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PEDIATRIC HEART TRANSPLANTATION AFTER A FONTAN PROCEDURE

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The Fontan procedure is a surgical technique used for hemodynamic correction of complex congenital heart defects (CHDs), and is used when radical correction of CHDs is anatomically impossible. In the long term – from 10 to 20 years – Fontan circulation can lead to "failing Fontan" characterized by heart failure symptoms, requiring adjustments to medical treatment and potentially surgical interventions, including heart transplantation (HT). Foreign studies indicate that HT is an effective method for prolonging life in patients with failing Fontan circulation. It stabilizes the patient's condition. This paper presents the first documented case of HT in a child following a Fontan procedure in the Russian Federation.

Keywords: heart transplantation, Fontan procedure, protein-losing enteropathy.

INTRODUCTION

The Fontan procedure is a hemodynamic, palliative surgical procedure designed to direct systemic venous blood flow to the pulmonary arteries bypassing the ventricle. It is typically performed for a range of complex congenital heart defects [1]. While the procedure often yields satisfactory medium- and long-term outcomes, it remains inherently palliative [2, 3]. Establishing univentricular circulation can significantly extend life expectancy; however, patients remain at lifelong risk for serious complications, including systemic ventricular dysfunction, arrhythmias, chronic hypoxia, thromboembolic events, protein-losing enteropathy (PLE), and plastic bronchitis. These complications can impair central hemodynamics, culminating in the development of the so-called "Failing Fontan" syndrome [4, 5]. According to published data, the incidence of heart failure after a Fontan procedure is 7% at 20 years, rising to 38% by the age of 40 [6].

Treatment strategies vary and include pharmacological management, endovascular interventions, and surgical procedures [7, 8]. Among the most advanced surgical options are left ventricular assist device implantation as a bridge to transplantation and orthotopic heart transplantation (HT). With improvements in surgical techniques for congenital heart defects, the number of people living with Fontan physiology has steadily increased, making the issue of failing Fontan increasingly relevant and urgent [9, 10].

However, HT in this patient population poses unique technical and clinical challenges, largely due to the complex surgical interventions performed before Fontan hemodynamic correction. Despite these complexities, numerous case series and observational studies in the international literature report encouraging outcomes in such patients. A meta-analysis of 426 Fontan patients who underwent HT revealed 1- and 5-year post-HT survival rates of 79.9% and 76.7%, respectively. The analysis encompassed studies conducted over a 22-year period, indicating that HT is a viable and effective treatment for this patient cohort, offering acceptable risk profiles and survival outcomes [11].

To date, no cases of HT for failing Fontan have been registered in Russia. Therefore, the present clinical case represents the first documented experience in the country.

OBJECTIVE

To present the first documented case of HT following a previously performed Fontan procedure in the Russian Federation.

CLINICAL REVIEW

Patient background

Patient P., a 14-year-old male, has been seen by a cardiologist at his place of residence since birth. He was initially evaluated and followed at Bakulev National Medical Research Center for Cardiovascular Surgery in Moscow for congenital heart disease: common atrioventricular canal, double outlet right ventricle, hypoplastic left heart syndrome, ventricular septal defect, and left pulmonary artery hypoplasia (Fig. 1).

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Beginning in 2010, the patient underwent multiple staged palliative surgical interventions, including: modified Blalock–Taussig subclavian-to-pulmonary anastomosis on the left using a PTFE (polytetrafluoroethylene) graft; bidirectional cavopulmonary anastomosis on the right side; pulmonary artery branch plasty and ligation of the main pulmonary artery under cardiopulmonary bypass (CPB); transluminal balloon angioplasty of the left pulmonary artery; embolization of major aortopulmonary collaterals (MAPCAs); left pulmonary artery stenting (Fig. 2); MAPCAs embolization. The Fontan procedure, representing the final stage of this palliative strategy, was performed subsequently. In February 2019, the patient underwent cardiac catheterization with intravascular ultrasound of the stent in the left pulmonary artery.

