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Liver-only Transplantation in a Patient With Complex Congenital Heart Disease: Case Report and Review of the Literature

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Background. Patients with liver failure due to or in addition to congenital heart disease (CHD) represent a growing population in need of organ transplantation. Traditionally, these patients received a combined heart and liver transplantation carrying a high risk of perioperative morbidity and mortality. **Methods.** We discuss a patient with complex cyanotic CHD and biliary atresia undergoing liver-only transplantation. Furthermore, a literature study was performed on combined congenital heart and liver disease in the setting of transplantation. **Results.** We describe a unique case of a patient with severe CHD undergoing orthotopic liver transplantation for biliary atresia. In the literature, congenital malformations affecting different organs seems not that infrequent. Liver-only transplantation has been described in mild CHD, although data in adult patients are scarce. In severe CHD, the liver usually suffers from congestion. The severity of liver disease and reversibility should be estimated to decide on combined heart-liver transplantation. **Conclusions.** Our case and a review of the literature demonstrate that a patient-tailored approach with liver-only transplantation may be an appropriate alternative to combined heart and liver transplantation in selected cases.

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INTRODUCTION

Because of the advances in the treatment of pediatric patients with severe congenital heart and liver disease, life expectancy of these patients nowadays transcends childhood.[1] Therefore, transplant programs are increasingly confronted with adult patients suffering from congenital defects. These patients are particularly challenging as frequently, congenital disease is not restricted to only 1 organ. As an example, patients with severe congenital heart disease (CHD), especially patients with a total cavopulmonary anastomosis (Fontan circulation), can develop congestive hepatopathy and even cardiac cirrhosis. In the end stage, these patients may require both heart and liver transplantation.[2] It is commonly accepted that in patients with total cavopulmonary anastomosis and advanced liver disease, a combined transplantation is indicated, since a heart-only transplantation can cause acute-on-chronic liver failure and the reversibility of liver disease is frequently difficult to predict. Likewise, a liver-only transplantation is contraindicated as the cause of liver disease would be left untreated.[3]

In another group of patients, congenital disease simultaneously affects different organs independently from each other. Biliary atresia and the Alagille syndrome belong to the leading indications for orthotopic liver transplantation (OLT) in children. Notably, biliary atresia is associated with CHD in 15% of the cases and Alagille syndrome in 24% of cases, whereas the overall incidence of CHD in the general population is only around 0.8%.[4,5]

We present a case of a patient with complex CHD and biliary atresia, in which a liver-only transplantation was performed. The patient gave informed consent and for this study approval from the ethics' board was not necessary.

CASE

A 26-year-old woman with a history of complex CHD and biliary atresia was referred to our hospital for combined heart-liver transplantation (CHLT).

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She had a history of transposition of the great arteries, ventricular septal defect, severe pulmonary stenosis, and a straddling tricuspid valve. After placement of bilateral modified Blalock Taussig Thomas shunts at 0 and 4 years of age, she had undergone a bidirectional cavopulmonary connection ("Glenn-circulation") at 11 years of age. Fontan completion had never been performed since she was doing well, and the pulmonary circulation was protected from systemic pressures by the pulmonary valve stenosis. Moreover, a Fontan completion would have inevitably increased downstream pressure for the liver. The latter was affected by congenital biliary atresia necessitating a hepatoportoenterostomy ("Kasai procedure") when she had been 1 year old. During the last 2 years before presentation, she had developed recurrent attacks of cholangitis with need for hospitalization and intravenous antibiotic therapy. Furthermore, in the preceding 6 months, the patient had developed jaundice with refractory pruritus. Given the frequent attacks of cholangitis, the patient was considered for liver transplantation. Preoperatively, she had mild cholestasis, a total bilirubin level of 1.25 mg/dL and a normal creatinine level. She had an MELD score of only 8. A preoperative ultrasound showed signs of fibrosis but normal portal, venous, and arterial flow. Magnetic resonance imaging showed irregular and dilated intrahepatic bile ducts but no suspected lesions. A liver biopsy was not performed.

