

CLINICAL CASE OF LIVER TRANSPLANTATION IN A KIDNEY TRANSPLANT RECIPIENT WITH HEPATOCELLULAR CANCER AND CORONARY ARTERY DISEASE

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Objective: organ transplantation is a highly effective and often the only possible definitive treatment for terminal diseases, significantly improving patient survival and quality of life. However, recipients have a higher risk of developing cardiovascular and oncological diseases, and are susceptible to decompensation of pre-existing diseases. Prevention and treatment of these conditions are becoming critical tasks in transplantology, requiring multidisciplinary collaboration. **Materials and methods.** This article presents a clinical case of the treatment of a patient with stage 5 chronic kidney disease, concomitant cardiologic pathologies and subsequently diagnosed hepatocellular cancer on the background of hepatitis C-related liver cirrhosis. Competent interaction and bridge therapy yielded successful consecutive kidney and liver transplantation with satisfactory outcomes. **Conclusion.** Our treatment experience has shown the effectiveness and necessity of a multidisciplinary approach, early diagnosis, therapy modification during transplantation and further treatment of patients with end-stage multiple organ dysfunction.

Keywords: *transplantation, chronic kidney disease, hepatocellular cancer, hemodialysis, bridge therapy.*

INTRODUCTION

Transplantation is a highly effective treatment for terminal diseases affecting various organ systems. Kidney transplantation (KT) can double the five-year survival rate of patients with stage 5 chronic kidney disease (CKD) compared to other renal replacement therapies (RRT) while significantly enhancing their quality of life [1–3]. Similarly, liver transplantation (LT) remains the only definitive treatment for many end-stage liver diseases, offering excellent immediate and long-term outcomes with no equally effective alternatives [4, 5]. Just over half a century ago, solid organ transplantation was an experimental field, with only isolated cases of clinical success. However, advancements in science, technology, immunology, genetics, and surgical techniques have transformed transplantation into a standard clinical practice in many transplant centers worldwide. Modern immunosuppressive therapy enables targeted suppression of the alloimmune response without causing severe immunodeficiency. While generally well tolerated by recipients, it is associated with adverse effects [6–8]. Solid organ transplant recipients face an increased risk of cardiovascular disease and cancer and are more susceptible to both the progression of preexisting conditions and

the development of new ones. Managing these risks is a critical challenge in modern transplant medicine, requiring a multidisciplinary approach. The presented clinical case underscores the significance of these considerations.

MATERIALS AND METHODS

Patient B., a 65-year-old man, was admitted to the cardiology ward at Botkin Hospital in Moscow on December 20, 2023, with complaints of irregular heart function, general weakness, and recurrent episodes of high blood pressure.

His medical history indicates that he has had arterial hypertension since 2005, with blood pressure reaching 200/100 mmHg. In 2014, he began experiencing leg swelling, progressive weakness, nausea, and vomiting. An outpatient examination revealed an elevated creatinine level of 1300 µmol/L, necessitating hospitalization for urgent medical care. He was diagnosed with stage 5 CKD due to hypertensive arteriolar nephrosclerosis.

In August 2014, an arteriovenous fistula was created, and chronic hemodialysis was initiated. The patient was informed about the irreversible nature of his condition and the advantages of kidney allotransplant over other

RRTs. Following a comprehensive evaluation, he was placed on the transplant waiting list.

During pre-transplant screening, the patient tested positive for hepatitis C virus (HCV) RNA, though there were no clinical, laboratory, or imaging signs of liver damage.

On November 21, 2015, the patient underwent deceased-donor kidney allotransplantation (DKAT) from a brain-dead donor. The early postoperative period was uneventful, with immediate and satisfactory graft function. The patient was discharged with a creatinine level of 120 $\mu\text{mol/L}$.

For long-term follow-up, a triple-drug maintenance immunosuppressive regimen was prescribed following the standard protocol: prolonged-release tacrolimus (target concentration 7–10 ng/mL), mycophenolic acid (360 mg twice daily), and methylprednisolone (4 mg once daily). Throughout follow-up, the patient showed no signs of significant kidney graft dysfunction or acute rejection.

