Chapter 11

Pentalogy of Cantrell

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Case Scenario

A 2-week-old neonate with unrepaired, prenatally diagnosed pentalogy of Cantrell presents to the general operating room for an omphalocele repair. She was born via cesarean section at 38 weeks weighing 2.9 kg, with Apgar scores of 6 and 8. She initially required continuous positive airway pressure support, but quickly weaned to nasal cannula. The omphalocele is large and contains mostly bowel but also parts of the stomach and liver. The umbilical sac is intact and covered by sterile gauze. The patient currently has one 24-gauge peripheral intravenous line and a nasogastric tube in place. She is on 1 L of oxygen per nasal cannula. On examination, she is noted to be tachypneic with paradoxical respiratory motion, and a pulsatile mass is seen under her skin just superior to the omphalocele sac.

Echocardiography reveals the following:

- *Moderately sized perimembranous ventricular septal defect with left-to-right shunting*
- *Elevated right ventricular pressures*
- *Preserved biventricular function*

Key Objectives

- Describe the five congenital defects that comprise pentalogy of Cantrell.
- Understand the surgical options, timing, and staging of repairs for this patient.
- Describe the preoperative assessment and studies necessary before surgery.
- Describe intraoperative concerns and management strategies.
- Describe postoperative destination and concerns.

Pathophysiology

What five congenital defects comprise pentalogy of Cantrell?

Pentalogy of Cantrell (POC) was first described in 1958 by James Cantrell and consists of the following findings:

1. A midline, supraumbilical abdominal wall defect
2. A congenital heart defect (CHD)
3. A lower sternal defect
4. An anterior diaphragmatic defect
5. A diaphragmatic pericardial defect [1]

William Toyama further classified the syndrome into three subcategories:

- **Class I** is considered definite, with all five defects as described by Cantrell.
- **Class II** is probable but incomplete, with four of five defects present, which must include both congenital heart and abdominal wall defects.
- **Class III** is incomplete phenotypic expression with various combinations of defects that must include a sternal malformation [2].

Various other malformations have been associated with POC, including craniofacial (cleft lip/palate), central nervous system (meningocele/hydrocephalus), limb (club feet), thoracic (lung atresia), and abdominal defects (pyloric stenosis/colon malrotation/cryptorchidism) [3].

What is the prevalence, epidemiology, and embryology of POC?

Pentalogy of Cantrell is a rare defect with reported incidences between 1/65,000 and 1/200,000 live births. The male/female ratio is approximately 2:1, and females tend to be more severely affected. Most cases are sporadic, although associations have been reported with trisomies 13, 18, and 21 and Turner syndrome, and some familial, X-linked cases have been reported. Pentalogy of Cantrell occurs between days 14 and 18 of embryonic life around the time of differentiation of the primitive mesoderm into the splanchnic and somatic layers, which give rise to the pericardium, myocardium, abdominal wall, diaphragm, and sternum. It is the abnormal differentiation, migration, and fusion of the mesoderm at this time that leads to the defects seen in POC [3, 4].

What types of abdominal wall defects are seen in POC?

Most patients with POC have an omphalocele, a ventral wall defect of the umbilical ring with herniation of the

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abdominal viscera covered by the umbilical sac. Other possible defects in the abdominal wall include wide diastasis of the abdominal muscles (diastasis recti), epigastric hernia, umbilical hernia, and gastroschisis (protrusion of the abdominal viscera through the defect to the side of the umbilical cord).

What are the various congenital heart defects seen with POC?

The most common intracardiac defects seen in POC are ventricular septal defect (72%–100%), atrial septal defect (53%), pulmonary stenosis (33%), tetralogy of Fallot (20%), and left ventricular (LV) diverticulum (20%). Complex congenital heart defects are present in 51% and include partial anomalous pulmonary venous return, transposition of the great arteries, truncus arteriosus, hypoplastic left heart syndrome, complete atrioventricular canal, and double outlet right ventricle. Other findings can include bilateral superior vena cava, single coronary anatomy, dextrocardia, and dextroversion. The most common pericardial defect is an absent pericardium, with the minority of patients having only a ventral defect [1, 3].

What is an LV diverticulum?

