Pediatric Liver Transplant

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Objectives:
The attendee will be able to do the following after this session:
1. Direct the preoperative assessment of the pediatric patient for liver transplantation.
2. Define the stages of liver transplantation.
3. Discuss the anesthetic management issues associated with each stage.
4. Describe the surgical options for anastomosing the new liver and the impact on anesthetic management.
5. Understand the etiology and management of the post reperfusion syndrome.

Stem Case – Key Questions

Your patient is a 14-month-old boy scheduled for orthotopic liver transplantation. Associated problems include marked jaundice and failure to thrive – he weighs only 8 kg. Past history includes a hepatic portoenterostomy (Kasai procedure), at 8 weeks of age, to treat his biliary atresia. During that surgery he was found to have a malrotation.

He has no known drug allergies. Total parenteral nutrition and intralipids are infusing thru a right subclavian portacath. Medications include furosemide. He finished dinner 3 hours ago.

Physical examination reveals the child to be awake and alert. He is in the semi recumbent position, slightly tachypneic, with a moderately protuberant abdomen. Oxygen saturation breathing room air (at sea level) is 93%.

What is biliary atresia? Are there associated congenital anomalies?
What are the implications of the previous Kasai procedure?
What, if any, additional work-up would you want prior to induction?
What blood products would you order prior to starting?

Preoperative labs include:
Hct. 30.2, plts 80k, PT 19.6, PTT 36.3, INR 1.9
Na 131, K 3.4, Cl 105, HCO3 19, BUN 30, Cr 0.9, Glucose 150
Alb 3.2, Total Bili 2.5

How will these results modify your perioperative management?
Formulate your anesthetic plan for this patient.
   How will you induce anesthesia?
   Is a rapid sequence induction appropriate? Why? / Why not?
   What kinds of monitoring will you use and when will you place those monitors?
   What drug regimen do you plan to use during maintenance of anesthesia?
Induction was uneventful. A Foley catheter was placed and vascular access established as follows:
- 22G R radial arterial catheter
- 22G R hand IV
- 20G L antecubital IV
- 5 Fr double lumen L subclavian

Anesthesia was maintained with oxygen/air, isoflurane, fentanyl, and vecuronium. The surgeons encounter a difficult dissection while removing the old liver. There is noticeable oozing, and the removal lasts 3 hours instead of the typical 1.

Laboratory results return:
- PT 20, PTT 60, INR 2, Hct 24%

What, if anything, will you do now?
What are the stages of liver transplantation?
- What problems are seen during each of these stages?

The hepatic artery is ligated and the surgeon is ready to clamp the IVC.

How will you manage the patient’s preload?
What are the surgical options for anastomosing the new liver?
- What are the anesthetic implications for each of the options?

An hour later the surgeon states that he will reperfuse the new liver in 5 minutes.

What preparations should you make prior to reperfusion?

The vascular clamps are removed. Within 1 minute a prolonged QT interval, peaked T waves, and a slowing of the HR are noted on the EKG, along with a decrease in BP.

What is the differential diagnosis?
- What will you do now?

Three hours later the case is coming to an end, the previous situation has resolved and the patient’s coagulation profile is normalizing. The surgeon asks you to start a low dose heparin infusion.

Why did the surgeon want the heparin infusion?
Would you extubate this patient in the OR? Why? Why not?
Once transferred to the Pediatric ICU, how would you manage this patient’s sedation and pain control?

**Discussion Outline**

Biliary atresia is the most common cause of neonatal cholestasis and the most frequent indication for liver transplantation in the pediatric population. It is due to a progressive fibro-inflammatory cholangiopathy that begins in early infancy and leads to the complete obliteration of the extrahepatic bile ducts. The pathogenesis has not been fully elucidated. Associated congenital anomalies may include: polysplenia, situs inversus, absent vena cava, malrotation, and cardiac anomalies. If there is no surgical intervention, i.e. Kasai procedure, then biliary cirrhosis, portal hypertension and end-stage liver disease will occur in about 50% of patients by 2 years of age. The Kasai procedure remains an important bridge until transplant. A previous Kasai procedure however may make for a difficult dissection of the native liver due to scarring and adhesions.
Additional work-up in this patient might include: CBC, blood chemistries, liver functions, coagulation profile, ABG, CXR, cardiac ECHO, and UOP.