The patient's medical history indicates that his blood pressure remained within the target range (130–139/70–79 mmHg) for an extended period while taking amlodipine (5 mg twice daily) and doxazosin (4 mg twice daily). In 2015, coronary angiography was performed as part of the pre-transplant evaluation, revealing no hemodynamically significant coronary artery stenoses.

Post-transplant diabetes mellitus was diagnosed in 2015, and the patient had been on vildagliptin for an extended period. However, due to sustained glycemic control, he discontinued anti-diabetic medication in mid-2023. Given his history of secondary hyperparathyroidism and electrolyte imbalances related to CKD and ongoing immunosuppressive therapy, the patient had also been on long-term supplementation, including calcium (1000 mg/day), potassium (99 mg/day), magnesium (500 mg/day), and vitamin D (10,000 IU every other day).

Given the previously diagnosed dyslipidemia, the patient has been on pitavastatin (4 mg daily) and ezetimibe (10 mg daily) for cardiovascular risk prevention. In 2017, routine outpatient biochemical testing revealed elevated hepatic transaminases (up to 200 U/L) and total bilirubin (56 mmol/L). Liver ultrasound findings were suggestive of cirrhosis, and HCV replication was confirmed in the blood.

Following hepatology consultation, liver function was deemed compensated with hepatoprotective therapy. An infectious disease specialist prescribed antiviral therapy (AVT) with sofosbuvir and daclatasvir. After six months of AVT, a sustained virological response was achieved, with an HCV RNA test on February 1, 2018, confirming viral clearance.

Upon admission, the patient was in a moderate but stable condition and fully conscious. His vital signs were as follows: height 170 cm, weight 70 kg (BMI 24.2 kg/m²), body temperature 36.7 °C, blood pressure (BP) 142/93 mmHg, and heart rate (HR) 62 beats per minute with a regular pulse. Bilateral pedal edema was noted. Auscultation revealed vesicular breath sounds and clear heart tones.

Electrocardiogram (ECG) conducted on December 20, 2023, showed sinus rhythm with a heart rate of 66 beats per minute. There was a marked leftward deviation of the electrical axis, a blockade of the anterior branch of the left bundle branch of His, and a first-degree atrioventricular (AV) block. Additionally, a single atrial extrasystole of the bigeminy type was observed.

Echocardiography conducted on December 20, 2023, revealed preserved global systolic function of the left ventricle (Simpson ejection fraction: 67%) with no local contractility impairments. Concentric left ventricular hypertrophy was observed (interventricular septum: 12 mm, posterior wall: 12 mm, LV mass index: 119 g/m²). Diastolic dysfunction was noted, following the abnormal relaxation pattern. Valve leaflets appeared thickened, with calcification of the non-coronary aortic valve leaflet. Minor pulmonary, mitral, and tricuspid regurgitation were present. The heart chambers were not dilated, and signs of hypovolemia were noted. Pulmonary artery pressure was within normal limits (systolic pulmonary artery pressure: 28 mmHg). No pericardial or pleural effusion was detected.

Daily blood pressure monitoring on December 21, 2023, revealed persistent systolic-diastolic arterial hypertension throughout the day. The degree of nocturnal BP decrease classified systolic BP as a “nightpeaker” pattern and diastolic BP as a “dipper”. The 24-hour average BP values were as follows: mean systolic BP – 156 mmHg, mean diastolic BP – 87 mmHg, and pulse pressure – 69 mmHg (elevated). Given the presence of uncontrolled hypertension, antihypertensive therapy was adjusted as follows: amlodipine was replaced with lercanidipine 20 mg once daily, doxazosin 4 mg twice daily was continued, and valsartan/sacubitril 50 mg twice daily was introduced.

