Perioperative Management of Acute and Recurrent Thrombosis of a Blalock-Taussig Shunt in a Neonate with Hypoplastic Left Heart Syndrome

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OBJECTIVES

1. Review the anatomy and physiology pertinent to the care of a neonate with hypoplastic left heart syndrome (HLHS) following stage palliation
2. Discuss the anesthetic management of neonates with HLHS for non cardiac surgery
3. Develop a differential diagnosis and management strategy for acute cardiopulmonary collapse in a neonate with a modified Blalock-Taussig Shunt (mBTS)
4. Discuss the work-up and subsequent management of recurrent thrombosis of a mBTS in a neonate
5. Review the various types of thrombophilias and their respective pathophysiology

CASE DESCRIPTION

A 7 wk old 4.5 kg male with HLHS s/p stage 1 palliation, with a 3.5mm gortex right MBTS, is scheduled for laparoscopic LADD operation due to intestinal malrotation. Baseline saturations are 86% with a NIBP of 86/37, HR of 135 and afebrile. Last weeks TTE reports qualitatively borderline systolic RV function with mild to moderate TV regurgitation, trivial neoaortic regurgitation, unrestrictive atrial communication and pulmonary venous return, as well as a patent mBTS with branch PA pulsatile blood flow.

Is there any other history you would gather or studies you would need prior to starting this case? What concerns you about proceeding with this case? What special considerations need to be taken to optimize the outcome for this infant with cardiac disease?

The infant is on Enoxaparin and aspirin therapy for a non-occlusive thrombus of the left femoral vein. The CBC shows a thrombocytosis with a platelet level of 529. Other studies and physical exam findings are as expected for an infant with HLHS s/p stage 1 palliation and bowl obstruction.

How do you plan to manage the patient's perioperative anticoagulation? What challenges can you expect with the laparoscopic approach? Would you prefer an open laparotomy, if so would you include a regional technique? How would you manage induction, maintenance, and monitoring during this case?

After induction, intubation, line placement, and monitoring is established, laparoscopic surgery is well underway, at which point significant hypoxia occurs.

What is your differential diagnosis for hypoxia in this infant? How will you begin your initial resuscitation?

Unfortunately the initial resuscitation efforts are not successful and the hypoxia continues to worsen.

At this stage how would acute mBTS thrombosis manifest itself and how would it be differentiated from other causes of hypoxia ie. hypoxia caused by pneumoperitoneum? If you strongly suspect acute mBTS thrombosis, what methods or therapies can you employ to confirm the diagnosis, mitigate complications and how would you involve the surgeon? When is an interventional cardiologist needed for possible intervention? What is your threshold for activating the ECMO team?

Profound refractory hypoxia has occurred despite all your best efforts to correct it and the situation is quickly deteriorating. The patient is placed on ECMO in rapid fashion, stabilized and taken for catheter-based intervention.

What new patient management challenges can you expect in transitioning a patient onto ECMO emergently and how would you manage them? What issues do you expect to encounter in taking this patient to the cath lab for intervention?

The diagnostic catheterization confirms the mBTS is thrombosed with no angiographic blood flow. A wire is passed and the shunt is emergently ballooned dilated and stented with good result. The patient is then transported on ECMO to the cardiac ICU for further management.

What is the ideal perioperative management of anticoagulants in those with shunt dependent circulation? What level of involvement do you have and should you have, in managing perioperative anticoagulants at your institution? Would you pursue a hypercoagulability workup given this scenario?

ECMO is weaned off within 24hrs. The infant appears to be neurologically intact by exam and by imaging without any end organ injuries. He is maintained therapeutic on a heparin infusion during which time he is extubated and a thrombophilia investigation is undertaken but pending. Five days after he has been decannulated from ECMO you are called to take him emergently to the cath lab, once again due to sudden progressive cyanosis. The mBTS is confirmed to have diffuse thrombus and it is balloon dilated with improved angiographic flow as well as greatly improved saturations. You then return the patient to the ICU.

