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Fetal Abdominal Wall Defects

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Additional information is available at the end of the chapter

Abstract

Abdominal wall defects (AWDs) represent a group of congenital anomalies that can be diagnosed early during pregnancy even at the time of the first trimester assessment, with direct impact on pre- and postnatal fetal prognosis and management decisions. The most frequent anomalies in this group are gastroschisis and omphalocele. The key method available, that allows the detection of any deviation from the physiologic midgut herniation, is the ultrasound (US) assessment. A precise algorithmic scan approach is imposed not only for an accurate detection of any abdominal wall defect, but also for a proper location of the defect and of the spatial relation to the umbilical cord insertion, fundamentally important in differentiating among various malformations. Other structural or chromosomal anomalies should be excluded. Suitable multidisciplinary counseling should be considered. Unfortunately, in utero surgery, in these cases, has not been yet successful. Postnatal early interventions are usually required in specialized pediatric centers.

Keywords: congenital anomalies, abdominal wall defect, gastroschisis, omphalocele, ultrasound

1. Introduction

Abdominal wall defects (AWDs) define a type of congenital anomalies characterized by the herniation of abdominal organs through an unusual opening surrounding the umbilical cord. The most common two types include omphalocele and gastroschisis. The omphalocele or exomphalos (in Greek, omphalos = umbilicus, kele = hernia, tumors) was firstly described in 1634 by Ambroise Pare, while gastroschisis (in Greek gastro = stomach—the term generally

used for abdomen; schisis = fissure, tear or gape) was first described by James Calder, a decade later. Other uncommon AWDS are ectopia cordis (EC), limb–body wall complex, cloacal and bladder exstrophy, urachal cyst, Prune belly syndrome and Cantrell pentalogy [1]. The correct prenatal detection and classification of these fetal malformations are extremely important for subsequent opportunities in parental counseling and pregnancy management. Nowadays, the intensive use of US assessment has allowed an increase in detection rates of AWDs, even from the first trimester nuchal translucency scan.

2. Embryology/pathophysiology and demographics

The embryologic developmental of the ventral body wall is reflected in its malformations. There are two types of defects, respectively, defects in the primaxial component and defects in the abaxial component. The first type of defects is often linked to neural tube-closure defects, whereas the second one manifest as limb–body wall or ventral body wall defects [2, 3]. Several hypotheses with respect to AWDS known as ventral body wall defects have been issued [4]. The embryologic origin of ectopia cordis, gastroschisis and bladder exstrophy is not yet known, but is thought to be more closely linked than that for omphalocele [5, 6]. It is considered that an abnormal closure of the ventral body wall folds during the 4th week of development is the main cause for these entities. In cases of gastroschisis, exposure to a teratogenic factor was suggested to be influential [7]. Some studies suggest that poor socio-economic status and prenatal care, as well as teratogens (e.g. recreational drugs, salicylates, paracetamol and pseudoephedrine) may be important contributors to the development of gas-troschisis [8, 9]. A combination of genetic and environmental factors was also thought to be involved in the origin of gastroschisis, and also ectopia cordis and bladder exstrophy [10–12]. Chromosomal abnormalities are diagnosed in 1.2% of infants with gastroschisis [13], whereas approximately half infants (54–57%) with omphalocele present with aneuploidies or gene disorders [14]. However, one risk factor associated with gastroschisis was identified in young maternal age, mothers under 20 years old having the highest risk [10]. The oldest embryologic hypothesis date from 1963, and state the potential teratogenic effect on the folds, which result in gastroschisis [15]. Another theory pleads for the rupture of the amniotic membrane at the base of the umbilical cord [16] or for the disruption of the omphalomesenteric (yolk-sac and vitelline) artery, resulting in infarction and necrosis at the base of the umbilicus [17]. As there is no evidence that for the amniotic rupture almost exclusively on the right side and that the omphalomesenteric artery offers blood supply to the paraumbilical region of the abdominal wall [18], the first and oldest theory may be overlooked [5]. On the other hand, omphalocele is a different entity, with a known etiology, thought to be the failure to return of the loops of bowel after the physiological herniation from the 6th to 10th week post-fertilization, when the fetal midgut extends into the extraembryonic celom, occupying the proximal segment of the umbilical cord [19]. A physiological hernia seldom exceeds 7 mm in diameter or rarely persists after 12 weeks of gestation, when the midgut returns to the abdominal cavity [20]. Other pathogenic theories include failure of complete lateral-body migration and closure of the body wall [15]. Omphalocele is more prevalent in older mothers.