Blood products to include, 4 units packed RBCs, 4 units FFP, and 6 units of platelets, should be readily available. Transfusion and lab support are both critical for successful liver transplantation, with lab personnel available to report serial measurements and process additional blood products as needed.

With the lab results presented for this patient and the previous history of Kasai, having the blood products available in the room and checked prior to incision would be necessary. The infusion of blood products would then be guided by the patient’s clinical appearance during the dissection and subsequent lab values. One IV to include D5W at a maintenance rate for glucose control might be considered.

Once the patient has been assessed and the O.R. is ready, midazolam 0.1 mg/kg might be considered for separation anxiety. In the O.R. the patient is preoxygenated and standard ASA monitors are applied. A rapid sequence induction with cricoid pressure should be strongly considered due to his NPO status and ascitic abdomen. Atropine, propofol and succinylcholine are commonly used to facilitate intubation and a cuffed ETT may be considered due to the variability in lung compliance secondary to the disease process and surgical procedure.

After induction, 1-2 large bore IV’s are inserted in the upper extremities (as the IVC may be cross-clamped) and a double lumen central line as well. (The portacath is useful for induction but not adequate for the procedure.) Fluid warmers and a rapid infusion system are added to the IVs. An arterial line is placed in the upper extremities, as the aorta may be cross-clamped.

Maintenance of anesthesia can be accomplished in a variety of ways; no technique has been shown to be the best. More importantly is the task of maintaining hemodynamic stability, fluid resuscitation, temperature maintenance, and correction of metabolic and coagulation abnormalities.

Coagulopathy is common in liver disease and the difficult dissection was not unexpected in this patient. FFP is most commonly used to correct coagulopathies. FFP is administered at our institution only if necessary clinically, not just based on lab values. This is due to the higher incidence of hepatic artery thrombosis in the pediatric patient. The anemia is corrected to keep the hematocrit around 30%.

There are three separate stages during liver transplantation. Anesthetic concerns vary depending on the stage of the procedure.

The **preanhepatic stage** (the “dissection”) – is characterized by the potential for large volume blood loss due to the coagulopathy and a difficult dissection, especially in those patients who have undergone a Kasai or other procedure, or previous liver transplantation. Maintenance of hemodynamic stability by adequate fluid and blood product administration and correction of coagulation abnormalities is essential. Cryoprecipitate is given if fibrinogen is low. Platelets are considered if FFP does not repair the clotting defect or if more than 2 blood volumes are transfused. Glucose homeostasis and temperature control is also of concern. Manipulation of the liver may obstruct major blood vessels and produce hypotension by decreasing venous return.

The **anhepatic stage** - begins with clamping of the IVC and portal vein, decreasing venous return. Most pediatric patients tolerate this well because of adequate collateral blood flow that developed secondary to the portal hypertension. Metabolic abnormalities may occur as a consequence of the absent liver and they need to be addressed: calcium may decrease because the citrate from blood products is not metabolized by the liver, metabolic acidosis can worsen because of high levels of lactate and citrate. Careful monitoring and correction of the pH, electrolytes, calcium, and glucose is necessary. Hyperventilation with adequate
volume resuscitation will improve the metabolic acidosis and hyperkalemia. An infusion of THAM will allow for correction of acidosis without a sodium overload. Once the new graft begins to function, the acidosis usually corrects. Volume resuscitation is guided by CVP, arterial pressure waveform and urine output. These may be challenging in patients that have pre-existent renal impairment, portopulmonary hypertension, intracardiac shunts or high ICP. In some centers, TEE is placed to guide volume resuscitation, inotrope administration and to provide real time monitoring of ventricular filling and contractile function. Reperfusion completes this stage and starts with removal of the suprahepatic clamp followed by the removal of the portal vein and infrahepatic clamps. Inadequate fluid resuscitation, inadequate flushing of the cold preservative solution and release of the vasoactive substances into the central circulation may cause hemodynamic instability. Hyperkalemia, hypocalcemia, and acidosis may develop. The cold solution may cause an acute increase in pulmonary vascular resistance and right ventricular dysfunction. Although rare, air embolism may occur with reperfusion.

