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Abdominal Wall Defects in the Newborn

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September 25, 2020

Introduction:

Hello, I am Zach Rumlow, a fourth-year medical student at Rocky Vista University. Doctor Paul Dube of Rocky Vista University and Doctor Melanie Lewis of the University of Alberta have assisted me with the creation of this podcast.

The purpose of this podcast is to review important clinical information as it pertains to the abdominal wall defects that are observed in fetuses and newborns.

Our objectives are:

1. Define umbilical hernia, omphalocele and gastroschisis
2. As it pertains to the fetal abdomen and the gastrointestinal tract:
    a. Review prenatal screenings
    b. Review normal embryonic development
3. Delineate the complications and comorbidities associated with neonatal abdominal wall defects
4. Review the operative and non-operative choices for management of neonatal abdominal wall defects
5. Explore the post-operative management and discharge criteria for patients with neonatal abdominal wall defects
6. Review the epidemiological data as it pertains to neonatal abdominal wall defects

Let's start with a case:

As a fourth-year medical student on a NICU rotation you are asked to attend a delivery with your attending for a G1P0 mother at 38 weeks gestation. Her only prenatal visit was at 12 weeks and showed a normal intrauterine pregnancy. On admission a fetal ultrasound demonstrated cephalad presentation but was otherwise inconclusive for fetal anatomy. Upon delivery the obstetrician notes that there are abdominal contents which are protruding from the abdominal cavity, and they appear to be freely mobile. What is the most likely diagnosis of this neonate? Please pause the podcast and continue once you have thought of the most likely diagnosis.

If you responded gastroschisis, you are correct!

If you did not guess gastroschisis, do not worry because in this podcast we will elucidate the presentation and treatment of gastroschisis along with the comparable anomalies including omphaloceles and umbilical hernias. Later, we will discuss these in greater detail; however, for those who are unaware of these terms, an umbilical hernia is a ventral, midline herniation of the intestines which are covered by skin, an omphalocele is a ventral, midline herniation of the intestines and potentially other viscera which is not covered by skin but is instead covered by a membrane, and gastroschisis is a ventral, lateral herniation of the intestines and potentially other abdominal viscera which is not covered by tissue.

Often, content that is taught during pre-clinical medical education is forgotten by the time students reach their clinical years and beyond. In part this is due to lack of differentiation and prioritization of pathology that results in clinical presentations. Fetal abdominal wall defects are a perfect example of embryology gone awry. To adequately prepare students and other providers, we will focus on the key features of the embryology of the gut that results in pathology in neonatal patients.

Normally, longitudinal and transverse folding of the flat, trilaminar embryonic disc occurs at gestational weeks 3-4. This transforms the disc into an elongated cylinder. Lateral folding is continued until the lateral body folds meet ventrally, in the midline, resulting in the formation of the primitive body tube with the outermost surface being composed of ectoderm and the innermost surface is composed of endoderm. The inner structure eventually forms the primary gut tube. The endoderm and the ectoderm and separated by the mesoderm which eventually forms the muscular abdominal wall. During this initial folding the ectoderm fails to connect over the umbilicus due to the connecting stalk and yolk sac which emerge from this region and form the umbilical ring. This failure allows for herniation of the primary midgut at gestational week 6. During this herniation the midgut rotates 90 degrees and then between weeks 10-12 it retracts and completes an additional 180 degrees of rotation. This rotation results in the anatomic configuration of the gastrointestinal tract. Abnormalities in these processes can result in the aforementioned congenital defects.[1,2]

Umbilical hernias are herniations of bowel through the midline umbilical ring which are smaller than 4 cm in diameter and are covered by the epidermis. They are the result of failed closure of the fascial and peritoneal layers over the umbilical ring.[3] ~~(4b)~~ Most commonly, they result spontaneous regression and closure, and therefore they are rarely managed with surgical techniques; however, this does not make them clinically insignificant. In the general neonatal population the prevalence of umbilical hernias is approximately 10-20% this is buoyed by the prevalence in the black population which is approximately 30%. Across all races the prevalence in neonates who are small for gestational age and premature is approximately 80%.[4] Further, neonates with Ehlers Danlos Syndrome, hypothyroidism, Beckwidth Wiedemann syndrome, trisomies 18 and