A decision was made to perform a hybrid surgical intervention under intensive care unit (ICU) conditions: Fontan procedure with extracardiac conduit modification, combined with transluminal balloon angioplasty of the left pulmonary artery stent.

In the early postoperative period, the patient developed signs of cardiopulmonary insufficiency, as well as prolonged transudation through the drainage systems, which required intensive pharmacological support.

Following discharge, the child remained under close surveillance by local cardiologists and specialists at Bakulev National Medical Research Center for Cardiovascular Surgery.

About 3 years after the Fontan procedure, the patient began to exhibit signs consistent with the failing Fontan syndrome, including: frequent watery stools (3–4 times daily for over one month), abdominal pain, and intermittent episodes of vomiting. The patient was hospitalized at the Russian Children's Clinical Hospital in response to these symptoms. Physical examination and diagnostic workup revealed: hepatomegaly (+2 cm below the costal margin), peripheral edema (notably in the shin), Signs of ascites, laboratory PLE (total serum protein – 42 g/L, serum albumin – 23 g/L), elevated fecal alpha-1-antitrypsin – >2250 mg/L, fecal calprotectin – 789 mg/kg (Fig. 3). Symptomatic therapy was administered. Due to

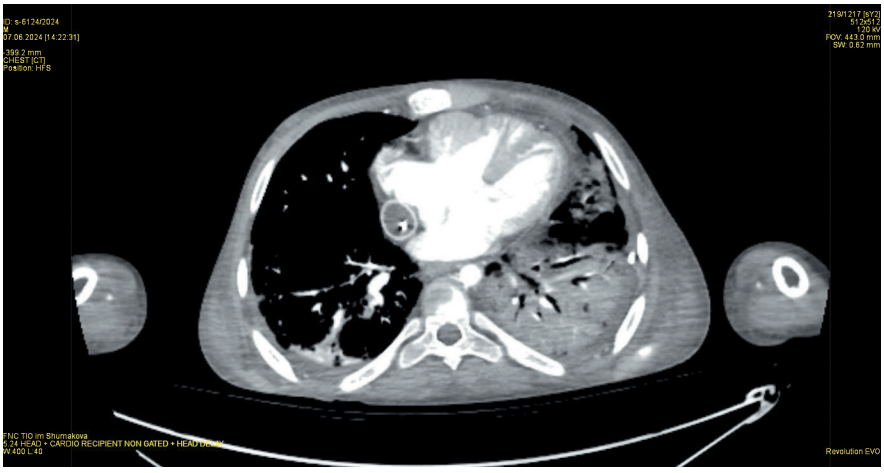

Fig. 1. Assessment of anatomy at the time of admission at Shumakov National Medical Research Center of Transplantology and Artificial Organs

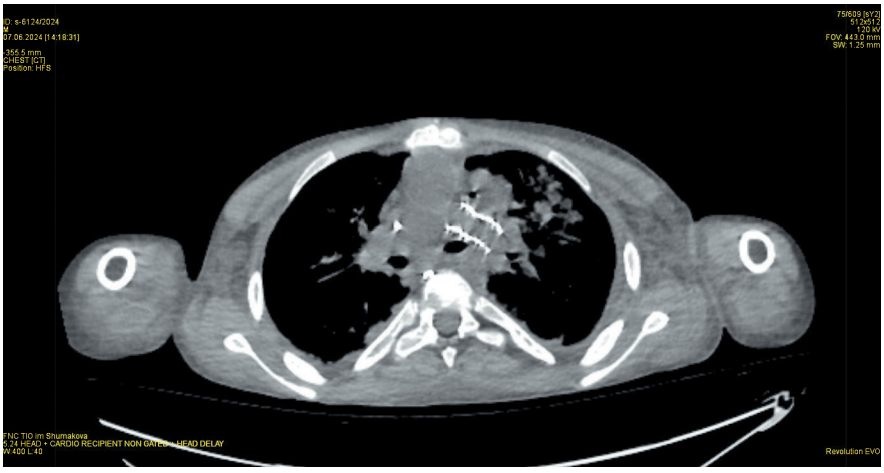

Fig. 2. Stent in the left pulmonary artery

the progressive accumulation of ascitic fluid, the patient underwent laparocentesis.

