between the ages of 30 and 45. The etiology remains unknown, although viral myocarditis, a positive family history (with up to 40% of cases being familial), and immunological disorders are considered significant contributing factors.

In suspected cases of DCM, diagnostic confirmation requires an electrocardiogram (ECG), echocardiography (EchoCG), stress echocardiography with dobutamine, cardiac catheterization and angiography, and endomyocardial biopsy. In most cases, two of the listed investigations are sufficient to establish the diagnosis [7].

The number of patients undergoing heart transplantation is steadily increasing. Following such surgery, the quality of life for individuals with cardiovascular disease improves significantly, and there is a noticeable trend toward a reduction in mortality from this condition both globally and in our country. However, for many general practitioners and internists, important questions remain unresolved—particularly regarding which patients should be referred for such procedures and how to manage diseases associated with the post-transplant period [1,8].

Another noteworthy aspect is the relative rarity of such patients in the general practice of primary care physicians. Tables 1 and 2 present the main indications and contraindications for heart transplantation.

Table 1 - Main indications for heart transplantation

Absolute readings
• A decrease in peak VO_2 to less than 10 ml/kg/min despite maximal medical therapy;
• Signs of severe myocardial ischemia that significantly limit daily activities, in patients for whom revascularization through coronary artery bypass grafting (CABG) or percutaneous coronary intervention is not feasible;
• Recurrent ventricular arrhythmias that are refractory to both medical therapy and electrophysiological treatment methods;
• Severe valvular heart diseases (when other surgical treatment methods are not possible), congenital heart defects, or cardiomyopathies that significantly impair daily activities and are associated with a greater than 50% risk of death within one year;
• Clinically proven chronic heart failure of NYHA class III–IV, refractory to medical treatment, with an estimated one-year survival of less than 50%.
Relative readings
• Decrease in peak VO_2 to less than 14 ml/kg/min despite maximal medical support;
• Frequent episodes of progressive unstable angina that are unresponsive to other forms of therapy;
• Heart diseases with signs of decompensation, refractory to both medical and surgical treatment, accompanied by irreversible pulmonary hypertension.

***VO_2 - Volume of Oxygen Consumed per Minute*

NYHA- New York Heart Association (Classification)

Table 2 - Main contraindications for heart transplantation

Absolute contraindications
• Autoimmune diseases;
• Age over 75 years in the presence of comorbidities that increase perioperative risk and worsen long-term prognosis;
• History of malignant neoplasms within the past 5 years (excluding non-melanoma skin cancers), or breast cancer stages I–IV or prostate cancer stages I–IV identified during preoperative assessment;
• Active smoker or quit smoking less than 6 months ago;
• Alcohol or psychoactive substance abuse;
• Presence of a local or systemic infection;
• HIV infection;
• Psychological or emotional instability, or a history of mental illness;
• Pulmonary hypertension with a transpulmonary gradient >15 mmHg or pulmonary vascular resistance >6 Wood units, refractory to medical therapy (NO, sildenafil) and/or mechanical support;
• Pulmonary function impairment (FEV_1 less than 1 L/min);
• Chronic renal/hepatic failure in the stage of decompensation.
Relative contraindications
• Age over 65 years, in the absence of comorbidities that increase the risk of complications during and after surgery;
• Acute pulmonary embolism;
• Grade II–III obesity;
• Decompensated liver/kidney disease (creatinine clearance less than 25 ml/min, bilirubin level greater than 25 mg/dL, transaminase levels elevated no more than 3 times above normal);
• Non-melanoma skin cancers within the last 5 years;
• Decompensated diabetes mellitus;
• Active peptic ulcer disease of the stomach or duodenum;
• Active diverticulitis;
• Cachexia;
• Coagulopathy;
• Recent infection (within 1 month; for hepatitis or severe pneumonia, within 6 months);
• History of acute cerebrovascular accident (stroke).

****HIV - Human Immunodeficiency Virus*

FEV_1 - Forced Expiratory Volume in One Second

During follow-up of transplant patients, it is essential to consider the possibility of late post-transplant complications such as postoperative infections, coronary artery disease, arterial hypertension, and others. Chronic rejection of the donor organ is also a potential concern. All of these require highly specialized and regular follow-up at the transplant center where the procedure was performed [9].