Is it unusual that the shunt re-thrombosed while therapeutic on a heparin infusion? What coagulation disorders might do this and what tests are used to identify them? What will you change about the anticoagulation management to prevent this shunt from clotting a third time while tests are pending?

You place the patient on aspirin in addition to heparin infusion. Laboratory analysis reveals: methylenetetrahydrofolate reductase mutation (MTHFR) is normal and homocysteine levels are normal, Factor V Leiden mutation is negative, anticardiolipin antibody studies are negative, prothrombin gene mutation is negative, however antithrombin levels are low, and protein C & protein S levels are also decreased from normal. FFP is administered to restore these factors to normal levels and the patient is transitioned back to Enoxaparin and aspirin.

MODEL DISCUSSION

Despite the first Blalock-Taussig shunt (BTS) being performed ~70yrs ago, the risk of thrombosis and sudden death remains alarmingly high. There are multiple variations of systemic artery to pulmonary artery shunts, each with advantages and disadvantages,. The most commonly employed is the mBTS, which consists of a gortex tube graft connecting the subclavian artery to the pulmonary artery. The mBTS has been shown to decrease morbidity as compared to the classic BTS however the mBTS has been adapted to its more common use today in complex single ventricle repair. In the case presented, a mBTS was used to provide a source of pulmonary blood flow as part of the first-stage palliation of a neonate with hypoplastic left heart syndrome (HLHS). HLHS consists of a severely underdeveloped aorta and left ventricle. Aortic arch augmentation is performed in the first-stage palliation with the addition of a shunt to provide a source of pulmonary blood flow (Norwood operation). This constitutes single ventricle physiology with systemic shunt dependent pulmonary blood flow. Single ventricle physiology at this stage requires a thorough knowledge of all factors influencing the dynamic balance between pulmonary blood flow and systemic blood flow and how to monitor and manipulate these factors to the patients benefit. These infants exist in a high cardiac output state as the single ventricle acts as a pump to the pulmonary and systemic circulation. Balancing the relative resistance between the pulmonary and systemic vascular bed is a fundamental concept in caring for these infants during the intraoperative period. As single ventricle physiology is not intuitive and presents a high degree of perioperative risk every effort should be made to optimize patient care.

Laparoscopic surgery has been demonstrated to be safe in neonates with HLHS. However there are several physiologic implications of pneumoperitoneum, which need to be understood in the context of single ventricle physiology. A pneumoperitoneum will inhibit pulmonary mechanics and worsen alveolar/arterial gradients, worsening hypercarbia as well as hypoxia. CO2 insufflation can be expected to lead to CO2 absorption making CO2 elimination more challenging. Hypercarbia is a potent pulmonary vasoconstrictor of which neonates and those with HLHS are readily susceptible. Pneumoperitoneum will increase SVR and decrease venous return, the degree of which depends upon the insufflation pressure and degree of trendelenburg position. These concepts hint that in the face of what appears to be adequate blood pressure and single ventricle saturations oxygen delivery can be severely impaired.

As was alluded to earlier, mBTS thrombosis remains a real concern and is reported to be as high as 17%. Anticoagulation guidelines cannot simply be extrapolated from the adult literature as

the underlying cause, location, and contributing factors in infant thrombosis is markedly different. Current recommendations regarding thrombosis prophylaxis after first-stage palliation with mBTS is to prescribe Aspirin rather than other antithrombotic therapies. Aspirin has been shown to lower the risk of death and shunt thrombosis overall, however thrombosis still remains high. When Clopidogrel was evaluated in addition to standard Aspirin therapy, no benefit was found. Unfortunately, there are no pediatric anesthesia perioperative anticoagulation guidelines at this time and therefore, institutional practices vary. Due to our unique skill set, it is important that anesthesiologists have input regarding perioperative anticoagulation management as this can improve patient safety. Recognizing intraoperative shunt thrombosis requires a high index of suspicion and a process of elimination of other potential sources, transthoracic echocardiography can be helpful in emergently evaluating shunt patency and branch pulmonary artery blood flow. However, thrombosis can progress rapidly requiring the clinician to make difficult decisions with incomplete information. Options for acute management of thrombosed mBTS include: surgical takedown and replacement, balloon angioplasty with or without thrombectomy or thrombolysis. ECMO may be required to stabilize the patient for these procedures to be performed safely.