Holter ECG monitoring on December 22, 2023, recorded a predominantly sinus rhythm with an average HR of 54 beats/min (maximum 85 bpm at 13:17, minimum 42 bpm at 06:25). Against this background, 213 polymorphic ventricular extrasystoles (two distinct morphologies) were recorded, including 6 paired and 10 episodes of bigeminy. Additionally, 674 supraventricular extrasystoles were observed, comprising 21 paired and 7 short runs of supraventricular tachycardia (up to 9 complexes), with a maximum HR of 144 beats/min. At 4:17 and 5:22, against the background of persistent first-

degree AV block (PQ interval up to 0.25 sec), episodes of third-degree AV block were recorded, characterized by idioventricular rhythm lasting up to 5 complexes at a frequency of 40 beats/min with AV dissociation. No diagnostically significant ST segment changes were observed during prolonged pauses. The maximum RR interval was 1.738 sec at 0:22.

Consultation with an arrhythmologist determined that there were no current indications for pacemaker implantation. However, it was recommended to conduct a repeat Holter ECG monitoring before any surgical intervention. If extensive surgical treatment is required, the possibility of temporary pacemaker placement should be considered based on indications. No antiarrhythmic therapy was deemed necessary at this time.

Laboratory findings indicated elevated creatinine (319 $\mu\text{mol/L}$) and urea (29 mmol/L) levels. Tacrolimus trough level on December 21, 2023, was 10.3 ng/mL. Kidney graft ultrasound on the same date showed no fluid accumulation in the transplant bed and no significant enlargement of the pelvicalyceal system. The kidney graft measured 99×57 mm, with clear and even contours. Doppler ultrasound revealed no signs of stenosis or thrombosis in the renal artery and vein, though cortical blood flow was somewhat reduced. The resistive index at the segmental arteries was 0.9. To determine the cause of graft dysfunction, a biopsy performed on December 21, 2023, confirmed acute tubular necrosis and signs of chronic transplant nephropathy, with no evidence of acute rejection. The findings suggested prerenal acute kidney injury and calcineurin inhibitor nephrotoxicity. Infusion therapy was initiated, and the tacrolimus dose was reduced. By discharge on December 29, 2023, creatinine and urea levels had improved to 146 $\mu\text{mol/L}$ and 13 mmol/L, respectively.

Lipid profile as of December 20, 2023, showed total triglycerides at 0.86 mmol/L, HDL at 1.45 mmol/L, LDL at 3.57 mmol/L, and total cholesterol at 5.11 mmol/L. Despite ongoing therapy with pitavastatin 4 mg and ezetimibe 10 mg, LDL cholesterol remained above target levels, necessitating an adjustment in lipid-lowering treatment. Considering the potential for drug interactions in a kidney transplant recipient, inclisiran was identified as the preferred therapeutic option.

Taking into account the history of post-transplant diabetes mellitus and the increase in fasting glucose levels to 7.9 mmol/L recorded during hospitalization, the patient was evaluated by an endocrinologist. As a result, dapagliflozin therapy at a dose of 10 mg once daily was prescribed, along with recommendations for a balanced diet with restricted intake of fast-digesting carbs.

A hepatology consultation was also conducted regarding liver cirrhosis secondary to chronic hepatitis C. Hepatobiliary ultrasound on December 24, 2023, revealed

diffuse liver changes characteristic of cirrhosis, signs of portal hypertension, liver asymmetry due to significant reduction in the left lobe, and a volumetric formation in segments 4–5, raising suspicion of hepatocellular carcinoma (HCC). Additionally, splenomegaly was noted.

An abdominal CT scan with intravenous contrast performed on December 25, 2023, showed a liver of normal size with an uneven, finely bumpy contour and normal density (55–65 HU). In the left lobe of the liver, early contrast enhancement of the portal vein branches was observed, indicative of arteriovenous shunting due to fibrotic changes. An inhomogeneous formation in segment 5 measuring 52×61 mm was identified, showing weak peripheral contrast uptake with washout in the delayed phase. No dilation of intrahepatic or extrahepatic bile ducts was noted. However, portogastric and portosplenic collaterals, as well as esophageal vein dilation, were present. The portal vein measured 19 mm (Fig. 1).