During inpatient treatment, two episodes of gastrointestinal bleeding were observed. These were attributed to hemostatic dysfunction, likely secondary to PLE. The bleeding episodes led to a critical drop in hemoglobin levels to 29 g/l. Management included multiple transfusions of erythrocyte suspensions, which contributed to clinical stabilization. Following improvement, the patient was discharged home, but recurrent symptoms necessitated readmission at Sukhanov Federal Center for Cardiovascular Surgery in Perm. There, cardiac catheterization was performed to assess Fontan circuit function. Based on the findings, it was decided to perform the following: stenting of the Fontan fenestration, and transluminal balloon angioplasty of the previously placed left pulmonary artery stent. The intervention was successful, and the patient was discharged in stable condition with positive clinical dynamics.

About six months later, the patient's condition deteriorated, with increasing weakness and dyspnea. He was hospitalized in Rostov-on-Don due to signs of worsening cardiovascular insufficiency. Clinical evaluation revealed severe hypoproteinemia and hypoalbuminemia, hemostatic abnormalities, and acid-base and electrolyte imbalance.

Due to unstable hemodynamics, arterial hypotension, and progressive edematous syndrome, the patient was transferred to the ICU, where cardiotonic therapy was initiated. Given the absence of viable options for further surgical correction, a decision was made to transfer the child to Shumakov National Medical Research Center of Transplantology and Artificial Organs. Upon admission to the ICU at Shumakov Center, the following diagnosis was confirmed: PLE following Fontan surgery with signs of decompensation, consistent with the failing Fontan clinical syndrome.

Echocardiographic findings on admission revealed moderately reduced ejection fraction (35–40%) of the single functioning ventricle, despite ongoing inotropic support.

A multidisciplinary council concluded that due to the prolonged course of PLE with signs of progressive decompensation and refractoriness to medical management, the patient was indicated for HT. He was subsequently placed on the emergency HT waiting list.

Heart transplantation and postoperative period

On June 8, 2024, the patient (initial weight: 40 kg, height: 160 cm) underwent orthotopic HT using the bicaval technique. The donor was a 27-year-old male with a weight of 90 kg. The cause of brain death was hemorrhagic stroke. The optimal donor was identified on day 3 following inclusion on the emergency transplant waiting list.

Graft ischemia time was 252 minutes, while CPB lasted for 177 minutes. Preoperative imaging and examination revealed two potential risk factors for perioperative and postoperative complications: tight adhesion of the aorta to the posterior surface of the sternum and narrowing of the left main bronchus, secondary to the presence of a stent in the pulmonary artery, respectively (see Fig. 4, Fig. 5, Fig. 6).

Despite the posterior position of the aorta, resternotomy proceeded without complications. However, pronounced adhesions in the mediastinum made surgical dissection challenging. The left innominate vein, in particular, was firmly adherent to the posterior sternal wall, making it difficult to isolate. Due to elevated venous pressure and thinning of the vessel wall, even minor trauma to the vein resulted in significant bleeding. One such major injury led to profuse hemorrhage, which was successfully controlled without the need for peripheral CPB initiation.

After prolonged cardiolysis, cannulation of the aorta, superior vena cava, and inferior vena cava was achieved, and CPB was initiated. Further cardiolysis in the region of the pulmonary artery branches and aorta was performed after establishing CPB.