The prevalence of the two most frequent entities of AWDs is reported to be for gastroschisis 3.09 per 10,000 births, with a live birth prevalence of 2.63 per 10,000 and for omphalocele 3.29 and 1.13 per 10,000, respectively [21]. The prevalence of gastroschisis has increased in the last years, whereas that of omphalocele has remained stable [22]. Regarding the prenatal diagnosis of AWDs, both omphalocele and gastroschisis are easily diagnosed at the 11–14 weeks nuchal scan. So, large studies report sensitivity for both congenital anomalies from 90 to 100% [23, 24]. In fact, reports show that 22 and 35% of the chromosomally normal cases of gastroschisis and omphalocele, respectively, were diagnosed before 14 weeks, and 50 and 30% between 14 and 23 weeks. The overall prenatal detection rate was 91.6% for gastroschisis and 83.3% for omphalocele [21].

3. Prenatal diagnosis and classification of fetal abdominal wall defects

3.1. Gastroschisis

Gastroschisis is an AWD characterized by the herniation of the abdominal viscera represented by bowel loops and occasionally parts of other abdominal organs outside the abdominal wall with no covering membrane or sac, to the right of the insertion of the umbilical cord, and rarely to the left side [25, 26]. Even if the condition is not generally associated with other major congenital or chromosomal anomalies, an accurate fetal anatomy assessment is required. The reported rate of the proportion of gastroschisis associated with major defects is about 10% [27], arthrogryposis being present in a minority of these fetuses [28], with a reported mortality rate of 5–10% in all cases of gastroschisis [29]. Others report a higher rate (14%) of additional associated anomalies, the central nervous system and cardiac malformations being the most common anomalies [30]. Gastroschisis is often classified into simple (as an isolated defect) and complex (as associated with bowel-related complications: intestinal atresia, perforation, stenosis or volvulus) [31]. In cases with intestinal complications, there is a relevant risk of increased morbidity, higher rates of complications, as respiratory distress or sepsis and of course an increased length of hospital stays [32]. The key to an accurate diagnosis is fetal US in routine antenatal care, which affects patient management and prognosis. In the past, the detection was higher in the second trimester, between 16 and 22 weeks of gestation, in approximately 60% of cases, with a false positive rate of 5.3% [33]. Misdiagnosis of gastroschisis as omphalocele has serious implications, as gastroschisis is rarely associated with chromosomal anomalies and unnecessary amniocentesis may be needed with additional risks to the procedure [34]. Nowadays, the diagnosis of gastroschisis can be facilitated ultrasonographically as early as the late first trimester, 12–13 weeks of gestation [35]. After correctly identifying a normal umbilical cord insertion using color Doppler, gastroschisis is detected as herniation of the bowel loops with no covering membrane (e.g. **Figure 1a**). In most cases, the defect is on the right side of the umbilical cord with a normal umbilical cord insertion. Beside the location of the defect, it is important to establish the size and content of the defect and if present, the associated anomalies.
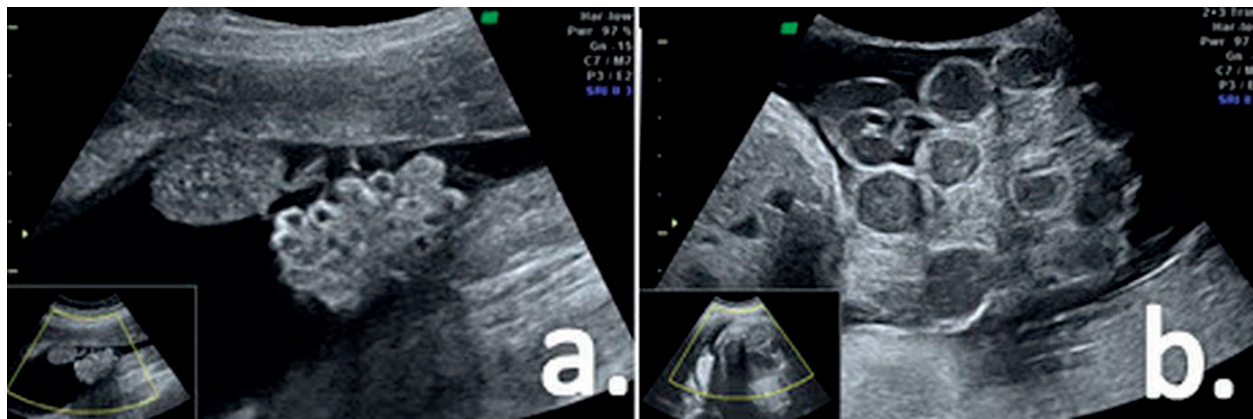
Figure 1. a. Ultrasound image of gastroschisis diagnosed in the second trimester (bowel loops floating in the amniotic fluid with no sac); b. Ultrasound image of gastroschisis diagnosed in the third trimester (thickened, echogenic bowel wall floating in reduced amniotic fluid).

