The Ochsner Journal 11:89–91, 2011

Orthotopic Liver Transplantation in a Pediatric Patient With Progressive Intrahepatic Cholestasis: A Coordinated Perioperative Subspecialty Approach

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ABSTRACT

This report discusses the perioperative anesthesia management of a pediatric patient with end-stage liver disease from progressive intrahepatic cholestasis, with particular emphasis on the coordinated, multidisciplinary approach our institution uses.

INTRODUCTION

At our institution, pediatric liver transplantation anesthesiology follows a team-approach model. The anesthetic team consists of a liver transplant anesthesiologist, a pediatric anesthesiologist, and 2 nurse anesthetists. We believe that the expertise the 2 anesthesiologists offer is the best possible option for successfully managing such highly complex patients. Patients undergo a consultative visit in the anesthesia preoperative center, at which time the patient receives a full evaluation in coordination with the abdominal transplant surgery group. The patient receives reevaluation on the day of surgery, after which the anesthesia team meets to formulate and discuss the anesthetic plan.

Pediatric liver transplant guidelines have standardized care, addressing many challenges associated with pediatric liver transplantation, such as coagulopathy, electrolyte disturbances, acid/base imbalance, vitamin deficiencies, growth retardation, and difficult vascular access. Although our case was uneventful, it illustrates many of these challenges. This report highlights the perioperative management of a pediatric patient with end-stage liver disease as a result of progressive intrahepatic cholestasis, with particular emphasis on the coordinated, multidisciplinary approach practiced at our institution.

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Key Words: Multidisciplinary subspecialty approach, pediatric liver transplantation, progressive familial intrahepatic cholestasis type 2

Financial disclosure: None of the authors has a financial or proprietary interest in the subject matter of this article.

CASE REPORT

The patient was a 10-year-old, 21.7 kg, Middle Eastern boy with a history of end-stage liver disease secondary to progressive familial intrahepatic cholestasis (PFIC) type 2. His history was significant for rickets, malnutrition, hypocalcemia, epistaxis, and anemia. The patient had no known drug allergies and no prior surgical history. Preoperative clinic consultation revealed a slightly anxious and malnourished male patient who exhibited both mental and physical developmental delays, and physical examination revealed a jaundiced patient with a systolic murmur. Upon chart review, the murmur was described as a functional murmur secondary to anemia. Cardiac echocardiography was normal. Significant laboratory values included a hemoglobin of 12 g/dL, international normalized ratio (INR) of 2.9, partial thromboplastin time (PTT) of 37.6 seconds, and a platelet count of $111 \times 10^3/\mu L$.

On the morning of surgery, the team reevaluated the patient in the intensive care unit, the anesthesiology team reviewed the chart, and informed consent was obtained. After the patient was transported to the operating room with a preexisting 22-gauge intravenous catheter in the right hand, we treated preoperative anxiety with titrated doses of midazolam to a Ramsay sedation scale of 2 to 3 using standard American Society of Anesthesiologists monitors. After preoxygenation, we induced anesthesia with midazolam, 1 mg; lidocaine, 20 mg; propofol, 100 mg; fentanyl, 100 μg; and pancuronium, 2 mg and intubated the trachea with a 6.0-mm internal diameter cuffed endotracheal tube without difficulty. We

inflated the endotracheal tube balloon cuff to the minimum pressure that allowed for adequate oxygenation and positive pressure ventilation and maintained anesthesia with isoflurane and oxygen. After the induction and intubation, we obtained intravenous and arterial access using an 18-gauge intravenous catheter in the right wrist, an 18-gauge intravenous catheter in the left antecubital fossa, a 22-gauge angiocatheter in the left radial artery, and a 7 French triple-lumen catheter in the right internal jugular vein with ultrasonography guidance. The patient's pressure points were carefully and thoroughly padded. We used all available mechanisms to maintain normothermia. Surgeons made the first incision approximately 60 minutes after induction. Per our pediatric liver transplant guidelines, vasoactive infusions included epinephrine and nitroglycerin that were titrated and adjusted to achieve and maintain acceptable hemodynamic parameters. The team assayed serial laboratory values throughout the case and when indicated, treated appropriately. The thromboelastogram was used to correct and maintain acceptable clotting parameters. Surgeons reperfused the portal vein 93 minutes after incision and the hepatic artery 118 minutes after incision and closed the abdomen 177 minutes after incision. Blood products administered included 543 mL of fresh frozen plasma, but no packed red blood cells were indicated. The hematocrit after induction was 36%, and the hematocrit at the end of the transplant was 30%. Vital signs and blood gases remained stable throughout all phases of the transplant. The only electrolyte disturbance was a potassium concentration of 2.7 mmol/L, treated with a series of titrated potassium infusions. Anesthetic management was unremarkable, and the patient was transported to the pediatric intensive care unit with positive pressure ventilation. The initial postoperative course was uncomplicated.