An LV diverticulum is either a muscular or fibrous appendix arising from the LV apex that extends beyond the myocardial border. The muscular type is associated with POC. It results in a narrow connection to the LV cavity (versus a wide connection in the fibrous type) that contracts synchronously with the true LV, although it is usually thin walled and hypokinetic. It often appears as a pulsating umbilical mass under the skin. The risks associated with LV diverticulum include spontaneous rupture, thrombus formation, and ventricular tachyarrhythmias. The left anterior descending coronary artery may also course through the diverticulum and put the patient at risk for LV failure after repair. Surgical intervention is indicated for those at high risk for rupture (dyssynchronous contraction), severe tachyarrhythmias, or progressive congestive heart failure (CHF) [5].

Clinical Pearl

Risks associated with LV diverticulum include spontaneous rupture, thrombus formation, and ventricular tachyarrhythmias. The left anterior descending coronary artery may also course through the diverticulum and put the patient at risk for LV failure after repair.

What sternal malformations are associated with POC?

Sternal malformations occur due to failed fusion of the mesenchymal plate during embryonic development and vary in significance from absence of the tip of the sternum (short sternum) to complete sternal absence. They are categorized according to location of the defect: (1) cervical, (2) thoracic, (3) thoracoabdominal, and (4) cleft or bifid sternum. Patients with sternal clefts have normal heart position and skin coverage and intact pericardium, and these malformations are typically more benign in nature, whereas those in the first three categories are associated with ectopia cordis [6].

Sternal instability may result in severe paradoxical movement of the mediastinum with respirations, leading to dyspnea, hypoxemia, and ventilatory failure in infants. In addition, sternal malformations leave the patient susceptible to respiratory infections and blunt or piercing trauma to the heart.

What is ectopia cordis?

Ectopia cordis (EC) occurs when the heart lies outside the thoracic cavity due to sternal, pericardial, diaphragmatic, and/or abdominal wall defects. It can lie partially or completely outside the chest and may also be deficient in both pericardial and skin coverings ("naked heart"). The apex of the heart is usually anterior and cephalad in both cervical and thoracic EC, both of which are nearly universally fatal [6]. Pentalogy of Cantrell is associated with thoracoabdominal EC, which often has a thin membrane/skin covering and the apex is typically not as rotated. In addition to being susceptible to infection and trauma, complete EC results in the development of a small chest cavity with associated lung hypoplasia. (See Figures 11.1 and 11.2.)

Clinical Pearl

In addition to susceptibility to infection and trauma, complete ectopia cordis results in the development of a small chest cavity with associated lung hypoplasia.

Are these patients at risk for pulmonary hypertension?

Patients with POC often have some degree of pulmonary hypoplasia and up to 55% present with pulmonary hypertension (PH) [7]. After birth they may require pulmonary vasodilators (inhaled nitric oxide [iNO], sildenafil) or respiratory assistance, including high-frequency oscillatory ventilation. Pulmonary hypoplasia may be attributed

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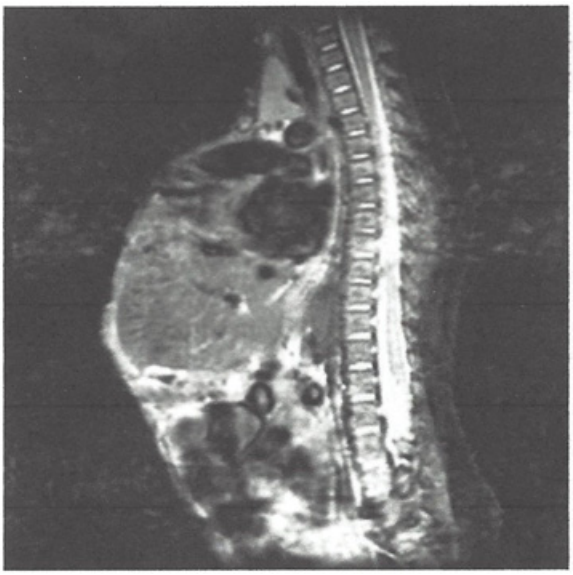

Figure 11.1 MRI, sagittal scan. The heart is located outside the thorax.