Other ultrasound features may include an abnormal position of the stomach, dilatation of the bowel loops with a thickened and echogenic bowel wall (e.g. **Figure 1b**). Regarding the amniotic fluid, a decreased amount is often reported, rather than an increased amount. Subsequent bowel atresia is a frequent complication in fetuses with gastroschisis, due to inflammation and direct trauma of the amniotic fluid, on the herniated bowel [36]. The significance of certain associated ultrasound features in determining fetal outcome is debated, as prenatal predictors of gastroschisis complications. There is an associated risk of intrauterine death in 5% of cases of gastroschisis [37], as well as an increased incidence of fetal growth restriction or small for gestational age weight fetuses [38]. Antenatal US features of gastroschisis, such as extra- and intra-abdominal bowel dilatation, stomach herniation, stomach dilatation, bowel matting, growth restriction, abnormal umbilical artery (UA) Doppler ultrasounds and abnormal amniotic fluid volume were studied as prognostic factors. However, only extra-abdominal bowel dilatation proved to be a statistically significant marker of complex gastroschisis and associated morbidity [39].The incidence of complex gastroschisis is reported to be 10% [40], with increased risk for complications such as perivisceritis [41], as the amniotic fluid is extremely toxic to the exposed bowel and ischemic injury, because of constriction at the level of the abdominal defect [42]. Regarding the risk of intrauterine demise (IUD), an intense surveillance protocol was proposed and demonstrated to reduce the rate of IUD by 2.2% [43]. The proposed modalities of monitoring included cardiotocography, even daily in the third trimester, and umbilical and middle cerebral artery Doppler [37]. On the other hand, the diagnosis of fetal growth restriction can be difficult, as abdominal circumference measurements are affected by the herniated bowel. Formulas that do not include abdominal circumference can be helpful in fetal weight estimation, but there are still on debate for the moment [44].