Once aortic clamping was feasible, the recipient heart was explanted. Despite a history of MAPCA closure and no significant recanalization or MAPCA development

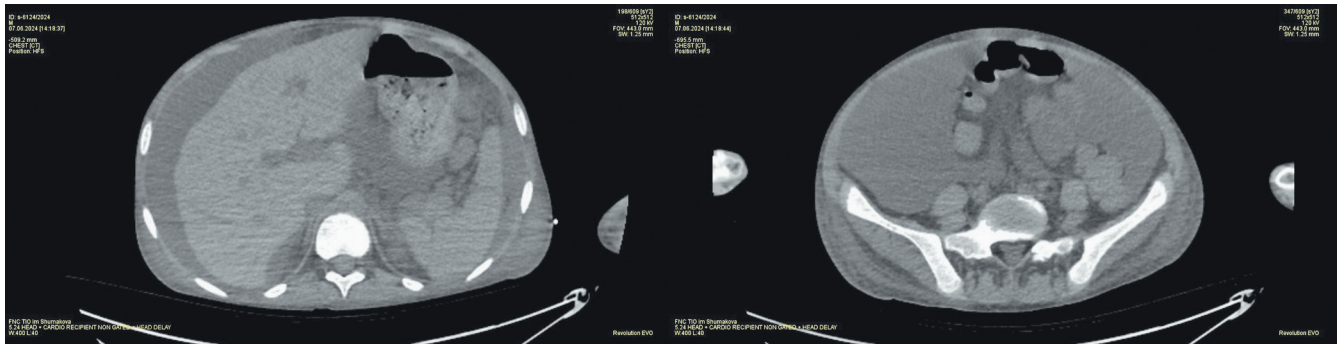

Fig. 3. Severe ascites

on preoperative CT, there was substantial pulmonary venous return, which complicated cardiac excision. The extracardiac conduit was then severed from the inferior surface of the right pulmonary artery, and the superior cavopulmonary anastomosis was also divided.

The resulting defects were combined into a single defect, which was then repaired using a xenopericardial patch. This stage was further complicated by pronounced blood return from the pulmonary arteries. Given the prolonged ischemia time and the stable, optimal positioning of the stent in the left pulmonary artery, the decision was made not to explant the stent, despite the potential for postoperative compression of the left main bronchus.