The postanhepatic stage is characterized by completion of the hepatic artery anastomosis and creation of the biliary drainage. There may be blood loss with split-liver grafts but it is not known until reperfusion how much bleeding there will be from the raw edge of the liver graft. It is important during this stage to avoid congestion of the new graft by too aggressive fluid resuscitation, and to maintain a hematocrit below 30% to minimize blood viscosity and decrease the risk of hepatic artery thrombosis. Patients less than 12 years old are started on a heparin infusion or low molecular weight heparin when PT is <20.

After IVC cross clamping, the preload is significantly decreased and is dependent on SVC flow rates. Careful fluid resuscitation to a CVP of 12-15 cm H2O before IVC cross clamping and the use of vasoactive drugs will help prevent a significant drop in the blood pressure.

Surgical innovations based on standard techniques for partial hepatectomy led to the use of reduced-size liver grafts, cadaveric split liver transplantation and living donor liver transplantation. Left or right lobe liver transplantation preserve the vena cava of the living donor so the donor hepatic vein is anastomosed directly to the recipient vena cava or hepatic vein. A low rate of arterial thrombosis has been achieved by using microvascular techniques to perform end-to-end arterial anastomosis. A portion of saphenous vein may be harvested from the donor to provide extension of the hepatic artery. The biliary anastomosis depends on the underlying diagnosis and the relative sizes of the recipient and donor liver. A Roux-en-Y anastomosis is obviously necessary in patients with biliary atresia because there is no native biliary tree. In addition the donor duct will be implanted into a Roux-en–Y limb in babies receiving segmental grafts and in older children with abnormal native biliary system (primary sclerosing cholangitis).

In anticipation of the electrolyte changes that may occur following reperfusion, sodium bicarbonate is given to neutralize serum pH. Calcium should be maintained around 1.1-1.2 mmol.l⁻¹ in order to mitigate the adverse effects of hyperkalemia and to maintain optimal cardiac output. Incremental doses of 10-20 mg/kg of calcium chloride or 30-60 mg/kg calcium gluconate may be required. If the serum K⁺ is greater than 5 mmol/l, an alkaline pH should be achieved with hyperventilation and/or administration of sodium bicarbonate solution prior to reperfusion. If the serum K concentration remains greater than 5 mmol/l in spite of an alkaline pH, furosemide 0.5-1.0 mg/kg should be given although its efficacy may be reduced if the vena cava is cross-clamped. An infusion of 0.25-0.5 g/kg of glucose and 0.2 Units/kg regular insulin should be administered to acutely reduce the serum K concentration.

The EKG changes are provoked by the rapid infusion of effluent from the transplanted liver, which is high in potassium and low in pH and temperature. In addition, infusion of air and/or microthrombi into the heart may precipitate acute pulmonary hypertension. Body temperature should be increased to 36-37º C if possible. Vigorous flushing of the liver with colloid solution followed by retrograde flushing with the recipient’s blood by the surgeon prior to reperfusion reduces the potassium concentration and acid content of the effluent. In addition, the FiO₂ should be increased to 1.0 and halogenated agents should be
discontinued 3-5 min prior to reperfusion. Epinephrine and atropine should be at hand for treatment of bradycardia. The circulatory changes associated with reperfusion usually subside within 10 min, provided that appropriate therapeutic measures are implemented. Blood must be prepared for immediate transfusion in the event of hemorrhage following removal of vascular clamps.