3.2. Omphalocele

Omphalocele is another AWDs represented by a midline defect that leads to a herniation into the amniotic cavity through the base of the umbilical cord. The herniated abdominal content is covered by a membrane presented by the peritoneum on the inner side, amnion

on the outer side and Wharton's jelly in between [26]. Omphalocele must be differentiated by the physiological midgut herniation that usually disappears before 11–12 weeks of gestation [45]. Omphalocele may be classified in terms of shape, as "conical", that includes hernia of the umbilical cord or "globular", with a large sac having a small diameter base. The size of the defect can be small, up to 5 cm, also called "minor" or more than 5 cm, called "major". The sac may contain bowel loops, small or large intestine, stomach, bladder or ovary or bowel loops and liver [6]. The covering membrane of the omphalocele can be intact, or it can rupture, and the bowel loops can float freely in the amniotic fluid and resemble gastroschisis. The differential diagnosis can include also cord hernia that has a normal insertion into the umbilical ring with intact skin, while in omphalocele the large defect has no muscles or skin. In term of associated anomalies, omphalocele can be syndromic or non-syndromic. About 75% of cases have associated chromosomal and non-chromosomal anomalies [46]. Some authors report a risk for chromosomal abnormalities of 30–40% [34], while other found a lower rate, of only 25% [30]. The most frequent chromosomal abnormalities associated with omphalocele include trisomy 18 (80%), trisomy 13, triploidy and trisomy 21. Other genetic findings described are 45,X, 47,XXY and 47,XXX, partial aneuploidy such as dup (3q), dup (11p), inv. (11), dup (1q), del (1q), dup (4q), dup (5p), dup (6q), del (9p), dup (15q), dup(17q), Pallister-Killian syndrome with mosaic tetrasomy 12p and Miller-Dieker lissencephaly syndrome with deletion of 17p13.3 and uniparental disomy (UPD) such as UPD 11 and UPD 14 [47]. The risk of aneuploidy does not change if the omphalocele contains only bowel or also the liver, but instead correlates with nuchal translucency thickness [14]. Non-chromosomal abnormalities include cardiac