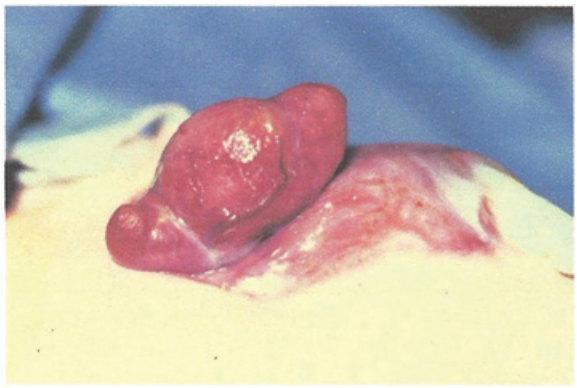

Figure 11.2 Cantrell's pentalogy (thoracoabdominal ectopia cordis). The heart is protruding from the thoracic cavity above an omphalocele. From Engum S. Embryology, sternal clefts, ectopia cordis, and Cantrell's pentalogy. *Semin Ped Surg* 2008; **17**: 154–60. With permission.

to the markedly decreased chest capacity but also to abnormal postnatal pulmonary growth. Pulmonary hypertension is more likely to occur with giant omphaloceles or when the liver is located inside the omphalocele sac. Pulmonary hypertension may also result from CHD due to cyanotic lesions resulting in hypoxia-induced tension on arterial smooth muscle and vascular remodeling, severe left-sided obstructive lesions, or lesions with significant left-to-right shunting. Pulmonary hypertension in POC has also been attributed to a possible genetic component, as it has been known to exist without the aforementioned comorbidities.

What surgical options and strategies should be considered in POC?

General Considerations The biggest challenge in caring for a patient with POC lies in consideration of the wide spectrum of anomalies with various complexities that complicate surgical planning. Planning dictates a multidisciplinary approach involving neonatology, cardiology, cardiac surgery, general surgery, anesthesiology, and pertinent subspecialties to determine the best course of action. Generally, corrective strategies include separation of the peritoneal and pericardial cavities with coverage of midline defects, omphalocele correction, repair of intracardiac lesions, and restoration of the heart into the thoracic cavity, all while preserving/establishing musculoskeletal structural integrity and hemodynamic stability. Early staged approaches are reserved for the most severe cases, while postponing surgery until after the more vulnerable neonatal period is advocated for less severe cases. In general, surgical mortality rates are higher in patients requiring early intervention. Alternative options include supportive/symptomatic care and comfort care/withdrawal.

Omphalocele An intact and well-epithelialized omphalocele does not necessarily need to be repaired immediately after birth, but early intervention is surgically easier. Smaller defects (<5 cm) can be repaired earlier by primary closure or with a synthetic mesh. Larger, more complex omphaloceles will require a staged approach with gradual reduction into the abdominal cavity to allow for growth within the cavity and to minimize the effects of increased intraabdominal pressure, especially in patients with significant cardiac malformations. Conservative management is preferred, if possible, for larger lesions to allow for epithelialization of the omphalocele sac and maturation of the lungs. This includes prophylactic antibiotics and coverage of the omphalocele to protect it from injury and desiccation.

Intracardiac Repair Unstable, hemodynamically significant intracardiac defects demand early intervention, which may include definitive surgical correction or surgical palliation. If possible, repair is delayed until there is sufficient growth of both the thoracic cavity and the lungs.

Left Ventricular Diverticulum Because of the risk of rupture and lethal arrhythmias, LV diverticula are repaired early. Repair of an LV diverticulum can be done concomitantly with EC and/or cardiac repair in less complex cases [5].

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Ectopia Cordis The main goal in repairing EC is to provide coverage to the heart and return it to the thoracic cavity to prevent fluid losses, desiccation, and trauma. This can be accomplished initially by primary closure for smaller defects or with the use of skin grafts or prosthetic material. Returning the heart into the thorax can cause compression or kinking of the great arteries and may have to be done in stages to allow for growth of the smaller thoracic cavity. The timing of intracardiac repairs in relation to reduction of the heart into the chest depends on the cardiac defect. Smaller, less significant lesions (such as an atrial or ventricular septal defect) may be repaired at the same time but more complex lesions may be delayed until the child is older and the thoracic cavity is large enough to accommodate the heart [4].