Cardiac allograft vasculopathy (CAV) is the leading cause of mortality in the post-transplant period. Due to the denervation of the transplanted heart, angina pectoris is typically absent. The only manifestations of this pathology may be silent ischemia or sudden cardiac death. Histological examination reveals progressive diffuse concentric hyperplasia of smooth muscle cells and the intima in coronary arteries. Studies indicate that initial ischemia of the donor organ increases the risk of coronary artery involvement. To prevent such complications, all patients presenting to outpatient clinics

must undergo thorough cardiac evaluation for early diagnosis of coronary pathology [2, 3, 10].

Infectious diseases remain the most frequent complications during the entire post-transplant period. The most commonly identified pathogens include Epstein–Barr virus (EBV), cytomegalovirus (CMV), herpes simplex virus (HSV), Toxoplasma gondii, Pseudomonas aeruginosa, Staphylococcus aureus, Pneumocystis carinii, Candida albicans, and Aspergillus spp. [2, 5].

CMV remains the primary infectious agent in heart transplant recipients. It is believed to play a key role in the accelerated development of CAV and transplant rejection. Long-term prophylactic therapy is prescribed accordingly. Plasma samples from all patients are tested using polymerase chain reaction (PCR) to detect viral DNA. Fungal infections such as candidiasis and aspergillosis are often etiological factors in severe pneumonia [5].

Various neoplasms, especially skin cancers and lymphoproliferative disorders, remain a serious concern for post-transplant patients. By eight years post-transplant, epithelial carcinomas are observed in 25% of patients [9]. The most widely accepted theory for the development of such malignancies involves long-term use of immunosuppressive drugs. CMV and EBV carriage may contribute to the malignant transformation of tissues [2, 4].

All heart transplant recipients seeking outpatient medical care for any reason must undergo a thorough skin examination, including mandatory biopsy of suspicious lesions, as well as lymphatic system assessment, followed by hematologist consultation if necessary [3].

In addition to new diseases, preexisting conditions may progress after transplantation. Arterial hypertension develops in 75% of patients within the first year post-transplant, rising to 95% over the subsequent five years. Renal insufficiency (RI) following heart transplantation arises primarily due to the chronic use of cyclosporine A. Approximately 2–3% of such patients require dialysis and eventually may need kidney transplantation. Hyperlipidemia is observed in 85% of this patient population. Furthermore, 35% of patients develop diabetes mellitus within 2–5 years post-transplant. This is likely related to the continuous use of immunosuppressants that stimulate gluconeogenesis. Additional side effects of immunosuppressive therapy include osteoporosis, avascular necrosis of the femoral head, musculoskeletal disorders, neurological conditions, epilepsy, and focal neurological seizures [9].

Nevertheless, post-transplant pharmacotherapy is prescribed based on vital indications, and any discontinuation or disruption in treatment can have fatal consequences. No clinical specialist other than the transplant physician is authorized to modify this regimen. Substantial efforts are currently underway to develop optimal immunosuppressive protocols that minimize the occurrence of these adverse drug reactions. Therefore, targeted screening of affected organs and systems is critical in all heart transplant recipients to detect and rule out specific post-transplant complications [8].

5. Conclusions

Thus, heart transplantation has currently become the treatment of choice for most patients with cardiovascular diseases in the stage of decompensation. The number of patients who have undergone such a procedure is increasing every year. Although heart transplantation and the subsequent pharmacological therapy involve a significant number of complications, this procedure greatly improves both the quality of life (based on our observations) and its duration.

To prevent and detect various conditions associated with heart transplantation, it is crucial for medical personnel—especially those in therapeutic specialties—to be well-informed, as patients most often seek help from these professionals. It is also important to note that the issue of organ transplantation touches on many aspects, including ethical ones, and is not only a medical matter but a broader social concern as well.

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Жүрек трансплантациясынан кейінгі науқастарды бақылау: Астана қаласындағы жүрек орталығының тәжірибесі

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Түйіндеме

Бұл клиникалық жағдайда бала кезінде митралды қақпақ пролапсы диагнозы қойылған науқас сипатталған. Кейіннен оған жүрек соғу фракциясының 20%-ға дейін төмендеуімен сипатталатын дилатациялық кардиомиопатия диагнозы қойылды. 2014 жылы науқасқа кардиовертер-дефибриллятор имплантацияланды.