On December 26, 2023, the alpha-fetoprotein (AFP) level was 67.02 ng/mL. Based on the presence of cirrhosis, a characteristic CT appearance, and elevated AFP levels, a diagnosis of hepatocellular carcinoma (HCC) was established. Given the clear radiological and biochemical findings, a puncture biopsy was not indicated.

Laboratory tests on December 26, 2023, revealed an elevated alpha-fetoprotein (AFP) level of 67.02 ng/mL. Based on the presence of cirrhosis, a characteristic CT appearance, and increased AFP levels, HCC of the liver was diagnosed. A puncture biopsy was deemed unnecessary.

Due to the newly detected malignant tumor, an oncological consultation was held, and a PET/CT scan was recommended to assess the presence of distant metas-

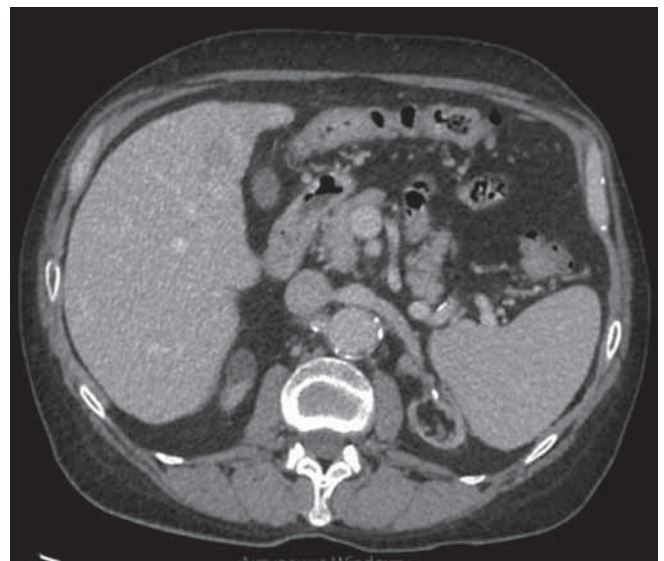


Fig. 1. Contrast-enhanced abdominal CT scan. Signs of liver cirrhosis, hepatocellular carcinoma, portal hypertension

tases. The PET/CT findings confirmed the absence of distant metastases.

According to current treatment guidelines for HCC, surgical intervention is the preferred approach in eligible patients. In cases of compensated liver cirrhosis (Child–Turcotte–Pugh (CTP) class A), both surgical resection and liver transplantation (LT) offer comparable long-term oncological outcomes. However, given the tumor's localization, achieving an R0 resection (complete removal with negative margins) would require extensive liver resection, posing a high risk of complications due to the underlying cirrhosis, potential liver decompensation, and worsening portal hypertension.

Furthermore, the tumor size exceeds the “Milan criteria”, which many transplant centers use as a benchmark for LT eligibility [9]. Nevertheless, the Metroticket 2.0 prognostic model estimates a five-year post-LT survival rate of 78.3%, which is considered an acceptable outcome [10]. Additionally, LT is acknowledged as the most suitable radical treatment of HCC for this patient because lifelong *de novo* immunosuppressive therapy is not required.

The patient was re-hospitalized on January 9, 2024, at Botkin Hospital for evaluation as a candidate for orthotopic liver transplantation (OLT). Comprehensive pre-transplant screening, including esophagogastroduodenoscopy, fibrocolonoscopy, and ultrasound of the lower limb veins, revealed no contraindications to OLT.