21 (otherwise known as Edwards and Down Syndrome respectively), and the mucopolysaccharidoses are at an increased risk of the disease.[3] Therefore, during newborn screening exams it is important to screen for the disease with a thorough physical exam with emphasis given to those at increased risk. Guardians should be informed of the diagnosis and reassured that the overall risk of complications is exceedingly low, but they should seek medical care if they notice signs of incarceration of umbilical hernia such as if the hernia is non-reducible, if it becomes painful to touch and/or changes in texture or color. They should also be made aware of signs of ischemia of the bowel including but not limited to hematochezia and/or melena, anorexia, abdominal pain, increased colic, and/or weight loss. Both ischemia and incarceration of the bowel are indications for immediate surgical intervention; additional indications of surgical intervention are defects which are larger than 1-1.5 cm and those which are present after 4 to 5 years of age as both of these cases are unlikely to spontaneously regress and close. [2,3,4,5] The overall risk of incarceration and ischemia is below 0.3% and the overall rate of necessary surgical repair is less than 10%.[4,6] In all cases laparoscopic or open techniques are well tolerated and result in low risk of recurrence.[7] The primary goals of surgery are to repair the structural defect of the abdominal wall and repair or remove any damaged bowel.[3]

Omphaloceles are the herniation of bowel and potentially the stomach and other viscera including the liver and less commonly the heart, bladder and female reproductive organs through the midline umbilical ring which are larger than 4 cm in diameter and are covered by an avascular peritoneal sac. The more commonly accepted hypothesizes for the development of omphalocele are failure of retraction of the abdominal contents at weeks 10-12, insufficiency of the lateral folding of the trilaminar disc which results in weakness of the resulting ventral ectoderm allowing for pathologic herniation of the abdominal contents, and/or failure of formation of the mesoderm which results in muscular weakness of the abdominal wall allowing for herniation of the abdominal contents.[1,2] In live births the rate of omphalocele is ~ 1:4,000-6,000. This rate is decreased secondary to spontaneous abortions, which in the case of omphalocele, are not uncommon and occur secondary to associated comorbid conditions.[2] Such conditions will soon be discussed in greater detail.

Gastroschises are the herniation of bowel and other abdominal viscera, but not typically the liver, which are lateral to the umbilical ring and are not covered by an avascular peritoneal sac. They most commonly occur on the right side of the abdominal wall. The more commonly accepted hypothesizes for the development of gastroschisis are insufficiency of the lateral folding that results in the formation of the ventral ectoderm allowing for pathologic herniation of the abdominal contents, failure of formation of the mesoderm which results in muscular weakness of the abdominal wall, and/or premature obliteration of the right umbilical vein (which normally occurs during the second trimester) or vascular accidents of the vitelline artery resulting in ischemia and infarction of the right abdominal wall allowing for pathologic herniation of the abdominal viscera.[1,3] Furthermore risk factors for the development of gastroschisis include pregnancy at an early age; with mothers under 20 having a sevenfold increase in the rate of

gastroschisis in their children. Additionally, the use of sympathomimetics (such as cocaine, methamphetamine, or more commonly used drugs like phenylephrine or methylphenidate) may increase the risk of the vascular accidents hypothesized as causing gastroschisis.[2] In live births the rate of gastroschisis is ~1:5,000 with that rate almost doubling over the last couple of decades.[1,2]