defects (50%) (atrial and ventricular septal defects (VSDs) and tetralogy of Fallot (TOF)) and gastrointestinal defects that are present in 40%. Omphalocele is a disorder that characterizes Beckwith-Wiedemann syndrome, together with macroglossia, macrosomia, hypoglycemia, visceromegaly and embryonic tumors [48]. The diagnosis is possible even from the first trimester, after 12 weeks of gestation, during the US genetic assessment (e.g. **Figure 2a** and **b**). Still, no aggressive management should be taken until the second trimester, as in some cases the omphalocele slowly disappears, although no spontaneous resolution have been reported in cases with herniated liver [14, 49]. Omphalocele looks like a smooth central mass, protruding from the anterior abdominal wall covered by membranes (e.g. **Figure 2a** and **b**.). It usually contains small intestine and liver, or other organs such as large intestine, bladder, stomach and spleen. The useful tool to demonstrate umbilical cord is a color Doppler. Polyhydramnios is a specific feature of omphalocele. Ascites can be present as well. Once the diagnosis is established, search for other associated anomalies should be considered. Invasive testing offer is mandatory. Studies have shown that 26–39% of cases are misdiagnosed as isolated omphalocele and actually, associated anomalies are demonstrated postnatally [50, 51]. Regarding the prognosis, it is driven by the presence and nature of the associated anomalies. Also, there is a higher risk for postnatal complications, such as pulmonary hypoplasia with consequently respiratory insufficiency. An omphalocele is considered giant if the defect contains more than 75% of the liver [52]. In cases of a small omphalocele and no associated anomalies, there is a very good prognosis, with a survival around 80–90%. In chromosomal and structural abnormalities associated cases, the mortality rate is around 80–100% [53]. An increased prevalence of deficits in
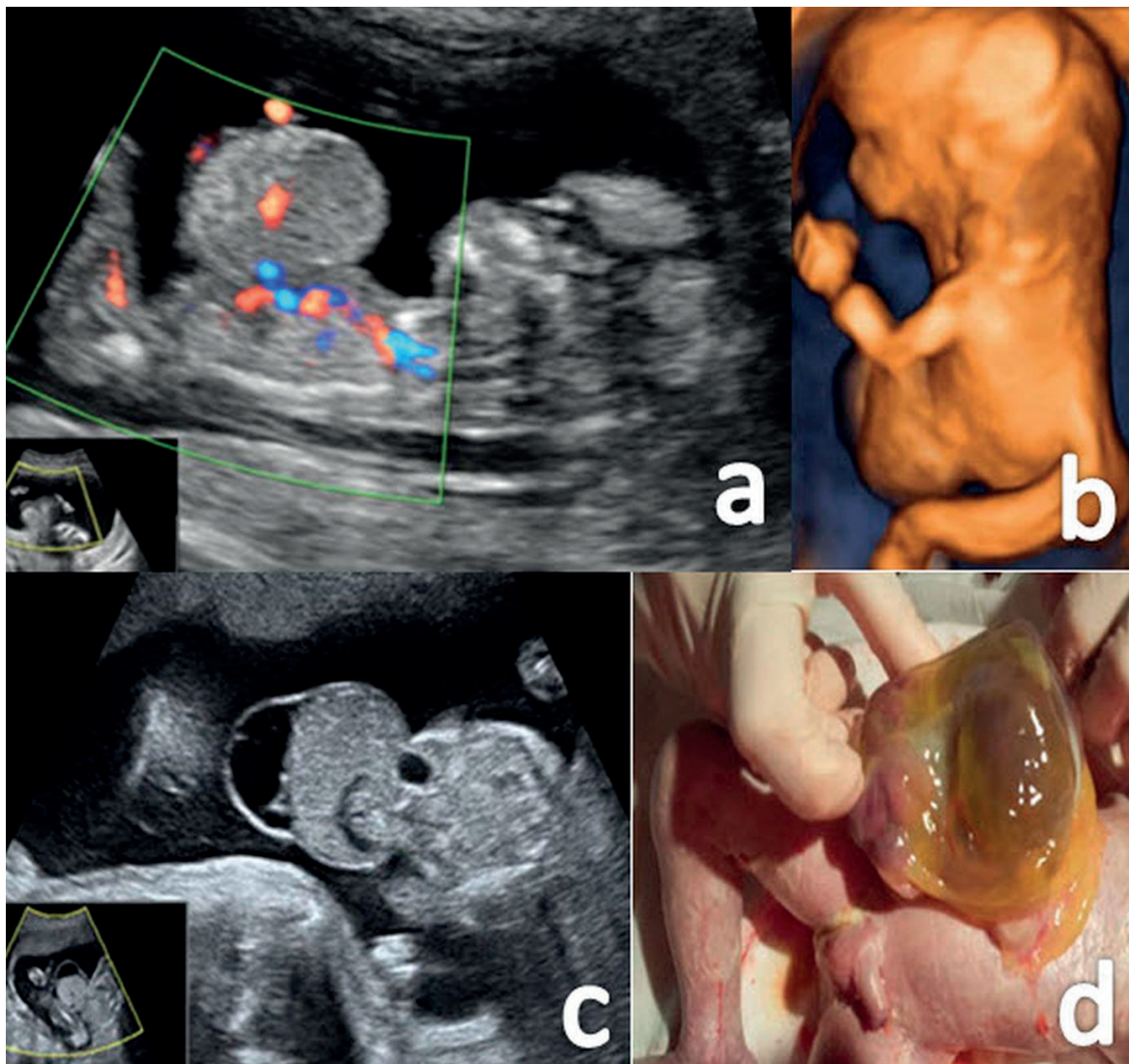
Figure 2. a. Ultrasound image of omphalocele diagnosed in the first trimester (a. Color Doppler image, b. 3D image); c. US image of omphalocele diagnosed in the second trimester; d. Postnatally image of omphalocele.