Given the patient's age and medical history – including stage 5 CKD, dyslipidemia, post-transplant diabetes mellitus, long-term smoking, arterial hypertension, and prolonged immunosuppressive therapy – a thorough cardiovascular assessment was warranted. A bicycle stress echocardiogram was performed, showing no initial signs of impaired local contractility. The end-diastolic volume was 95 mL, and the ejection fraction was 60%. At peak exercise, arrhythmias were recorded on ECG, including

unstable runs of supraventricular tachycardia (up to 6 complexes), ventricular extrasystoles, and one short (3-complex) unstable run of ventricular tachycardia. Following rhythm restoration, two zones of impaired local contractility were identified: hypokinesis of the basal and middle posterolateral segments, which were clinically painless.

Coronary angiography performed on January 1, 2024, revealed hemodynamically significant stenoses: 80% in the middle segment of the anterior descending artery, 70% in the proximal third of the right coronary artery, and a subtotal lesion of the posterior interventricular branch (Fig. 2, a). Based on these findings, the patient was diagnosed with coronary artery disease with painless myocardial ischemia.

Based on coronary angiography and stress echocardiography findings, a decision was made to proceed with percutaneous coronary intervention. Transluminal balloon angioplasty and stenting were performed on the posterior descending artery (PDA) and right coronary artery (RCA) using Promus Premier 2.25×28 mm and Promus Premier 4.0×28 mm stents, respectively, with a favorable angiographic outcome (Fig. 2, b).

To evaluate the functional significance of the atherosclerotic lesion in the anterior descending artery (ADA), another stress echo was conducted, yielding a negative result. No indications for additional revascularization were identified at the time of assessment. The patient was prescribed dual antiplatelet therapy (DAPT) for a minimum of three months.

The prolonged waiting time for transplantation due to coronary artery stenting and the need for DAPT posed a risk of tumor progression and potentially poor oncologic outcomes. Consequently, a decision was made to initiate bridge therapy. Selective transarterial chemoembolization (TACE) was chosen as the preferred method. The procedure was performed on January 16, 2024, using

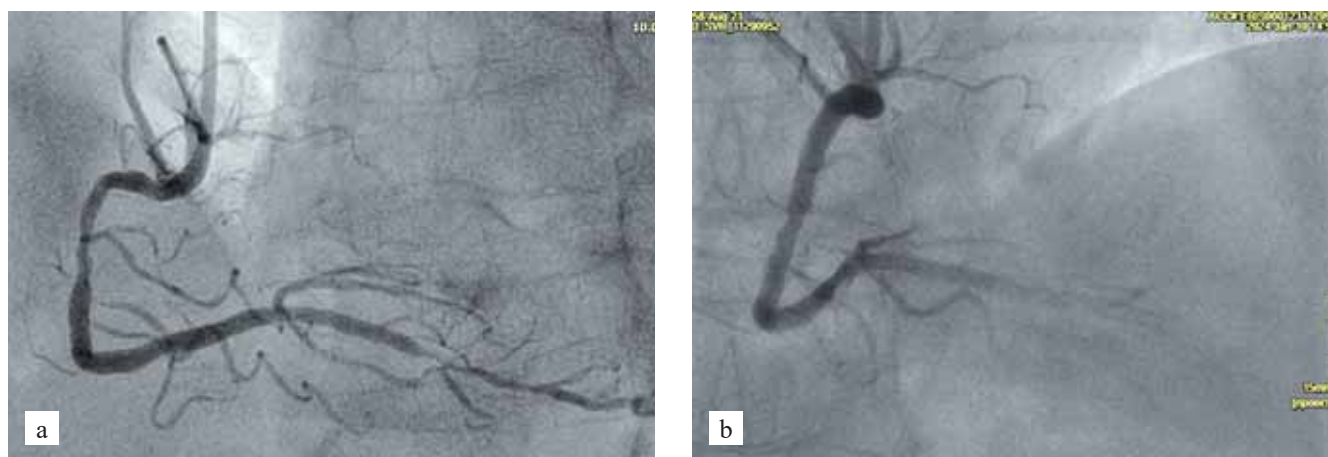


Fig. 2. Coronary angiogram: a, multilevel stenoses of RCA, PDA and ADA are detected; b, Promus Premier 2.25×28 mm and Promus Premier 4.0×28 mm coronary stents were positioned and implanted in the area of PDA and RCA stenoses

DC Bead microspheres (100–300 microns) loaded with doxorubicin (50 mg) to target the liver tumor. The angiographic findings are presented in Fig. 3.