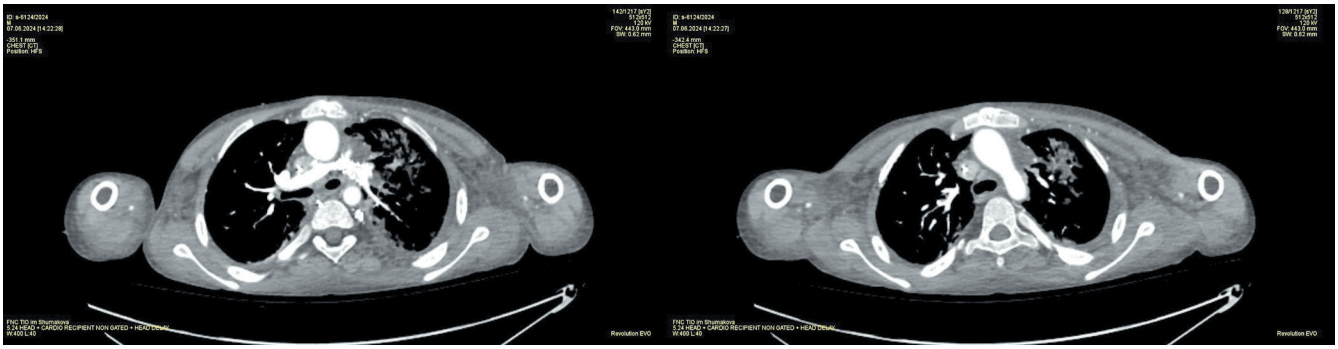

Fig. 4. Retrosternal location of the aorta

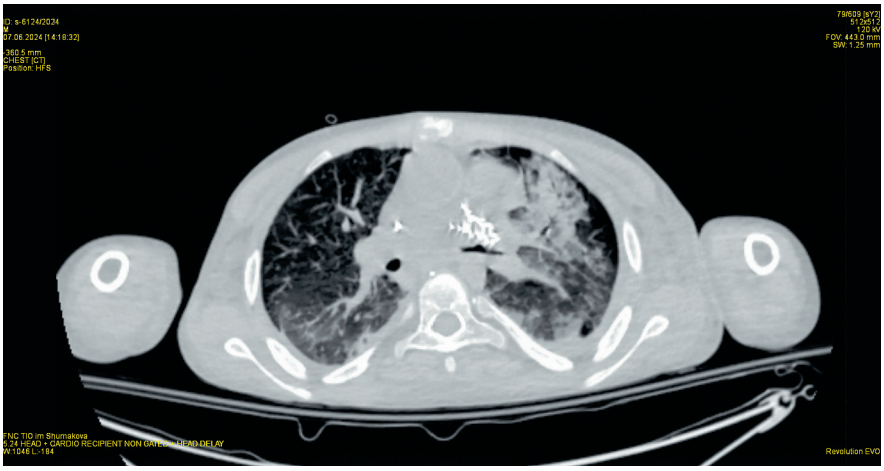

Fig. 5. Narrowing of the left main bronchus due to a neighbouring stent in the left pulmonary artery, before transplantation

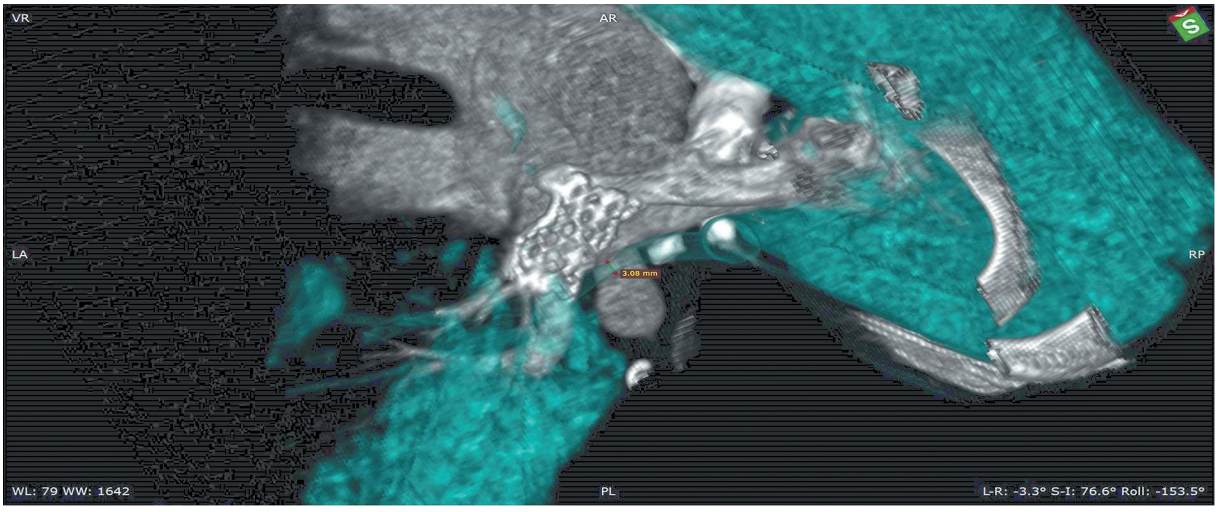

Fig. 6. 3D model of left main bronchus stenosis before transplantation

Graft implantation proceeded in the following sequence: left atrium, pulmonary artery, inferior vena cava, superior vena cava, and aorta. After aortic clamp removal, transesophageal echocardiography confirmed good graft function. The sternum was sutured immediately. The total duration from skin incision to skin closure was 6 hours.

In the immediate postoperative period, inotropic support with dobutamine was initiated at 2 mcg/kg/min, with gradual tapering as myocardial function stabilized and signs of graft insufficiency resolved. Basiliximab was administered as induction therapy in accordance with current guidelines for the management of patients following HT.

Given the presence of preoperative risk factors, the patient underwent fibrobronchoscopy prior to tracheal extubation, which revealed narrowing of the left main bronchus with a pulsating structure along the anterior bronchial wall (Fig. 7). The most likely cause of this finding was the presence of a stent in the left pulmonary artery. The total duration of mechanical ventilation was 26 hours. Following extubation, the patient developed dyspnea and worsening respiratory insufficiency, particularly in the supine position (Fig. 8).