developmental achievements has been demonstrated in neonates with omphalocele [53]. An accurate prenatal diagnosis includes combining US evaluation with invasive testing. Even if high suspicion of omphalocele in the first trimester, the definitive diagnosis should be established after reevaluating the fetus in the second trimester. Besides karyotyping, also cytogenetic investigations should be offered. Termination of pregnancy is recommended after proper counseling, especially in cases of a large defect and severe associated anomalies.

3.3. Ectopia cordis

Ectopia cordis (EC) is a rare congenital AWD with poor prognosis. The defect is located in the anterior chest wall and abdominal wall, with abnormal placement of the fetal heart outside the thoracic cavity, with associated defect in the parietal pericardium diaphragm,

sternum and in most cases cardiac malformation [54] (e.g. **Figure 3a**). The most frequent intracardiac defects include ventricular septal defect (VSD, 100%), atrial septal defect (ASD, 53%), tetralogy of Fallot (TOF, 20%), left ventricular diverticulum (LVD, 20%) and pulmonary hypoplasia [55, 56]. The term of ectopia cordis was described for the first time in 1706, as a generally sporadic malformation [57]. Rarely, it is reported an association with chromosomal abnormalities like trisomy 18, Turner syndrome, 46,XX and 17q+ [58]. The condition affects 5–8/1 million live [59]. EC is classified into different types such as cervical (5%), cervicothoracic and thoracic (65%), thoracoabdominal (20%) and abdominal (10%) [57, 60]. Also, EC can be "partial", if the heart can be visualized pulsating through skin and "complete" when the heart is outside, naked, without the pericardial membrane [55]. The thoracoabdominal EC is one of the five features of pentalogy of Cantrell. The diagnosis of EC is possible using ultrasound assessment as early as the first trimester, even before 11 weeks of gestation [61, 62]. Still the associated abnormalities can be better evaluated in the early second trimester in nearly 90% [63]. Three-dimensional (3D) scan can improve the accuracy in detection of EC in rare cases of minor forms of ectopia cordis [64]. Invasive diagnosis of associated aneuploidy is mandatory in each case of EC [65]. This rare malformation has a poor prognosis, needing intensive care right from delivery, which includes resuscitation and coverage of the exposed heart with saline-soaked gauze pads wrappings, followed by aggressive surgical correction [66]. In most infants, this anomaly is fatal in the first hours or days after birth due to infection, cardiac failure or hypoxemia [67]. Early precise diagnosis of EC is necessary and essential, for a multidisciplinary team to provide optimal parental counseling. The couple must decide whether they opt for termination of pregnancy or for continuing it, despite the poor prognosis. There is no consensus regarding the mode of delivery, and parents should also decide autonomously if they prefer vaginal birth acknowledging the risk for fetal demise during labor. However, the alternative of performing a cesarean section does not change the outcome [63]. Prenatal care and accurate early ultrasound diagnosis is required especially in developing countries, in which the health care system is lacking currently important physical and material resources.
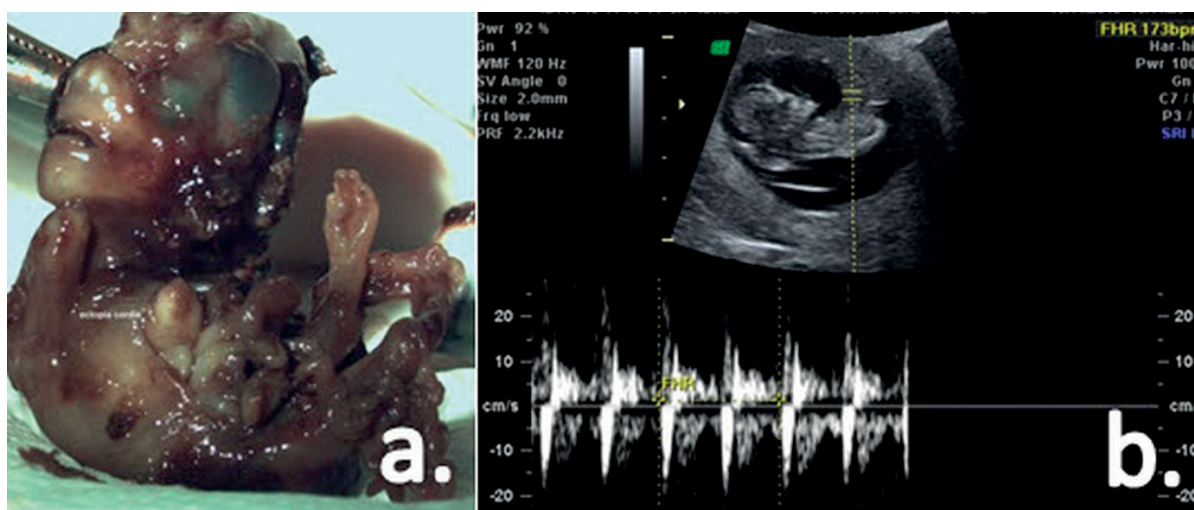