Congenital heart disease is at increased risk for developing thrombosis for a variety of reasons, including low flow & turbulent flow states, surgical tissue disruption and contact activation, presence of foreign materials, and even a higher presence of intrinsic thrombophilia. With this risk of thrombosis and the state of parallel circulation, there is a great risk of embolic stroke continually present. When thrombosis occurs despite adherence to standard anticoagulation management and without acquired risk factors, such as central line presence, then consideration should be given to an intrinsic thrombophilia investigation.

The predisposition to forming clots inappropriately is a complex interaction involving a myriad of procoagulant factors and coagulation inhibitors. An imbalance can be both genetic and acquired. Neonates have lower baseline concentrations of antithrombin and protein C, which places them among the highest risk pediatric age group for developing thrombosis. It is well recognized that those with congenital heart disease are at high risk for developing thrombosis. Evidence suggest that deficiencies of the protein C anticoagulant pathway, such as Factor V Leiden & protein C deficiency, are likely to play an important role in early thrombosis development in those with congenital cardiac disease. Factor V Leiden gene defect is a single amino acid substitution affecting Factor V, which leads to a diminished ability to deactivate Factor V by activated protein C. Activated protein C inactivates activated factor V and VIII. In the coagulation cascade activated factor V and VIII are critical for efficient thrombin generation. Deficiencies of antithrombin, protein C, and protein S also lead to a prothrombotic state. Protein S is a cofactor of activated protein C. Other important hypercoagulable states include Hyperhomocysteinemia and Antiphospholipid antibody syndrome. Hyperhomocysteinemia is an independent risk factor for thrombosis and it can be both genetic and acquired. The most common genetic hyperhomocysteinemia is a variant of methylene tetrahydrofolate reductase (MTHFR). Antiphospholipid antibody syndrome is an autoimmune hypercoagulable state caused

by antiphospholipid antibodies and detected by anticardiolipin antibody studies. This list is only a primer as the testing can become quite extensive and a thrombophilia workup should be conducted with the assistance of a pediatric hematologist.

REFERENCES:

1. Pearl J. First-stage palliation for hypoplastic left heart syndrome in the twenty-first century. J Thorac Surg 2002;73:331-339
2. Walker A. Anesthesia for major general surgery in neonates with complex cardiac defects. Pediatric Anesthesia 2009;9:199-125
3. Petrucci O. Risk factors for mortality and morbidity after the neonatal Blalock-Taussig shunt procedure. Ann Thorac Surg 2011;92:642-652
4. Monagle P. Thrombosis in children with BT shunts, Glenns, and Fontans. Progr Pediatric Cardiology 2005;21:17-21
5. Khan S. Hereditary thrombophilia. Thrombosis J 2006;4:15-27
6. McCrory MC. Thrombotic disease in critically ill children. Pediatr Crit Care Med 2011;12(1):80-9
7. Slater B. Outcomes after laparoscopic surgery in neonates with hypoplastic heart left heart syndrome. J Pediatr Surg 2007;42(6):1118-21
8. Wessel DL. Clopidogrel in infants with systemic-to-pulmonary-artery shunts. N Engl J Med 2013;368(25);2377-84
9. Monagle P. Antithrombotic therapy in neonates and children: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2012;141(2 suppl):e737S-801S
10. Li JS. Clinical outcomes of palliative surgery including a systemic-to-pulmonary artery shunt in infants with cyanotic congenital heart disease: does aspirin make a difference? Circulation 2007;116(3);293-7