Due to the clinical signs of respiratory failure, the radiographic evidence of atelectasis, and the bronchoscopic confirmation of bronchial narrowing, a CT scan was performed to assess the extent of bronchial stenosis and determine the feasibility of stent placement in the left main bronchus (Fig. 9).

Following the imaging assessment, endoscopic stenting of the left main bronchus was successfully performed using a nitinol stent with an 8 mm diameter (Fig. 10). The patient was transferred to the cardiothoracic department on postoperative day 10 for continued monitoring and treatment.

At the time of transfer, echocardiography revealed satisfactory global systolic function of the left ventricle,

Fig. 7. Fibrobronchoscopy before extubation showing compression of the left main bronchus along the anterior wall

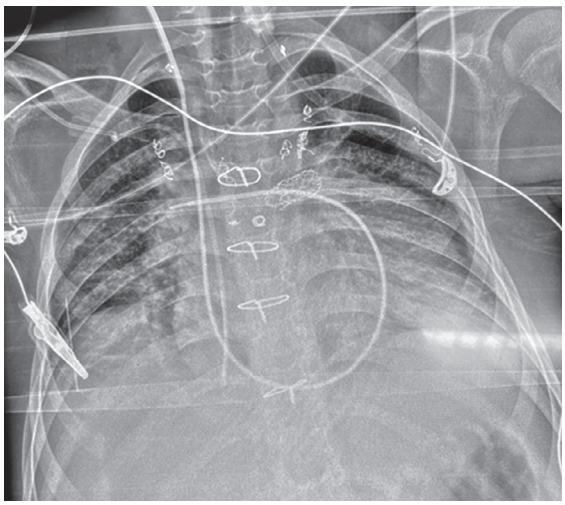

Fig. 8. Pneumonography immediately after extubation

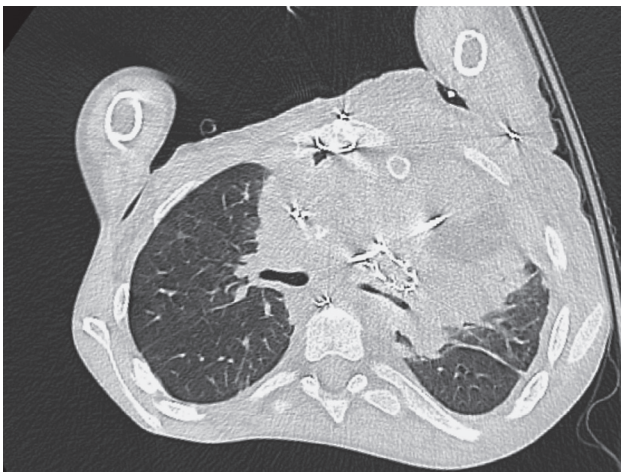

Fig. 9. Computed tomography assessing bronchial narrowing and feasibility of stenting

with a left ventricular ejection fraction (LVEF) of 64%. Dobutamine inotropic support was discontinued on postoperative day 5 in the ICU.

A triple-drug immunosuppressive maintenance regimen was initiated, consisting of a calcineurin inhibitor (tacrolimus), an antimetabolite (mycophenolate mofetil), and corticosteroids (methylprednisolone).

To monitor for cardiac graft rejection and evaluate for donor-transmitted coronary artery disease, both coronary angiography and endomyocardial biopsy were performed. It revealed no signs of acute cellular or antibody-mediated rejection of the cardiac graft. Additionally, coronary angiography showed no stenotic lesions in the coronary arteries of the transplanted heart.

During postoperative week 1, serum levels of total protein and albumin normalized, and diarrheal episodes resolved. However, 10 days after transfer to the general ward, there was a decline in total protein and albumin levels (to 34 g/L and 19 g/L, respectively), along with reappearance of loose stools. This clinical presentation was regarded as recurrent PLE.

A comprehensive evaluation was conducted to exclude alternative causes of the recurrent PLE. Symptomatic therapy and a fat-free diet were initiated. During hospitalization, serial assessments were performed to monitor the bronchial stent position and presence of granulations in the left main bronchus.

