Living related donor liver transplantation in a patient with Alagille's Syndrome with severe pulmonary stenosis: a case report

Pelin KARAASLAN[1], Selma ÖZGÜR[1], Tümay Uludağ YANARAL[1], Esra KUTLU[1], Hamdi KARAKAYALI[2], Emine Arzu KÖSE[1]

[1]Department of Anesthesiology and Reanimation, Medipol University Hospital, Istanbul, Turkey
[2]Department of Surgery, Transplantation Service, Medipol University Hospital, Istanbul, Turkey

Abstract

Alagille's syndrome (AGS) is a multisystem disorder affecting liver, heart, face and skeletal system. Approximately 25% of AGS patients may need liver transplantation (LT) in childhood. Unfortunately AGS patients have multisystem pathologies and they should be carefully evaluated before LT. Especially congenital heart defects in AGS patients may cause hemodynamic effects perioperatively in transplantation surgery. In this case report we aimed to discuss successful anesthetic management for living related donor liver transplantation (LRDLT) in a patient with Alagille's syndrome and severe pulmonary stenosis. Successful anesthetic management of a growth retarded 11-months old, 5110 grams infant for LT is a challenge especially with coexisting cardiac pathologies. Complete preoperative evaluation and careful perioperative monitoring of the patient resulted in stable circulation.

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Introduction

Alagille's syndrome (AGS) has characteristics including chronic cholestasis; typical peculiar facies; posterior embryotoxon; butterfly-like vertebral-arch defects; and cardiovascular malformations [1,2]. Approximately 21-31 % of AGS patients develop end-stage liver disease leading to the need for transplantation [3-7]. End-stage liver disease causes low systemic vascular resistance and liver transplantation may cause cardiovascular instability and huge hemorrhage [8]. This may lead to perioperative problems especially in coexisting cardiovascular pathology patients. Cardiac abnormalities, most commonly pulmonary stenosis, are found in 85-100% of AGS patients [3,9]. Congenital heart defects in AGS patients may cause hemodynamic effects perioperatively in transplantation surgery [5]. In this case report we aimed to discuss successful anesthetic management for living related donor liver transplantation (LRDLT) in a patient with Alagille's syndrome and pulmonary stenosis.

Case report

The patient The patient was a 54 cm female infant of 11 months weighing 5100 grams with AGS, end-stage liver disease and severe pulmonary stenosis (PS). She was diagnosed with severe bilateral pulmonary stenosis by echocardiography soon after birth. Her echocardiography record also showed supravalvular mild aortic stenosis (maximum gradient was 30 mmHg), mild hypoplasia of descending aorta and atrial septal defect. The electrocardiogram (ECG) showed sinus tachycardia with right ventricular hypertrophy (RVH). She also had a cleft lip and palate. Although pediatric cardiology department reported high risk potential for transplantation, in order to correct cardiac pathologies first step of strategical approach was liver transplantation. Her mother was chosen as the donor. The patient had severe jaundice (total bilirubin=19.484 mg/dL), pruritis, coagulopathy (aPTT=34.8 sec) and hypercholesterolemia (total cholesterol=437.8 mg/dL) (Table 1 and 2). After ECG and pulse oximetry monitoring, anesthesia was induced with ketamine 3 mg/kg, fentanyl 3 mcg/kg and maintained with sevoflurane 2% in a mixture of 50% O2 + air. Neuromuscular block was achieved with vecuronium. Central venous catheter via right internal jugular vein, arterial monitoring via left radial artery and pulse contour cardiac output (PICCO) monitoring via the right femoral artery were performed. Urine output and nasopharyngeal temperature were monitored. In order to prevent right to left shunt due to hypercapnia, ventilation and oxygenation were followed by end-tidal CO2 and arterial blood gas analysis. Dopamine was infused continuously with a dosage strategy depending on PICCO monitoring guidance. During operation, systolic arterial pressure was 80-140 mmHg, CVP was 7-10 mmHg and CI was 2.61-2.89 liter/min/m2.

The inferior vena cava was partially clamped during liver transection and hepatic vein reconstruction. The lateral segment of her mother's liver was transplanted. At the time of reperfusion of portal vein, the systemic arterial pressure was protected in normal range by dosing dopamine infusion and volume loading with crystalloid fluids. No additional catecholamine infusion was needed. Total operation time was 6 hours 35 minutes, total anesthetic duration was 7 hours 55 minutes, total infused volume was 250 mL, total albumin volume was 60 mL, total blood transfusion was approximately 150 mL (Htc: 22-31%) and fresh frozen plasma was 150 mL. Urıne output during anesthesia was 440 mL. The postoperative course was uneventful. She was extubated 15 hours after surgery. Total bilirubin decreased to 10.63 mg/dL on the first day after operation. She was discharged from hospital on day 12.