After careful consideration by a multidisciplinary team (hepatologists, transplant surgeons, cardiac anesthesiologists, congenital cardiac surgeons, and cardiologists), we decided that in the particular situation of the patient, a liver-only transplant was a better option than a combined heart-liver transplant.

From a cardiac perspective, she was in NYHA class I with an oxygen saturation of 88% at rest and had a normal sinus rhythm on ECG. Echocardiography showed a normal biventricular systolic function, a nonrestrictive ventricular septal defect, moderate tricuspid valve regurgitation, a peak instantaneous gradient across the pulmonary valve of >90 mm Hg, and a patent Glenn anastomosis. Exercise testing showed a peak oxygen consumption of 15.3 mL/min/kg (or 52% predicted) with normal evolution of heart rhythm and blood pressure. Serum levels of NTproBNP were 508 ng/L. Cardiac catheterization showed a ventricular end-diastolic pressure of 11 mm Hg, a pulmonary capillary wedge pressure of 17 mm Hg, mean pulmonary artery pressure of 19 mm Hg, right atrial pressure of 8 mm Hg, and a pressure in the Glenn circuit of 16 mm Hg.

As such, her condition could be entirely attributed to the consequences of a failing Kasai with associated recurrent cholangitis. We, therefore, opted for a liver-only transplantation for several reasons: (1) the patient had an overall acceptable cardiac function with expected good long-term outcome, (2) absence of prominent hepatic congestion, and (3) higher upfront risk and nonsuperior long-term outcome of a combined heart-liver transplant. Concerns included cardiac performance during liver transplantation, paradoxical embolization perioperatively, and reperfusion injury of the donor liver.

After 8 months on the waiting list, the patient was successfully transplanted using a conventional caval reconstruction technique with the use of veno-venous extracorporeal membrane oxygenation. For the latter, the outflow cannula was inserted in the left axillary vein, and the inflow cannula was placed in the inferior caval vein. In our center, liver transplants are routinely performed with the use of veno-venous bypass during the anhepatic phase to decrease venous congestion. In this particular patient, we used veno-venous extracorporeal membrane oxygenation to additionally safeguard oxygenation and ventilation and consequently, low pulmonary vascular resistance. Moreover, use of the ECMO would have ensured lung perfusion with oxygenated blood via the Glenn anastomosis in case of sudden pulmonary arterial hypertension (eg, during reperfusion of the liver). Hemodynamic stability was achieved by the administration of in total 4000 mL balanced crystalloid infusions and 1500 mL human albumin 5%. No blood products had to be transfused. During the operation, the patient received a continuous infusion with norepinephrine 0.05–0.15 μg kg^{-1} min^{-1}. The patient's cardiac status was monitored during the transplantation with transesophageal echocardiography; this showed no significant changes in cardiac function and hemodynamics during the procedure. During the procedure, there were neither surgical nor cardiac complications. The venous cannulas could be removed at completion of the arterial anastomosis. At the end of surgery, the patient was tracheally extubated in the OR and admitted to the intensive care unit. She recuperated well and was discharged from the ICU after 4 days. After 8 days on the regular surgical ward, she was discharged home. There were no serious complications during her recovery, and her cardiac situation remained stable. The pathology report of the explant liver described typical signs of congenital bile duct atresia and no signs of congestion. Now—17 months after surgery—she remains in good general health. Liver function is good without any episodes of cholangitis. A routine MRI of the liver 1 year postoperatively showed no bile duct abnormalities and a good vascular status of the liver. Following liver transplantation, when the hepatic failure physiology was reversed, she remained in NYHA class I. We observed no change in biventricular systolic function with stable moderate tricuspid valve regurgitation at 6 and 12 months.

DISCUSSION

To the best of our knowledge, this is the first report of a patient with cyanotic CHD palliated with a bidirectional Glenn undergoing liver-only transplantation.