However, surveillance ultrasonography indicated a progressive decrease in hepatic artery blood flow, unresponsive to fluid loading. The patient returned to the operating room on postoperative day 7 for an exploratory laparotomy and intraoperative ultrasonography. Intraoperative ultrasonography confirmed a continued decrease in hepatic artery blood flow, with flow restriction within the allograft at the splenic artery and gastroduodenal artery of the proper hepatic artery. It was unclear whether this represented obstruction to flow from a stenotic lesion or vascular spasm. After careful dissection of adventitial tissue with intrahepatic balloon dilatation, hepatic artery blood flow improved substantially. Five days later, the patient was discharged with normalized serum aminotransferases and no signs of solid organ rejection.

DISCUSSION

PFIC is a heterogeneous group of autosomal recessive cholestatic disorders. PFIC begins within the neonatal period or in the first years of life. The 3 types of PFIC are defined by different mutations located in the gene responsible for bile flow through the intrahepatic canalicular transporter system.[1] PFIC1 and PFIC2 are characterized by low γ-glutamyl peptidase (GGT) levels. Despite having different gene mutations, PFIC1 and PFIC2 have few clinical differences, and both are caused by the absence of a gene product required for canalicular export and bile formation.[1] In PFIC3, patients have a similar clinical presentation, but laboratory results reveal an elevated serum GGT. Rather than defective bile salt export, patients with PFIC3 have deficient hepatocellular phospholipid export.[2] The lack of phospholipids produces unstable micelles that have a toxic effect on the bile ducts, leading to bile duct plugs and biliary obstruction.

The main clinical presentations of PFIC are cholestasis, jaundice, pruritus, and progressive hepatic failure secondary to fibrosis.[3] Growth failure is another presenting symptom. Ninety-five percent of patients have short stature. Perennial asthma-like disease and recurrent epistaxis in the absence of thrombocytopenia or coagulopathy are common presenting problems because of exceedingly high circulating levels of biliary salts. Fat-soluble–vitamin deficiencies are prevalent in untreated patients.[4] PFIC is a diagnosis based on clinical suspicion, pertinent biochemical findings, advanced imaging techniques that rule out more common hepatic disorders, and histologic confirmation.

Our patient had PFIC2, caused by a mutation in the *ABCB11* gene on 2q24 that encodes the bile salt export pump mechanism (BSEP). BSEP, the major canalicular bile acid pump, is necessary for the effective mobility of bile salts through the bile canaliculi, which eventually reach the duodenum or the gallbladder. Loss of BSEP function results in severe hepatocellular cholestasis. Once intrahepatic cholestasis develops, patients rapidly progress to liver failure. PFIC2 is also associated with hepatocellular carcinoma in children. PFIC1 and PFIC2 are rare, with fewer than 200 cases reported in the literature. All forms of PFIC are lethal if untreated. Few untreated patients have survived into the third decade of life. PFIC1 and PFIC2 have been reported in all races. PFIC3 has been found in Western Europe and North African Arabic populations. Males and females are equally affected. Our patient has an older female sibling with the same diagnosis and disease progression. She is currently on the United Network for Organ Sharing transplant list.[1-4]

Our approach to this patient's perioperative care illustrates our institution's emphasis on highly coordinated care. Preoperatively, the patient benefited from extensive preparation and planning that included conferences with our surgical colleagues to discuss perioperative management and our visit with the patient months in advance of the surgical encounter. We performed a review of systems and a thorough physical examination, reviewed pertinent laboratory data, and assessed the airway and vascular access. Intraoperatively, we adhered to our pediatric liver transplant guidelines, including maintenance of low central venous pressure to decrease venous congestion, blood loss, and perhaps blood usage.[5-7] Two subspecialist anesthesiologists worked together to offer the best anesthetic care possible. A liver transplant anesthesiology subspecialist, a pediatric anesthesiologist, and members of our specialty certified registered nurse anesthetist team cared for the patient.

We believe that this care model offers distinct advantages for such complex patients. The liver transplant anesthesiology team does not routinely care for pediatric patients; therefore, incorporating a pediatric subspecialist brought additional knowledge, experience, expertise, and skill to the liver transplant arena. The 2 anesthesiologists shared line placement and together made decisions, adjustments, and interventions based on individual and shared knowledge, skill, and experience. The pediatric anesthesiologist is fellowship trained. Specific examples of this benefit include experience with pediatric line placement, pediatric drug dosing, and an in-depth knowledge of pediatric physiology. Also, the liver transplant anesthesiologist has a thorough knowledge of the pathophysiology of end-stage liver disease, the physiology associated with clamping the suprahepatic vena cava and infrahepatic vena cava, coagulation cascades, and the derangements associated with the hepatectomy, anhepatic, reperfusion, and completion stages of liver transplantation.[8,9]

In summary, this case illustrates how a coordinated multidisciplinary subspecialty approach to pediatric liver transplantation can promote safe and effective care for the complex pediatric patient undergoing orthotopic liver transplantation. This approach is feasible in a highly subspecialized practice setting and promotes optimally collegial interactions across the participating subspecialties. More important, it allows us to take care of our patients to the best of our ability by using all available tools and resources at our disposal, including personnel, knowledge, experience, procedural skill, and unique expertise.

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