Importantly, and unlike in the case of gastroschisis, omphalocele is associated with a greatly increased risk of congenital comorbidities which increase the rate of mortality. In live births the overall mortality of isolated omphalocele is < 5%; however, > ½ of all patients with omphalocele have associated congenital defects including cardiopulmonary defects which are the most commonly associated comorbidity and cause of mortality.[2] 10% of all cases of complicated omphalocele are associated with Beckwith Wiedemann syndrome [which as a reminder, includes the constellation of Wilms Tumor Secondary to a mutation to the Wilms Tumor 2 gene, hypoglycemia due to excessive IGF-2 and insulin production, organomegaly, and macroglossia in addition to omphalocele]. Approximately, 1/3 of all patients with omphalocele have associated trisomies 13, 18, or 21 (Patau, Edwards, and Down syndrome Respectively).[1,7] Importantly, although rare, one of the most fatal associations with omphalocele is Pentalogy of Cantrell which presents as the pentad of omphalocele, inferior sternal, anterior diaphragmatic, and intra and pericardial defects.[2,7] In patients with Pentalogy of Cantrell the heart is often found within the omphalocele and the degree of cardiac defect is often the determining factor in survivability. It is present in approximately 1:200,000 live births. Due to the high rates of perinatal mortality, we will not discuss in great detail additional syndromes associated with omphalocele. However, it should be noted that there are numerous proposed genetic mutations and syndromes that are associated with omphalocele.[8] Even though as intrauterine risk factors of omphalocele continue to be fleshed out, there are some notable ones that should be addressed. Notably due to omphalocele's association with neural tube defects, the association with modified function of the methylenetetrahydrofolate reductase gene and its gene products should not be ignored. Although not a standardized recommendation, the use of vitamins B_9 and B_{12} (folate and cobalamin respectively) has been shown to reduce the risk of omphalocele.[8] This is likely associated with their respective effects on the methylenetetrahydrofolate reductase gene and its gene products. Additionally, intrauterine exposure to valproic acid (brand name: Depakote), has been shown to increase the risk of omphalocele along with neural tube defects. This is also, likely due to modified function of the methylenetetrahydrofolate reductase gene and its gene products. Lastly, there are proposed findings of hereditary omphalocele and gastroschisis via autosomal dominant and recessive pathways along with x-linked recessive pathways.[8] Although it is not the sole responsibility of a pediatrician to ensure adequate prenatal counseling of mothers, it is important for pediatricians to recognize risk factors that may increase the risk of fetal complications especially when there is a known family history of disease.

As stated, the rate of congenital comorbidities associated with gastroschisis is limited. The primary means of morbidity and mortality of gastroschisis is small bowel necrosis

and ileus.[2] Due to the irritating nature of amniotic fluid and the resulting ileus that occurs from exposure to it, both oligohydramnios and polyhydramnios are not uncommon complications that result from gastroschisis.[2] In the case of omphalocele, the protective nature of the avascular peritoneum makes this is an uncommon complication, but its risk is elevated in the case of perforation of the peritoneal covering.[2] Additionally, increased risk of torsion of the bowel in patients with gastroschisis can result in increased risk of ischemia and necrosis which inherently increases mortality.

Knowing this, it follows that, the most appropriate prenatal management of these diseases involves detection and diagnosis of these defects, detection and diagnosis of associated comorbid conditions, and appropriate and timely management of these defects and their comorbidities. As discussed, omphalocele is a normal finding up until 12 weeks of gestation and therefore it is not diagnosed prior to that point.[1,2] Both omphalocele and gastroschisis are associated with elevated maternal, serum alpha-fetoprotein levels (with levels in patients with omphalocele ~ 4x the upper limit of normal and those with gastroschisis ~7x the upper limit of normal). In most cases, maternal, serum alpha-fetoprotein is tested at the 18-20 week prenatal visit as part of the quad screen for maternal, serum alpha-fetoprotein, hCG, inhibin A and estriol. These tests are used to assess for trisomies 13, 18, and 21; monosomy of the sex chromosome; and fetal abdominal wall and neural tube defects. At the same time the fetal anatomy scan is used for both screening and diagnosis of these defects as it has approximately an 80% sensitivity and a 95% specificity for detection of omphalocele and gastroschisis.[1,9] In addition, fetal MRI can be used to confirm diagnosis and rule in and out other congenital defects associated with omphalocele.[9,10] Further, due to both being midline in nature and both being covered by tissue it is not uncommon for omphalocele and umbilical hernias to appear similar on initial imaging and therefore it in the case of either disease it is appropriate to consider fetal MRI for further differentiation. It is important for obstetricians to note the presence of abdominal wall defects as they require precaution when clamping the umbilical cord so as to not accidentally clamp the bowel. Beyond normal maternal screening, once diagnosed, treatment and diagnosis of omphalocele includes recommendation of a 22 week fetal echocardiogram due to high rates of associated cardiopulmonary defects.[6] In addition, it is noteworthy that omphalocele and gastroschisis increase the risk of fetal complications including but not limited to fetal growth restriction, bowel ischemia and necrosis, oligo or polyhydramnios, and cardiopulmonary defects. Therefore, it is recommended that beginning at week 32 mothers undergo either weekly or biweekly non-stress tests and/or biophysical profiles to identify such pathologies. Lastly, although in the cases of isolated omphalocele or gastroschisis preterm and/or premature along with cesarean deliveries are not recommended, and are associated with increased risk of fetal and maternal mortality, associated complications including intrauterine growth restriction, giant omphaloceles, or those which contain the liver are indications for their use. [7,8,10] Additionally, any maternal complications(such as: preeclampsia, placental abruption, placenta previa) are indications for delivery as specified by the obstetrics team.[4] As with all congenital conditions, screenings for associated diseases should be discussed appropriately with appropriate parental parties, as some of the complications and comorbidities of