Several authors have described liver-only transplantation in pediatric patients with CHD. Similar to our patient, most of these cases had an indication for OLT due to biliary disease. However, the majority of these patients suffered only from mild-cardiac disease.

In a cohort study comparing perioperative outcome of OLT in pediatric patients *with* (n = 41) and *without* (n = 181) minor CHD (shunt lesions and obstructive lesions, no major defects), there was no difference in outcome including the incidence of graft failure, graft rejection, surgical complications, and infections.[6] There was no difference in mortality. This study suggested that mild to moderate cardiac lesions do not need correction before OLT.

Another study including 23 children with well-controlled CHD undergoing living donor liver transplantation showed that transplantation was safe.[7] There were no perioperative cardiac complications, and cardiovascular disease did not increase the operative risk nor did the cardiovascular status worsen postoperatively. This study showed that compensated CHD is not a risk factor for living donor liver transplantation.

In adult patients, the literature is relatively silent on liver transplantation in the presence of severe underlying structural cardiac disease. There are data on the assessment of coronary artery disease in OLT candidates, especially in the context of an increasing incidence of nonalcoholic steatohepatitis as indication for OLT and the aging OLT recipients.[8] Left ventricular hypertrophy is also associated with poor outcome in OLT.[9,10] In patients with complex CHD, preoperative assessment of cardiac function and estimation of the postoperative outcome are relatively difficult. Therefore, every transplant candidate with CHD needs to be assessed individually.

From the cardiac perspective, heart transplant has been described as a good therapeutic option for failing Fontan patients.[11,12] Nevertheless, heart transplantation can be challenging after previous congenital heart surgery, especially in the situ-ambiguous patient.[13]

In patients with congestive hepatopathy being palliated with a Fontan circulation, one of the most challenging questions is to estimate the reversibility of liver disease. In many patients with Fontan circulation, heart-only transplantation will suffice to reverse hepatopathy. However, in advanced liver disease, it can be detrimental to choose for heart-only transplantation with the risk of losing both the patient and the organ.[3] The clinical tools that are currently available to estimate the severity (and potential reversibility) of liver disease all have limitations. Serological markers (serum fibrosis scores and MELD-XI), imaging, and liver stiffness assessment tools have overall only poor to moderate correlation with fibrosis.[14] Transjugular biopsy and hepatic venous pressure gradient measurements are anatomically not always possible, and pressure measurements can be obscured by the presence of collaterals. Biopsies in general have the limitations that sampling error can occur.

If advanced liver disease is present, a CHLT is necessary and seems feasible. In a cohort of 20 failing Fontan patients, 5 patients (25%) had biopsy-proven cirrhosis or advanced fibrosis with clear signs of advanced liver disease (eg, ascites, varices, and splenomegaly in a higher extent than expected to be due to the Fontan).[15] Those 5 patients underwent CHLT and had similar outcomes compared with the heart-only subgroup. Only the postoperative hospital stay was longer in CHLT patients.

These data are further supported by another cohort of 17 failing Fontan patients with liver fibrosis.[16] In this study, 7 patients (41%) received CHLT, which was shown to be an acceptable therapeutic option.

CONCLUSION

Careful assessment of both liver and heart function is necessary when considering CHLT. We report on a unique case with cyanotic CHD in which liver-only transplantation was feasible. After weighing long-term outcome of her CHD versus the risk and outcome of CHLT and given the absence of hepatic congestion, liver-only transplantation was performed with excellent clinical outcome. We realize that this is a unique case with a rare form of combined heart and liver disease that was managed with a novel approach. But since patients with CHD tend to live longer and concomitant liver disease is frequent, similar cases could occur in the future. This case could be a good example of a patient-tailored approach, but the decision should always be made on a case-by-case basis by a multidisciplinary team. The option to avoid the added risk of a combined heart and liver transplant in future cases should be explored.

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