At three months post-stenting, a scheduled removal of the stent from the left main bronchus was successfully

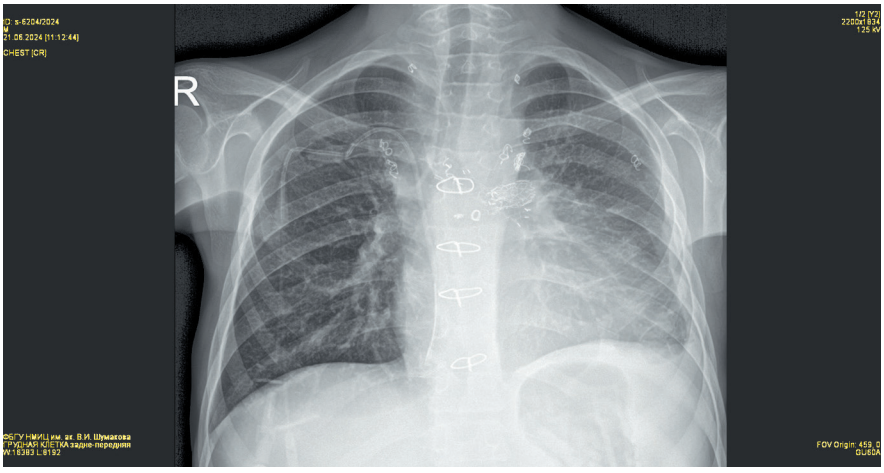

Fig. 10. Pneumonography after stenting of the left main bronchus

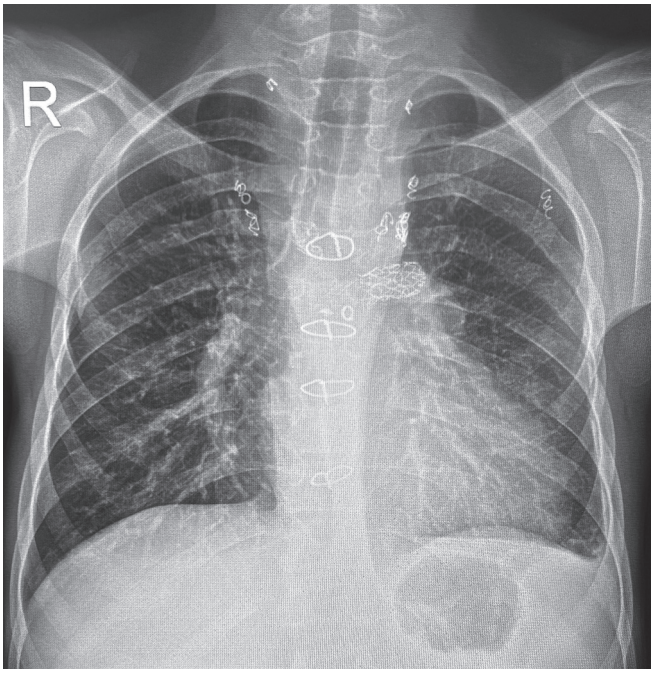

Fig. 11. Pneumonography after stent retrieval from the left main bronchus

performed (Fig. 11). Postoperative bronchoscopy revealed that the structural patency of the left main bronchus was preserved. In the context of ongoing therapy for PLE and adherence to a fat-free diet, albumin infusions were discontinued on day 174 post-transplant due to stable laboratory values of total protein and albumin. However, subsequent monitoring showed a moderate decline in these parameters.

At the time of discharge (on day 201 post-transplant) from Shumakov National Medical Research Center of Transplantology and Artificial Organs, the patient demonstrated no clinical or echocardiographic evidence of cardiac graft dysfunction. Final laboratory values at discharge were: total protein – 57.2 g/L, and albumin – 35.5 g/L.

