Cardiac arrhythmias during repair of a congenital diaphragmatic hernia in a critically ill neonate.

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Goals
1. Understand the embryology, classification, prognostic measures and surgical therapies in neonates with congenital diaphragmatic hernia (CDH)
2. Appreciate the challenges of providing anesthesia in the NICU environment
3. Understand the role of ventilation (conventional ventilation, HFOV) and ECMO strategies
4. Understand the cycle of pulmonary hypertension in CDH
5. Understand cardiac rhythm disturbances in neonates and how to manage them intra-operatively

Case Description:
The patient is a 3-day-old, 3kg, term female neonate with a right side CDH. The patient is in the NICU ventilated with HFOV.

Questions:
What is a congenital diaphragmatic hernia? What types exist? Why does it occur? What is the incidence? What are the typical outcome/survivability odds? What are some common co-morbidities in survivors? Are there other associated anomalies?

Case Description continued:
Current medications include iNO 20ppm, dopamine, epinephrine, milrinone, vasopressin, prostaglandin and cisatracurium. Surgeons have requested to perform the repair in the NICU.

Questions:
What treatment options exist? Should in-utero treatment have been considered a viable option since there was a prenatal diagnosis? Should medical optimization or emergency surgical intervention be the primary course of action? How do you optimize medically? What happens to respiratory
mechanics and hemodynamics in the immediate postoperative period? Are they better? Worse?
What is different about performing an anesthetic in the NICU versus the operating room? Is there
value in routine and familiarity of the environment? Does the benefit, if any, out way the risk in
transporting such a critically ill infant?

**Case Progression - Physical Exam:**
Foreign bodies include a right side ante-cubital fossa PIC line, UAC, UVC and OETT. Baseline vitals
are BP 91/57, HR 115 and saturations 96%. Pertinent lab results include: Na 127, K 2.9 and
Bicarbonate 31.

**Questions:**
Any concerns about access, hemodynamics or labs? Do you proceed with the case now? Parents want
to know if the surgery should be delayed a little longer to allow their daughter to "get stronger"? Do
you place additional lines? If so, which ones? What other studies would you obtain or how would you
further optimize the infant?

**Case Progression - Laboratory studies and tests:**
Pre-operative CXR shows displacement of the liver and loops of bowel into the right chest cavity
with resultant left shift of the mediastinum. Pre-operative ECHO shows small PDA with
bidirectional flow, severe tricuspid regurgitation and a moderately flattened inter-ventricular
septum.

**Questions:**
What is the typical cycle of pulmonary hypertension in infants with CDH? What ECHO findings are
indicative of pulmonary hypertension? How do you treat pulmonary hypertension? Which options
are currently recommended? Is there a role for prophylactic hyperventilation? How does iNO work?
If medical management is failing, when do you consider ECMO? Which patients are appropriate
candidates for ECMO? What are other common indications for ECMO? What types of ECMO exist?
What are the risks associated with ECMO? How does ECMO affect CDH outcomes, i.e., is survivability
improved, unchanged or worsened?

**Case Progression:**
The decision is made to proceed with case in the NICU as the infant has exhibited significant
improvement in hemodynamic stability over the past 24 hours. The NICU providers and surgical
staff all feel as though this is the patient’s window of opportunity.

**Questions:**
Does the surgical approach, thoracic versus abdominal, affect any of your decisions? Would the
surgical plan for a primary repair of an abdominal incision cause any concerns? What is your
anesthetic plan? Any agents you would avoid? What is the importance of temperature control in
these infants? What common pulmonary complications should you be watching for in patients with
CDH?

**Case Progression – Intra-operative Events:**
Shortly after surgical exposure during retraction of the abdominal contents from the thoracic
cavity to the abdomen, the heart rate abruptly changes to 240 and the BP decreases to 65/30. A
diagnosis of SVT is made.
Questions: What is the differential diagnosis of “SVT”? What are common causes of SVT? What are the most likely causes in this particular patient? How do you treat SVT? How common is unstable SVT seen in the neonatal population?

Case Progression – Intra-operative Events Continued: The patient receives adenosine twice. The rhythm changes to a new rate of 180 and appears to be irregularly irregular. Magnesium is administered and an amiodarone load is given. The heart rate continues to decrease but remains irregular while the blood pressure improves slowly. An amiodarone infusion is begun.

Questions: What other treatment options are available? Are they safe in neonates?

Case Progression - Postoperative Events: As the surgery concludes, cardiology is consulted and a diagnosis of atrial fibrillation is confirmed. The decision is made to cardiovert the patient. Cardioversion is successful after the second attempt.