Three months after undergoing percutaneous coronary intervention, the patient was placed on the active LT waiting list. A multidisciplinary consultation with a cardiologist, transplantologist, nephrologist, and hepatologist was conducted, leading to adjustments in the immunosuppressive therapy regimen, including the withdrawal of mycophenolic acid preparations in preparation for extensive surgery. Kidney transplant function was satisfactory.



Fig. 3. Selective transarterial chemoembolization of liver tumor



Fig. 4. Dual hypothermic oxygenated machine perfusion (DHOPE)

LIVER TRANSPLANTATION

On May 18, 2024, the transplant ward was notified of a potential brain-dead donor. The donor was a 66-year-old man, 180 cm tall and weighing 92 kg, who had died from acute ischemic stroke. Laboratory parameters, including aspartate transaminase (AST), alanine transaminase (ALT), total bilirubin, creatinine, and urea levels, were within normal limits. The donor had been on mechanical ventilation for 72 hours.

During visual assessment at multi-organ retrieval, the liver appeared medium-sized, with a smooth, shiny surface and a yellowish trace upon palpation. Its consistency was dense and elastic, and vascular anatomy was standard (Michel's type I). Instant histopathology revealed macrovesicular steatosis of 40–50%. The organ was deemed suitable for transplantation and was immediately offered to the patient (Fig. 4).

Given the donor's classification as suboptimal and the borderline characteristics of the liver graft, indications were established for dual hypothermic oxygenated perfusion (DHOPE) using a heart-lung machine upon organ delivery to the transplant ward's operating room. The total cold ischemia time was 5 hours and 13 minutes, with the final 2 hours and 10 minutes dedicated to DHOPE. Perfusate AST and ALT levels at 30 minutes of perfusion were 934 U/L and 523 U/L, respectively.

During surgical planning, it was evident that complete inferior vena cava (IVC) clamping, as required in the classical OLT technique, could cause significant hemodynamic instability in a patient with a complex cardiac history. To mitigate this risk, a decision was made to perform hepatectomy while preserving the IVC, followed by caval reconstruction using the Belghiti technique (Fig. 5).

Hepatectomy was performed without technical difficulties. The graft was placed into the surgical field, and

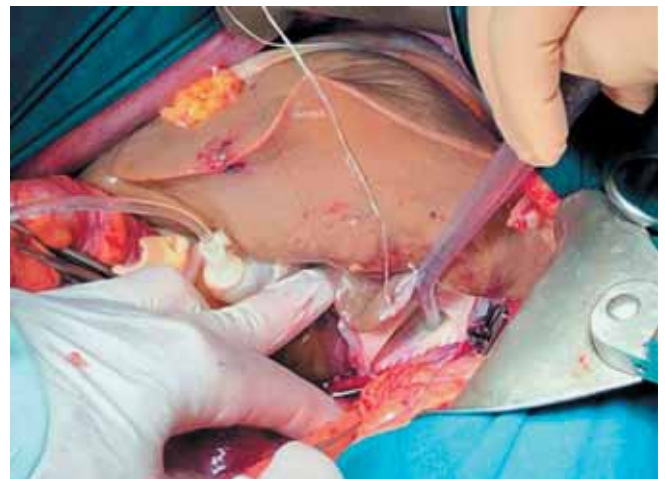


Fig. 5. Liver transplantation: caval reconstruction using the Belghiti technique

sequential anastomoses of the IVC and portal vein were completed. Following an intravenous injection of methylprednisolone 500 mg, reperfusion was initiated. The liver rapidly turned cherry-colored and exhibited satisfactory turgor, with no signs of postreperfusion syndrome.