Sternal Malformations Repair of sternal malformations in the neonatal period is preferred because the compliant chest wall becomes more rigid by the age of 3 months, making surgery more complicated. Simple malformations can be repaired by primary closure, but complex lesions may require a staged approach because of the risk of cardiac compression/decompensation secondary to the limited size of the small chest cavity. Various techniques such as the use of autologous tissue (rib, costal cartilage, clavicle), sliding/rotating chondrotomies, and pectoralis major myoplasty may be used [4].

Clinical Pearl

Pentalogy of Cantrell has a wide spectrum of anomalies with various complexities; therefore surgical planning dictates a multidisciplinary approach.

Anesthetic Implications

What preoperative information is necessary before surgery?

A preoperative evaluation for a patient with POC must include a multidisciplinary discussion prior to surgery. Imaging including echocardiogram, cardiac catheterization, computed tomography/magnetic resonance imaging studies, and ultrasound to assess cardiac/sternal/abdominal defects will help with anesthetic planning. The child's cardiorespiratory status should be evaluated for signs of compromise including shunting, arrhythmias, congestive heart failure (CHF), low cardiac output, aspiration, respiratory failure, and PH, as early and aggressive support may be necessary. Patients may require mechanical ventilation at birth, as well as inotropic support, the use of iNO, and systemic pulmonary vasodilators. Patients are also at risk for sepsis, dehydration, hypothermia, and renal failure.

Clinical Pearl

A thorough preoperative investigation of available imaging to ascertain the presence and severity of associated anomalies is paramount. The cardiorespiratory status should be evaluated for signs of compromise, as early and aggressive support may be necessary.

What are the intraoperative concerns regarding omphalocele repair in a patient with POC?

The main concern with an omphalocele repair in a patient with POC is the effect of increased intraabdominal pressure (and translated increase in intrathoracic pressure) on reduction of viscera into the abdominal cavity. This increase in abdominal pressure and physical presence of additional viscera in the abdomen may compress the exposed heart and lungs, compromise alveolar ventilation, induce arrhythmias, and reduce venous return to the heart. This, in turn, may worsen right-to-left shunting (or reverse left-to-right shunting), induce a PH crisis, decrease cardiac output, or hinder the ability to ventilate effectively. The potential for severe cardiac compromise is magnified in patients with EC and LV diverticula, who may not tolerate even mild increases in intraabdominal pressure or direct compression.

Clinical Pearl

The increase in intraabdominal pressure and physical presence of additional viscera in the abdomen may compress the exposed heart and lungs, compromise alveolar ventilation, induce arrhythmias, and reduce venous return to the heart.

What are the intraoperative concerns regarding sternal malformation repair?

Large sternal malformation repair, especially in patients with EC, significant CHD, or LV diverticulum, may lead to rapid blood loss, arrhythmias, impaired cardiac function, and pneumothorax. Internalization of an EC or further reduction of the heart into the thoracic cavity may increase intrathoracic pressure enough to impair ventilation and reduce venous return to the heart or may twist or kink the great vessels. Intraoperative echocardiography may be necessary to assess cardiac function.

The operating room setup should consist of a typical setup for a neonatal omphalocele repair. The room should be warmed, blood should be available, and dextrose-containing intravenous fluids should be administered.

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A naso- or orogastric tube is necessary to decompress the stomach. In patients with significant CHD/PH, it is wise to have vasoactive drugs available (epinephrine, milrinone, vasopressin, phenylephrine, and calcium chloride) both in bolus form and as infusions. Nitric oxide should also be readily available. In patients with an LV diverticulum who are at risk for arrhythmias, antiarrhythmic drugs such as adenosine and amiodarone should be available and defibrillation pads should be placed. Ventilation can prove challenging and it may be necessary to use an intensive care unit (ICU) ventilator intraoperatively.

What types of vascular access and monitoring are necessary intraoperatively?

The type of vascular access and monitoring necessary will be determined by the severity of the cardiac lesion(s) and the size of the abdominal wall defect. Anesthesia for repair of a small omphalocele with a simple cardiac defect and no significant hemodynamic compromise or shunting (such as a small atrial or ventricular septal defect) can be accomplished with one or two peripheral intravenous (IV) lines and standard American Society of Anesthesiologists monitoring. However, placement of arterial and central venous access is warranted for either primary closure of a large omphalocele with reduction into the abdominal cavity or in the presence of complex, hemodynamically significant cardiac lesions as the potential for cardiac compromise, arrhythmias, need for vasoactive medications, fluid shifts, and concerns for respiratory compromise and PH crisis exist. It should also be noted that an electrocardiogram (ECG) tracing in patients with EC (especially when the heart is completely outside the chest) may not be possible. Heart rate and rhythm may have to be assessed through direct visualization.