Questions: How do you cardiovert a neonate? Dose? How do you make the decision for cardioversion versus medical management? Is there additional risk given the patient’s history and nature of surgery?

Case Progression - Postoperative Events Continued: Initially, on 12 lead EKG it is thought the rhythm has changed to atrial flutter but after pausing the HFOV it is determined to be sinus rhythm.

Questions: How does HFOV work? Why would it affect the EKG?

Discussion

Case History The patient is a 3-day-old, 3kg, term female neonate with a right side CDH. The patient is in the NICU ventilated with HFOV and iNO 20ppm. Current medications include dopamine, epinephrine, milrinone, vasopressin, prostaglandin and cisatracurium. Foreign bodies include a right side ante-cubital fossa PIC line, UAC, UVC and OETT. Pre-operative CXR shows displacement of the liver and loops of bowel into the right chest cavity with resultant left shift of the mediastinum. Pre-operative ECHO shows small PDA with bidirectional flow, severe tricuspid regurgitation and a moderately flattened inter-ventricular septum. Baseline vitals are BP 91/57, HR 115 and saturations 96%. Pertinent lab results include: Na 127, K 2.9 and Bicarbonate 31.

Questions

1. What is the incidence and classification of CDH? CDH is a rare congenital anomaly with an incidence of around 1 per 3,000 live births. The true incidence is probably much higher, 1 in 15,000 if stillbirths are included.
There are three broad anatomic types of CDH:

a. Posterolateral (Bochdalek) Hernia
   - 80% of all hernias with 85% on the left side, 10% on the right and 5% bilateral

b. Non-posterolateral hernia
   - Morgagni hernia anterior retro-sternal
   - Pentalogy of Cantrell anterior hernia (CDH and defects in the supra-umbilical midline abdominal wall, lower sternum, diaphragmatic pericardium and heart (ectopia cordis)).
   - Central hernia, rare

c. Diaphragmatic eventration
   - Incomplete muscularization of the diaphragm resulting in a thin fibrous sheet of tissue. Mild forms may present later with respiratory symptoms such as recurrent pneumonias.

2. What is the normal embryological development of the diaphragm?
Development of the diaphragm takes place during the 4th and 12th weeks of gestation. It probably forms from two main components:
   a. Central and anterior portion
      - Develops from the septum transversum, which is initially fused to the liver and later becomes the central tendon of the diaphragm
   b. Posterolateral portion
      - Develops from the pleuroperitoneal folds

3. What are the causes of CDH?
This is not completely understood and it is likely multi-factorial:
a. Environmental causes
   Vitamin A deficiency may cause disruption of the retinoic acid signaling pathway and is associated with CDH
b. Chromosomal abnormalities
   10% of patients with CDH have a chromosomal abnormality – chromosome 'hot spots' include 1, 8p23, 8q22 and 15q26.
   - Pallister-Killian Syndrome (CDH, short limbs, high forehead, ocular hypertelorism, low set ears, seizures, developmental delay)
   - Fryns Syndrome (CDH, coarse facial features, hypoplasia of nails and terminal phalanges, congenital cataracts, cardiac anomalies)

Disruption of normal diaphragm formation and resultant herniation of abdominal viscera into the chest may cause compression of the ipsilateral lung and pulmonary hypoplasia. However, there is also abnormal lung tissue development in-utero as well. It is this combination of lung hypoplasia and abnormal morphology of the lung vasculature with leads to severe respiratory insufficiency after birth.

4. What prenatal factors influence prognosis?
   Early detection of CDH is possible by fetal ultrasound and occurs at a mean gestation of 26 weeks with a detection rate of 50%. It is more difficult to detect right-sided CDH with ultrasound. Early diagnosis before 24 weeks gestation is usually associated with large defects and poor prognosis. Numerous methods exist for predicting survival, the most important are:
   a. Lung-to-head circumference ratio (LHR)
      If > 1.0 survival reaches 92% with optimal post-natal therapy
   b. Liver position
      If the liver is up (herniated into the thoracic cavity) the prognosis is worse (43% survival if up vs 93% survival if down)
   c. Fetal MRI
      More reliable than ultrasound. Useful to accurately measure lung volumes and predict ECMO use post-delivery and measure response to in-utero interventions.

Associated anomalies are present in about 50% of CDH babies including cardiac malformations (15%), renal, and CNS.