Arterial reconstruction was performed using an end-to-end technique with ligation of the gastroduodenal artery. Biliary reconstruction was completed via end-to-end choledochoduodenostomy with interrupted PDS 6-0 sutures. The surgery lasted 5 hours and 38 minutes, with a total blood loss of 900 mL. The early postoperative period was uneventful, and the patient stayed in the intensive care unit for 48 hours. Peak AST and ALT levels reached 1232 U/L and 1923 U/L, respectively, indicating a moderate degree of ischemia-reperfusion injury. No signs of early graft dysfunction were observed. Immunosuppressive therapy followed a standard protocol, with basiliximab induction and reintroduction of prolonged-release tacrolimus from postoperative day 3. The total hospital stay was 13 days, with both grafts functioning satisfactorily.

Three weeks after wound healing, mTOR inhibitor everolimus was introduced into the immunosuppressive regimen, maintaining a target level of 4–6 ng/mL, while the tacrolimus target level was reduced to 3–5 ng/mL. Oral methylprednisolone therapy was continued at 4 mg once daily.

RESULTS

At 3-month follow-up, the patient remained in stable and satisfactory condition with no complaints. Despite prior interventions and a complex comorbid background, he maintains an active lifestyle. Liver and kidney transplant functions were stable, with a creatinine level of 120 μ mol/L and an AFP level of 4 ng/mL. A contrast-enhanced abdominal CT scan revealed no signs of recurrent HCC.

DISCUSSION

This clinical case illustrates the complex medical journey of a patient whose prognosis would have been extremely poor without comprehensive and well-coordinated care. Long-standing uncontrolled hypertension led to nephroangiosclerosis and, ultimately, end-stage CKD. KT was the optimal treatment, allowing the patient to regain a high quality of life for over eight years – an outcome unlikely to be achieved with chronic hemodialysis.

However, prolonged immunosuppressive therapy, despite adequate prophylaxis, contributed to the development of obstructive coronary artery disease (CAD), diabetes mellitus, and the progression of chronic hepatitis C to cirrhosis and HCC. During hospitalization for cardiovascular pathology, the patient required a multidisciplinary care from at least seven specialists, including

a cardiologist, transplant surgeon, hepatologist, nephrologist, endocrinologist, oncologist, and interventional radiologist. These specialists not only managed existing conditions but also diagnosed two additional life-threatening diseases: multivessel CAD with hemodynamically significant stenoses and a malignant liver tumor.

LT was identified as the optimal treatment for cirrhosis and HCC, but proceeding without prior correction of obstructive CAD would have posed a high risk of cardiovascular complications. The use of minimally invasive percutaneous coronary intervention provided effective treatment and rapid rehabilitation. Moreover, bridge therapy with TACE controlled tumor progression, allowing LT to be performed within acceptable criteria and ensuring favorable overall and recurrence-free survival.

Solid organ recipients face a heightened risk of specific complications, stemming both from their underlying disease and the long-term immunosuppressive regimen. In response, the global trend is shifting toward integrating transplant programs within multidisciplinary hospitals, where patients can receive comprehensive, specialized care across multiple medical disciplines simultaneously [11].

Organ transplantation is no longer confined to isolated, highly specialized institutions; it has evolved into a high-tech yet accessible therapeutic option for patients. However, availability of transplant care remains closely tied to efficient organization of organ donation processes and adoption of advanced technologies that maximize the viability of each organ. In this case, the use of cold oxygenated perfusion played a crucial role in reducing the risk of early graft dysfunction and primary non-function, ensuring the successful transplantation of an organ from a suboptimal donor.

CONCLUSION

Transplantation is a highly effective treatment for end-stage diseases of various organ systems. However, solid organ transplant recipients face an elevated risk of complications due to both the underlying disease that necessitated the transplant and the lifelong need for immunosuppressive medications. Prevention and management of these complications represent a primary challenge that requires a coordinated effort from a multidisciplinary team of specialists.

The authors declare no conflict of interest.

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