What are the anesthetic induction and intubation considerations for this patient?

An IV induction is warranted when an omphalocele is present because of possible delayed gastric emptying and risk for aspiration. Induction goals for these patients should be tailored toward the specific cardiac lesion. Epinephrine should be drawn up and immediately available in the event of cardiovascular collapse on induction of anesthesia. The abdomen must be decompressed to minimize aspiration risk and bowel distension. Care must be taken to ensure the omphalocele sac and exposed heart are covered and not compressed during mask ventilation and intubation. Intubation may be difficult in patients with severe EC due to the heart sitting on the chest and the anterior/cephalad direction of the heart. There may be little to no room for the laryngoscope handle to be placed while manipulating the blade into the oropharynx. When appropriate, a difficult airway cart with fiberoptic intubating equipment should be present.

Clinical Pearl

Intubation may be difficult in patients with severe EC due to the heart sitting on the chest and the anterior/cephalad direction of the heart. There may be little to no room for the laryngoscope handle to be placed while manipulating the blade into the oropharynx.

What ventilatory strategies should be planned for this patient?

These patients are already at risk for ventilatory failure, as they often have pulmonary hypoplasia and some degree of PH, a deficient anterior chest wall, and a diaphragmatic malformation. Significant left-to-right shunting with fluid overload and CHF further compromise ventilation. Cardiopulmonary compromise is made worse with the reduction of the omphalocele into the abdominal cavity. Even slight pressure on the lower sternum or abdomen during positioning can impair ventilation. Permissive hypercapnia with a higher respiratory rate and lower tidal volumes and peak inspiratory pressures may be indicated to minimize reduced venous return to the heart as well as pulmonary hyperinflation and lung injury. Caution should be exercised, however, in patients with PH, as hypercapnia may lead to an increase in pulmonary vascular resistance and a pulmonary hypertensive crisis may ensue. It may be necessary to use an ICU ventilator during the procedure.

Clinical Pearl

Permissive hypercapnia with a higher respiratory rate and lower tidal volumes and peak inspiratory pressures may be indicated to minimize reduced venous return to the heart as well as pulmonary hyperinflation and lung injury.

What is abdominal compartment syndrome?

During an omphalocele repair an increase in abdominal pressure >20 mm Hg and/or an increase in central venous pressure (CVP) >4 mm Hg places the patient at risk for abdominal compartment syndrome (ACS). Abdominal compartment syndrome occurs when an increase in intraabdominal pressure results in hypoperfusion to the splanchnic circulation leading to lactic acidosis, renal

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failure, intestinal ischemia, reduced cardiac output, and impaired ventilation. Signs of intraoperative ACS include difficulty with ventilation, lower extremity edema or duskiness in color, failure of the SpO_2 monitor in the lower extremities, oliguria, decreased femoral pulses, and differences in upper versus lower extremity blood pressures. Close monitoring of intraabdominal pressure and/or CVP is helpful in guiding surgical repair in patients who are at higher risk for ACS.

What are the postoperative concerns for this patient?

Postoperative concerns include ACS, low cardiac output syndrome, CHF, arrhythmias, LV diverticulum rupture, respiratory failure, PH/pulmonary hypertensive crisis, hypoxemia, infection/sepsis, small bowel obstruction, feeding difficulties/parenteral nutrition dependence, fluid and electrolyte abnormalities, and hypothermia. Because of the significant postoperative concerns, most infants remain intubated and recover in the intensive care unit after surgery.

What is the prognosis for patients with POC?

Owing to the low incidence and extreme heterogeneity of POC, it is difficult to approximate the prognosis, but it is generally poor. Recent data state a survival rate between 37% and 61%, depending on the type and severity of associated malformations and intracardiac defects. Risk factors for high mortality include Class I POC, younger age at first operation, respiratory failure exceeding 100 days, hypoxia, complex CDH, and complete EC. The causes of death are cardiac failure, tachyarrhythmias, ruptured LV diverticulum, CHF, respiratory failure, and sepsis [3, 8].

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