5. What prenatal therapies are available?
   Prenatal surgical intervention has evolved through four phases:
   a. Open fetal surgical repair
   b. Open surgical tracheal occlusion
      - Occluding the fetal tracheal prevents the normal efflux of lung liquid and results in rapid pulmonary growth
      - Requires delivery via EXIT procedure due to tracheal occlusion
   c. Endoscopic external tracheal occlusion
      - Requires delivery via EXIT procedure
   d. Endoscopic fetal endoluminal tracheal occlusion (FETO)
      - Utilizes a detachable balloon which can be punctured endoscopically at 34 weeks gestation

All of the above prenatal therapies have associated risks for the mother as well as premature rupture of membranes and pre-term labor. These fetal interventions have been reserved for the most severely affected fetuses. The survival rate for all fetal interventions is around 20%.
6. **What are the immediate post-delivery procedures and treatments?**

Ideally delivery should be as close to term as possible to ensure lung maturity. To avoid transportation of unstable neonates, delivery should take place at a tertiary center with both neonatal intensive care and pediatric surgery available. After delivery the infant should be intubated immediately without bag and mask ventilation to avoid inflation of the stomach, which may further compromise lung expansion. Early placement of an orogastric tube will help decompress the bowel. Vascular access should be obtained including a UVC and arterial line. As pre-ductal PaO2 measurements reflect cerebral oxygenation, the arterial line should be inserted into the right radial artery if possible. There is no evidence to support routine surfactant replacement. Other standard neonatal resuscitation measures should also be remembered such as to warm and dry the infant, glucose monitoring etc.

7. **What are the classic physical findings in a newborn infant with CDH?**

In addition to cardio-respiratory distress a physical examination may reveal a barrel-shaped chest, a scaphoid abdomen, absence of breath sounds on the side of the CDH, shifted cardiac sounds and bowel sounds in the chest. A CXR may show lung hypo-expansion on the side of the CDH (often hyperexpansion on the contra-lateral side) and herniated abdominal contents filled with air or fluid.

8. **How should ventilation be managed in the NICU?**

Permissive hypercapnia and a ‘gentle ventilation’ strategy are necessary. A ventilation strategy aiming for pre-ductal saturations between 85-95%, post-ductal saturations above 70% and PaCO2 between 45-60 mmHg is well accepted. Adequate organ perfusion is indicated with a pH above 7.2 and a lactate <5 mmol/l and urine output >1ml/kg/hr. If conventional ventilation is used PIPs should be limited to <25cmH2O with a PEEP of 2-5cmH2O and a rate of 40/min. Many centers now use high frequency oscillatory ventilation (HFOV) early on. The physiological rationale for HFOV derives from its ability to preserve end-expiratory lung volume while avoiding lung over-distension, and therefore lung injury. A CXR should be done to avoid lung hyperinflation as defined by a >8 ribs visible above the diaphragm. Typical initial HFOV settings are MAP 13-17 cmH2O, frequency 10Hz, delta p 30-50 cmH2O.

9. **What are the criteria for ECMO in a neonate with CDH?**

The following should be considered:

- Inability to maintain pre-ductal sats >85% or post-ductal sats >70%
- Increased PaCO2 and respiratory acidosis with a pH <7.15 despite optimal ventilation management
- PIPs >28cmH2O or MAP >17cmH2O required to maintain sats >85%
- Inadequate oxygen delivery with metabolic acidosis as measured by elevated lactate >5mmol/l and pH<7.15
- Systemic hypotension resistant to fluid and inotropes resulting in urine output <0.5ml/kg/hr
- Oxygenation index >40 (mean airway pressure x FiO2 x 100/PaO2)

10. **What factors influence the timing of surgical repair?**

Survival rates in infants with CDH undergoing surgical repair after preoperative stabilization range from 80-92%. Rather than early surgical intervention, the emphasis is now on pre-surgical optimization. Surgery may not occur until the infant is 3-10 days old. Repair on ECMO can be considered. The usual surgical approach is trans-abdominal. The routine use of a chest tube post-
op is not necessary as an effusion quickly fills the pleural cavity on the affected side. A chest tube promotes infection in the pleural space. Occasionally, a pleural effusion after repair may compromise pulmonary function and ventilation, necessitating chest tube placement.