DISCUSSION

Patients with failing Fontan can be broadly categorized into two groups based on the underlying cause: reduced ventricular function (RVF), and impaired Fontan hemodynamics (IFH). RVF is typically defined as a single ventricular ejection fraction less than 30%. On the

other hand, IFH refers to a constellation of clinical and hemodynamic abnormalities despite preserved ventricular function. Conditions that suggest IFH include severe growth retardation, impaired systolic function with evidence of low cardiac output, PLE, plastic bronchitis; Fontan-associated liver disease, and pulmonary arteriovenous malformations [12, 13]. PLE is specifically defined as hypoalbuminemia (albumin <30 g/L) lasting more than 3 months, accompanied by clinical signs or symptoms like ascites, pleural effusion, edema, diarrhea, or abdominal pain, persisting for more than 3 months [14]. In our case, the primary indication for HT was the development of severe PLE. The interval between the Fontan procedure and the onset of PLE was 3 years, 6 months, and 5 days.

A review of several multicenter studies involving patients with failing Fontan who underwent HT revealed in-hospital and early mortality rates ranging from 15% to 23% in cohorts of over 70 patients [15–18]. However, our single case report does not permit definitive conclusions regarding these outcomes.

According to a 2006 multicenter study, more than 60% of patients with failing Fontan underwent HT within 6 months of clinical deterioration. In our observation, the waiting list duration was only 3 days. Following transplantation, albumin levels normalized within 30 days, consistent with previous findings in PLE patients [16].

In our observation, normalization of total protein and albumin levels, as well as cessation of diarrhea, occurred during the first week following HT. However, 10 days after transfer to the ward, there was a decline in total protein and albumin levels (to 34 g/L and 19 g/L, respectively), accompanied by reappearance of liquid stools. This clinical presentation was regarded as a recurrent PLE.

According to a study involving 7 individuals who experienced recurrent PLE after HT, the primary causes identified included acute or chronic rejection, graft dysfunction, anastomotic site stenosis, vascular thrombosis, infectious complications (including cytomegalovirus enteritis), and post-transplant lymphoproliferative disorders [19]. All possible causes of the recurrent PLE were excluded. Symptomatic therapy and a fat-free diet were initiated. At present, the patient demonstrates positive clinical dynamics, evidenced by a gradual increase in total protein and albumin levels.

Some studies have reported an association between shorter waiting list times and more rapid normalization of protein and albumin levels, suggesting that a shorter time on the transplant waiting list may be linked to faster recovery of these parameters post-transplant [14]. In our case, however, despite the exceptionally short waiting period (3 days), normalization of protein and albumin levels after relapse required more than 6 months, indicating a prolonged recovery.

It is important to note that this patient cohort – although quite common – often lacks early diagnosis, which can delay listing for transplantation. In our observation, about 5 months after transplantation, echocardiography confirmed satisfactory graft function, with an LVEF of 64%, and no episodes of pulmonary hypertension were observed. No episodes of rejection were recorded in the patient during the 7-month follow-up period.

Two studies assessing 1- and 5-year survival rates after HT in patients with failing Fontan were reviewed. The first study, covering the period from 1990 to 2002, demonstrated lower survival rates in the Fontan group compared to those without prior Fontan surgery: 1-year survival was 71% in the Fontan group versus 83% in the non-Fontan group, while 5-year survival was 60% versus 74%, respectively. In contrast, a more recent study spanning 22 years reported improved outcomes, with 1-year and 5-year survival rates of 79.9% and 76.7%, respectively, in patients who underwent HT for a failing Fontan [11, 15]. These data suggest that careful patient selection, early referral for surgical intervention prior to the onset of irreversible target organ damage, and the use of lower-intensity initial immunosuppressive regimens may significantly enhance post-transplant survival in this high-risk population [11, 14, 15, 20].

CONCLUSION

Our clinical case shows the feasibility and potential success of HT in patients with a failing Fontan, even in the presence of significant technical challenges and frequent preoperative decompensation. However, it is important to recognize that the resolution of associated complications, such as PLE, may be prolonged – even in the absence of identifiable precipitating factors.

The authors declare no conflict of interest.

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