omphalocele and gastroschisis such as trisomy 18 and Pentalogy of Cantrell along with severe bowel necrosis are often incompatible with life.[2] Prior to delivery it is appropriate for these patients to be referred to specialists including but not limited to geneticists and maternal fetal medicine to discuss the most appropriate and available clinical options to them.[2]

Finally, we will address the most appropriate management of these neonates once they are born. As discussed previously, umbilical hernias often require minimal management, while gastroschisis and omphalocele can present as either severe surgical emergencies or as cases that should be managed appropriately but may pose little threat to neonatal viability.

As we have discussed, maternal fetal medicine will be consulted on these cases, additionally, the neonatal and surgical teams will be consulted about the upcoming delivery. As otherwise noted the decision for vaginal versus cesarean delivery will depend upon the safety of the mother and the associated complications of the diseases.

Once born, these neonates will be admitted to the NICU for continuous monitoring of cardiopulmonary, gastrointestinal, and hemodynamic function. All neonates should be thoroughly examined and NG suctioning is appropriate to reduce the volume and pressure of the viscera.[2,10] As discussed cardiopulmonary function may be diminished in either case but special focus should be given in patients with omphalocele.[10] Patients with omphalocele may need to be intubated and placed on a ventilator or CPAP, and additional cardiac resuscitation and management will likely be required.[10] Meanwhile, gastroschisis presents with the added complication of ileus and may require parenteral nutrition and therefore early central line placement will likely be indicated.[10] In the case of either disease it is important to maintain the integrity of the bowel and/or the peritoneal sac. Both omphalocele and gastroschisis should be managed by placing the lower portion infant in a bowel bag filled with warm saline and if unavailable the herniated organs should be covered in a sterilized, saline soaked, plastic wrapping. In patients with gastroschisis, it is important to place them in a lateral decubitus position with the side of the defect being downward so as to not contribute to vascular compromise and strangulation of the ectopic organs.[2,7,10] Due to the high rate of comorbid complications that can impact the viability of the repair of omphaloceles it is important to consider the presence of other congenital abnormalities. Additionally, surgeons should note the location of the liver relative to the omphalocele as rupture during manipulation can result in fatal hemorrhage.[2,8,10] In the case of omphalocele it is important for surgeons to note the size of the defect, as all defects between 4 and 10 cm are termed omphaloceles and are more likely to be successfully repaired using a staged closure while those which are larger than 10 cm are termed giant omphaloceles and are likely to require a delayed, staged closure.[2,5] In the case of a staged repair, the abdominal contents are typically placed inside of a one-piece plastic silo which is sutured to the surrounding fascial layer. The abdominal contents are kept under pressure and allowed to gradually fill the abdominal cavity. The pressure should be kept below 20 cm H_2O so as to not contribute to compromise, and the entire process takes ~

1 week to complete. Once the viscera is completely replaced inside the abdominal cavity primary closure of the abdominal wall is performed.[5,10] As mentioned delayed, staged repair is primarily used in the case of giant omphalocele or in the case of other significant malformations which are associated with omphalocele. The primary benefit of a staged closure is the allowance of a more gradual filling of the abdominal cavity and promotion of enlargement of the thoraco-abdominal cavities, which in severe cases experience blunted intrauterine growth. In general, patients are subjected to daily dressing changes during which silver sulfadiazine is applied to gauze and then to the defect. [10] This process allows for eschar formation over the surrounding peritoneal membrane, contraction of the contents into the abdominal wall, and then repair of a resulting ventral hernia once the process is complete.[5]