11. How can pulmonary hypertension in the neonate with CDH be managed?
The physiological basis of pulmonary hypertension in infants with CDH is:
   a. Pulmonary hypoplasia
   b. Abnormal pulmonary alveolar and vascular architecture
   c. Newborn elevation in pulmonary vascular resistance (PVR)
Echocardiography is extremely useful to help evaluate pulmonary hypertension in the neonate, in particular right ventricular dysfunction and overload. After optimization of fluid status, inotropic support and red cell mass, additional therapies should be considered. Inhaled nitric oxide (iNO) is usually the first choice. It is a selective pulmonary vasodilator that can be administered via the ventilation circuit. In neonates with persistent primary pulmonary hypertension, iNO improves oxygenation and decreases the need for ECMO. In the presence of systemic or suprasystemic pulmonary hypertension right ventricular failure may develop (right ventricular dilation and leftward shift of the interventricular septum). This can lead to left ventricular failure. To protect the right ventricle from overload due to increased afterload, PGE1 should be started to maintain ductal patency. Another therapy that can be considered is sildenafil, a PDE-5 inhibitor.

12. How are you going to prepare for delivering an anesthetic to this critically ill neonate in the NICU?
Many neonates with CDH are too sick for transport to the operating room for surgical repair. Often it is safer to repair the CDH at the bedside in the NICU. Standard preparation should include a thorough review of the chart (history, labs, CXR, ECHO etc) and examination of the patient. Discuss access options with the bedside nurse. Enlist the help of the neonatologist, especially if the baby is on HFOV. You are not expected to know everything – often the neonatologist has been looking after the baby for several days and is aware of many of the nuances of current management. Make sure you have a dedicated line for access, preferably central. Attach a long micro-bore tubing to this access point and have a flush syringe and stop cock on the other end where you can administer drugs, blood, etc. Make sure blood is checked and at the bedside in a cool box. If the baby is on ECMO discuss options for blood products and what the ACT target range is with the perfusionist. Have all of your drugs with you including; pancuronium, fentanyl, atropine, epinephrine (1mcg/ml), calcium, saline flushes etc. Make sure you have re-intubation equipment
13. What is your diagnosis? What is your initial management?
A sudden increase in heart rate resulting in hemodynamic change requires intervention. This is most likely a SVT. It is unusual to routinely place external defibrillation pads prior to incision on these patients so although there is an acute hemodynamic change it was elected to pharmacologically manage this rhythm. Adenosine 0.1mg/kg is a typical starting dose which can doubled for a second dose if there is no effect. Note that adenosine will not convert atrial fibrillation or flutter.

14. What are the possible causes of SVT in this neonate?
   a. Direct surgical stimulation of the heart
   b. Atrial stretch during movement of the abdominal contents out of the chest cavity and subsequent shift in the heart position
   c. Right side PIC line
   d. Abnormal electrolytes
   e. High dose inotropes
   f. Right heart overload and stretch from pulmonary hypertension
   g. Maternal hyperthyroidism

15. Is atrial fibrillation common in infants?
Atrial fibrillation in neonates with normal hearts is very rare. The main reason that atrial fibrillation is rare among small children may be their small cardiac and atrial mass. There needs to be adequate myocardial mass for the multiple wavelet theory to be fulfilled ie electrical waves which start in the atrial myocardium are fragmented into many other wavelets.

16. Why did it take two attempts to cardiovert this patient?
Atrial flutter waves in the neonate can have a frequency between 200-600 beats/min. This patient was on HFOV with a frequency setting of 10Hz - which is 10 cycles per second or 600 cycles/min. This HFOV frequency looked like atrial flutter on the first post-cardioversion EKG. Once the HFOV was paused, the rhythm was clearly a successful sinus rhythm cardioversion.
See the two attached 12-lead EKGs. The first EKG shows the HFOV artifact and the second EKG is taken seconds later with the HFOV on pause.

17. What are some of the long-term problems that survivors of CDH have?
Almost all CDH survivors have long lasting problems. They are at risk of developing surgical problems in later life, such as CDH recurrence or bowel obstructions because of adhesions. Associated cardiac or chromosomal anomalies in children with CDH may involve a wide range of problems, which may need multidisciplinary follow-up. Specific problems related to CDH include:
   • Pulmonary
     o Chronic lung disease
     o Persistent pulmonary hypertension
     o Recurrent respiratory tract infections
   • Gastrointestinal
     o Gastroesophageal reflux
     o Feeding problems and failure to thrive
     o Reflux related pulmonary problems
- Esophageal dysmotility
- Neurological
  - Neurodevelopmental delay possibly secondary to hypoxia, ECMO etc
  - Sensorineural hearing loss possibly due to ototoxic medications etc
EKG taken on HFOV showing artifact.
This could erroneously be interpreted as atrial flutter or fibrillation
EKG taken one minute later with HFOV on pause showing sinus tachycardia
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