Discussion

Alagille's syndrome Alagille's syndrome is a multisystem disorder affecting liver, heart, face and skeletal system [5]. Approximately 25% of AGS patients may need liver

Table 1: *Perioperative data of the patient.*

	Preoperative	Anhepatic phase	Postoperative 5th day
Hemoglobin (g/dL)	9.8	6.7	8.6
Platelet (10e3/uL)	279.000	189.000	105.000
Wbc (10e3/uL)	9.2	5.09	12.09
BUN (mg/dL)	34.2	27	25
Creatinine (mg/dL)	0.16	0.39	0.23
AST (U/L)	593.1	1009	628
ALT (U/L)	528.3	454	270.4
Bilirubin, total (mg/dL)	19.484	10.63	2.9
Bilirubin, direct (mg/dL)	16.447	8.9	2.2
Sodium (mmol/L)	133	146	135
Potassium (mmol/L)	4.1	3.6	4.7
Calcium (mg/dL)	10.2	13.2	9.85
INR	0.99	1.1	1.39
Cholesterol, total (mg/dL)	437.8		169.6
Triglyceride (mg/dL)	265.8		138.5
Lactate (mmol/L)	0.7	8.3	2.1

BUN: *Blood urea nitrogen;* AST: *Aspartate aminotransferase;* ALT: *Alanine aminotransferase*

Table 2: *Haemodynamic variables during surgery.*

	Induction	Anhepatic phase	Reperfusion
CI (L/min/m^2)	2.81	2.81	2.61
GEDI (mL/m^2)	335	315	192
ELWI (mL/kg)	18	18	11
SVRI (dyne s/cm^5)	1524	1731	2073

CI: *Cardiac index;* GEDI: *Global end diastolic index;* ELWI: *Extravascular lung water index;* SVRI: *Systemic vascular resistance index*

transplantation (LT) in childhood [5-7]. Most AGS cases that needed LT compromised the complications of cholestasis, severe hypercholesterolemia and osteodystrophy. Published series describe 1-year survival after LT ranging between 71-100 %. Success rate of LT absolutely depends on the severity of the cardiac anomaly. Pretransplantation cardiac evaluation should be performed perfectly. Besides possible intraoperative problems, it should be kept in mind that long-term use of anti-rejection therapy drugs may lead to nephrotoxicity, bone changes and atherosclerosis. There are studies reporting experiences in which PS and RVH did not cause intraoperative problems during LT [10,11]. Inferior vena cava clamping may increase the fluid requirements resulting in acute heart failure [5]. Cardiovascular instability is usually observed both during caval clamping and reperfusion phases. We used partial clamping during both liver transection and hepatic vein reconstruction. Thus, there was no need to overload fluids or blood products. Another major problem for end-stage chronic liver disease patients is peripheral vasodilatation which may worsen after reperfusion phase [5]. After reperfusion, pulmonary vascular resistance may increase leading to poor graft reperfusion and graft dysfunction. In order to avoid this condition, throughout all the operation, we monitored the cardiac index, systemic vascular resistance and global end diastolic index.

Maintaining stable and normal body temperature is very important in transplantation patients because it is well known that hypothermia results in coagulopathy and thromboembolic complications [3]. Even though normal levels of clotting factors and normal clotting test results are provided, hypothermia may present with decreased platelet activity and inhibited enzymatic reactions of coagulation cascade. In our patient we provided normothermia throughout the operation by warming the transfused fluids and using blankets.

Unfortunately AGS patients have multisystem pathologies and they should be carefully evaluated before LT. Unremitting cholestasis, resistant pruritis, extensive xanthomatosis, bone fractures and growth retardation are major indications for LT [12,13]. In this patient LT was indicated due to jaundice with pruritis and growth retardation. Success rate of LT depends on a strict preoperative multidiciplinary planning and perioperative management. The pediatric cardiology team indicated that no preoperative treatment or correction was needed for this patient before LT. Intraoperative CVP around 10 mmHg and stable hemodynamic parameters were maintained via proper fluid resuscitation and vasopressor infusion. The patient was discharged from hospital on day 12 but long-term prognosis is uncertain due to effects of immunosupressive treatment on renal and vascular disease.

In conclusion, successful anesthetic management of a growth retarded 11-months old, 5110 grams infant for LT is a challenge especially with coexisting cardiac pathologies. Complete preoperative evaluation and careful perioperative monitoring of the patient resulted in stable circulation.

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***Correspondence to:**

Pelin Karaaslan
Department of Anesthesiology, Medipol University Hospital Istanbul
Turkey
Tel: +905057657550
Fax: +902124607831
E-mail: drpelinsesli@hotmail.com