The repair of gastroschises is not entirely different from the repair of omphaloceles. The most common forms of repair of gastroschises are immediate repair with primary closure or a staged repair with use of a silo followed by primary closure.[2,5,7] In the case of gastroschises with minimal herniation it is possible to replace the abdominal viscera into the abdominal cavity and perform primary closure. It is still important to ensure low intraabdominal pressure to prevent ischemia and necrosis of the bowel and other viscera which can impact cardiopulmonary and urogenital function. Just as in the case of omphalocele a one-piece plastic silo can be placed and can allow for gradual filling of the abdominal cavity. This is often required for larger defects with greater amounts of visceral ectopy.[2,7]

In the instances of either disease, infection can be a key player in mortality. Therefore, all manipulation of the ectopic contents should be performed in a sterile fashion. Neonates should receive 48 hours of antibiotic prophylaxis of skin flora with ampicillin and gentamicin. This can be discontinued following negative blood cultures.[7]

The discharge criterion for patients with gastroschises and omphalocele are variable, but depend upon successful nutrition of patients along with management of their possible comorbid conditions.[7,10] Recognize, that due to low rates of ileus in patients with uncomplicated omphalocele, it is common to start early enteral feeding; however, due to high rates of comorbidities it is important to continue to monitor a neonate's tolerance of enteral feeding, their fluid status, and their cardiopulmonary function.[2] Due to the comorbidities associated with omphalocele, feeding is typically not the only factor that dictates the discharge criteria of these patients, and they will often require management by multiple specialties. This differs from patients with gastroschises as comorbid conditions are uncommon, but due to high rates of ileus, early enteral feeding is often more complicated and will need to be supplemented with parenteral nutrition. Importantly, patients who fail enteral feeding are more likely to have longer hospital stays and have increased rates of morbidity and mortality.[11] Preliminary research shows that rates of necrotizing enterocolitis, sepsis, and prolonged hospital stays are reduced in patients who successfully progress from total parenteral nutrition and early trophic feeds to total enteral nutrition.[11] Factors improving the success of this progression are term delivery, female sex, primary closure of the defect (therefore not performing a

delayed closure via a silo), and starting feeds at an earlier age.[11] Students and providers should recognize that although these risk factors are often out of their control they should be considered when evaluating the prognoses of these patients. As noted, there is limited research surrounding the topic of feeding and nutrition of neonates with abdominal wall defects, and therefore treatment plans of patients with these diseases should utilize multidisciplinary approaches that consider all presently available literature.[2, 7,10, 11] As we have previously discussed, it is exceedingly rare to observe complicated forms of umbilical hernias and therefore prior to discharge these patients rarely require management exceeding the pediatric hospitalist group.[4,5]

The conclusion of our patient's case was a successful manual replacement and primary closure of a gastroschisis which was limited to the terminal ileum. After delivery a central line was placed to begin total parenteral nutrition; however, beginning at 24 hours they were advanced on trophic feeds and feeding was advanced to total enteral nutrition by day 22 at which point their central line was removed and they were discharged. They will plan to follow up with the surgical team along with their pediatrician.

In conclusion:

- We reviewed and contrasted the definitions of omphaloceles, gastroschises and umbilical hernias
- We compared and contrasted their likely embryological origins
- We discussed the important role of normal prenatal testing in the screening for and diagnosis of the pathologies
- We differentiated the comorbid diseases that often present with umbilical hernia and omphalocele from the complications that are caused by gastroschisis
- We provided an overview of the operative and non-operative management of omphaloceles, gastroschises and umbilical hernias providing insight into the importance of management of comorbidities and complications of the diseases
- We briefly explored the growing evidence surrounding appropriate feeding of patients with omphalocele and gastroschisis
- We recognized that each disease has its own epidemiological and clinical nuances that differentiate their management and follow up
- I would again like to thank Doctors Paul Dube and Melanie Lewis for assisting me with the creation of this podcast! Thank you for your time!

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Developed by Zachary Rumlow, Dr. Paul Dube, and Dr. Melanie Lewis for PedsCases.com. September 25, 2020.

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