Hepatic artery thrombosis (and other vascular thrombotic complications) is directly related to the size of the vessels and thus is most likely in the smallest pediatric recipients. Early suspicion and evaluation with duplex sonography, MR angiography, or angiogram, and immediate exploration and successful thrombectomy may salvage the graft. Bile leaks resulting from bile duct ischemia secondary to early hepatic artery thrombosis require retransplantation. Surgical intervention is generally chosen over lytic therapy because of the risk of bleeding from lytic therapy. Chartier et al. reported a superior survival rate after lytic therapy with tPA- 77% survival, vs. surgical embolectomy -53%, radiological embolectomy -50%, and heparin -38%.

Patients less than 10 kg are commonly ventilated for 12-24 h or more following the surgery but those less than 5 kg may require a longer duration due to diminished power of breathing and, in many cases, greater restriction of lung function because of a proportionately larger liver graft. Pleural or pericardial effusions and splenomegaly cause a reduction in lung volume in children with liver failure. Intrapulmonary right-to-left shunting through abnormally dilated pulmonary arterioles and impaired hypoxic pulmonary vasoconstriction may cause severe hypoxemia. A decrease in pulmonary diffusion capacity has also been described, further contributing to hypoxemia. After large amounts of blood products transfusion there is the potential for transfusion related–acute lung injury (TRAL). Large fluid shifts will occur in these patients because of hypoalbuminemia and aggressive fluid resuscitation therefore pulmonary edema is a possibility. Also, the decreased hepatic clearance of opioids and the increased free fraction of benzodiazepines will result in significant postoperative sedation.

In some studies done in adult patient population there is a decreased need for postoperative narcotics. One explanation is the lack of sensory input from a denervated donor liver. In addition, there seems to be an increase in neuropeptides involved in pain modulation, specifically met-enkephalin, resulting in a decrease in pain sensation. Also, the large doses of steroids administered for immunosuppression have a central euphoric effect. However, the postoperative pain requirements in pediatric liver transplants have not been studied. Multimodal approach should be employed. IV PCA controlled by proxy is used in most institutions. Caudal block with morphine has been reported to provide good postoperative analgesia with minimal complications in these coagulopathic patients and to allow a rapid extubation. Wound infiltration with local anesthetics may help for the first few postoperative hours.

References:
8. UpToDate: AASLD guideline: Liver transplantation; Living donor liver transplantation; www.uptodate.com

Questions
1. What are some concerns for the biliary atresia patient going for liver transplant?
   a. Previous Kasai procedure
   b. Possible associated congenital anomalies
   c. Coagulopathy
   d. All of the above

2. Which of the following is important in the care of the pediatric liver transplant patient?
   a. Adequate laboratory support
   b. Adequate blood banking support
   c. Adequate IV access in the upper extremities
   d. All of the above

3. During the anhepatic stage, the anesthetic concerns include:
   a. Maintaining adequate CVP after the IVC is cross clamped
   b. Possible administration of inotrope to maintain adequate ventricular filling
   c. Correction of hypocalcemia
   d. All of the above

4. Problems that may ensue with the post reperfusion syndrome include all of the following EXCEPT:
   a. Hypokalemia
   b. Air embolism
   c. Increase in pulmonary vascular resistance
   d. Release of vasoactive substances into the central circulation

5. During the postanhepatic stage, the anesthetic concerns include all of the following EXCEPT:
   a. Possible bleeding from split-liver grafts with reperfusion
   b. A decreased incidence of hepatic artery thrombosis if the PT is over corrected.
   c. Maintaining a hematocrit < 30% to minimize blood viscosity
   d. Initiation of a heparin infusion when the PT is < 20