Уақыт өте келе, жүрек жеткіліксіздігінің белгілері күшейіп, жүргізілген консервативті терапияның айтарлықтай әсері болмағандықтан, жағдайы нашарлады. Дәрігерлік консилиум шешімімен 2015 жылдың ақпанында науқасқа жүрек трансплантациясына көпір ретінде HeartMate III сол жақ қарыншаны қолдау құрылғысы имплантацияланды. Отадан кейінгі ерте кезең оң жақ қарыншалық жеткіліксіздікпен асқынды.

2017 жылдың шілде айында, механикалық қолдауда 2,5 жыл өткен соң, жасанды қанайналым мен гипотермия жағдайында ортотопиялық бикавальды жүрек трансплантациясы жүргізілді. Отадан кейінгі ерте кезең жедел бүйрек жеткіліксіздігімен күрделеніп, науқас ұзақ уақыт бойы гемодиализ сеанстарын қабылдады, сонымен қатар трансплантаттың жедел гуморальды (және жасушалық) кері қағу эпизоды тіркелді.

Метилпреднизолонмен (3 күн бойы 1 г) пульс-терапия жүргізілгеннен кейін науқастың жағдайы жақсарды. Өмір бойына арналған иммуносупрессивті терапия тағайындалды: такролимус (Програф), метилпреднизолон, микофенол қышқылы (Майфортик), сондай-ақ операциядан кейін алғашқы 6 ай бойы валганцикловирмен (Вальцит) профилактикалық терапия жүргізілді, кейін ацикловирге ауыстырылды. Қосымша қолдаушы терапия ретінде антиагрегантты, гиполипидемиялық және гастропротективті дәрілер тағайындалды.

Қазіргі таңда науқас үнемі ацетилсалицил қышқылын (Тромбо АСС), β-блокатор (бисопролол), сондай-ақ біріктірілген гиполипидемиялық терапияны (Розулип Плюс) қабылдайды.

Түйін сөздер: дилатациялық кардиомиопатия, созылмалы жүрек жеткіліксіздігі, жүрек трансплантациясы, операциядан кейінгі кезең, иммуносупрессивті терапия.

Ведение пациентов после трансплантации сердца: опыт Центра сердца в Астане

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Резюме

В данном клиническом случае описан пациент, которому в детском возрасте диагностировали пролапс митрального клапана. Впоследствии был установлен диагноз — дилатационная кардиомиопатия с прогрессирующим снижением фракции выброса до 20%. В 2014 году пациенту был имплантирован кардиовертер-дефибриллятор.

С течением времени наблюдалось ухудшение состояния в связи с нарастанием симптомов хронической сердечной недостаточности и отсутствием выраженного эффекта от проводимой консервативной терапии. По решению врачебного консилиума в феврале 2015 года была выполнена имплантация устройства поддержки левого желудочка HeartMate III как моста к трансплантации сердца. Ранний послеоперационный период осложнился правожелудочковой недостаточностью.

В июле 2017 года, после 2,5 лет на механической поддержке, была проведена ортотопическая бикавальная трансплантация сердца в условиях искусственного кровообращения и гипотермии. Ранний послеоперационный период был осложнен острой почечной недостаточностью, в связи с чем пациент длительно получал сеансы гемодиализа, а также эпизодом острого гуморального (и клеточного) отторжения трансплантата.

После была проведена пульс-терапия метилпреднизолоном (1 г в течение трех дней), что привело к стабилизации состояния. В дальнейшем назначена пожизненная иммуносупрессивная терапия, включающая такролимус (Програф), метилпреднизолон, микофеноловую кислоту (Майфортик), а также профилактическая терапия валганцикловиром (Вальцит) в течение 6 месяцев после операции с последующим переходом на ацикловир. Дополнительно проводится сопроводительная терапия: антиагрегантная, гиполипидемическая и гастропротективная.

В настоящее время пациент постоянно принимает ацетилсалициловую кислоту (Тромбо АСС), β-блокатор (бисопролол), а также комбинированную гиполипидемическую терапию (Розулип Плюс).

Ключевые слова: дилатационная кардиомиопатия, хроническая сердечная недосататочность, трансплантация сердца, послеоперационный период, иммуносупрессивная терапия.