Figure 3. a. Ectopia cordis in a post-abortum fetus; b. Body stalk syndrome (ectopia cordis, fetus attached to the placenta).

3.4. Body stalk syndrome or limb: Body wall complex

Body stalk syndrome (BSS) represents the rarest and most severe AWD. This syndrome was described for the first time in 1987, as an association of three main features: exencephaly, facial clefts or encephalocele, thoraco or abdominoschisis and limb defects [68]. The anomaly is lethal, as there is a herniation of the peritoneal cavity in the extraembryonic coelomic cavity, with the fetus attached to the placenta [69] (e.g. **Figure 3b**). This is due to a large wall defect and due to a short or absent umbilical cord [26]. BSS is also known as the amniotic band syndrome, short umbilical cord syndrome or limb–body wall complex syndrome [70]. Usually, there is no association with chromosomal anomalies; still placental trisomy 16 or maternal uniparental disomy 16 have been reported [71]. The recurrence rate has been demonstrated to be low, and there is no correlation with parental age or fetal gender [68, 72]. The reported prevalence is 0.12 cases per 10,000 births (alive and still births) [73] or even higher 1 in 7500 pregnancies [74]. Two phenotypes have been described, respectively, as placento-cranial and placento-abdominal [75]. The diagnosis of BSS can be established by the end of the first trimester US scan [76] or at 11 weeks' gestation [77]. The US features of BSS show: the fetus is located (in its entirety or partially) outside the amniotic cavity, with an abnormal fetus, that cannot be separated from the placenta, and has lost his anatomic landmarks (**Figure 4a**, **b**). There can be also thoracoabdominal defects, spinal cord abnormalities, positional limb deformities and abnormalities of umbilical cord and membranes. As the US appearance can be confusing, the examination of the amniotic continuity, content of both the amniotic sac and coelomic cavity and a short umbilical cord helps in differentiating this condition from other AWD [77]. The differential diagnosis includes other polymalformative conditions, such as pentalogy of Cantrell, omphalocele-exostrophy-imperforate anus-spinal defects and isolated gastroschisis [78]. Also, kyphoscoliosis is often seen [74] and oligohydramnios can be present in the second and third trimester, situation in which only MRI can elucidate the anatomic structures [79]. Another finding is the presence of constriction rings, which can entangle the fetus [80]. Also, the fetuses with BSS present an increased nuchal thickness, a short umbilical cord and internal organ malformation, like abnormal mesodermal development [80]. So, the early diagnosis (at 11–13 weeks' gestation) is possible and necessary, as the anomaly is lethal and termination of pregnancy is offered. There is also a risk of spontaneously abortion reported, but in such cases an accurate diagnosis is often impossible. In the special situation represented by a twin pregnancy with a fetus with BSS and another unaffected fetus, the prenatal care should focus only on the healthy twin [80].

3.5. Cloacal and bladder exstrophy

Cloacal exstrophy (CE), even if rare, is a complex anomaly of the urogenital tract and intestinal tract that involves a low AWD with the exstrophy of all the structures that form the cloaca (rectum, bladder and lower genitourinary tract). The main embryologic event that is attributed to CE is represented by the premature rupture of the cloacal membrane before fusion with the urorectal septum. Still, many theories regarding the pathogenesis have been issued such as abnormal overdevelopment of the lower cloaca that prevents mesenchymal tissue migration [81, 82], abnormal fusion of the genital tubercle below the cloacal membrane or
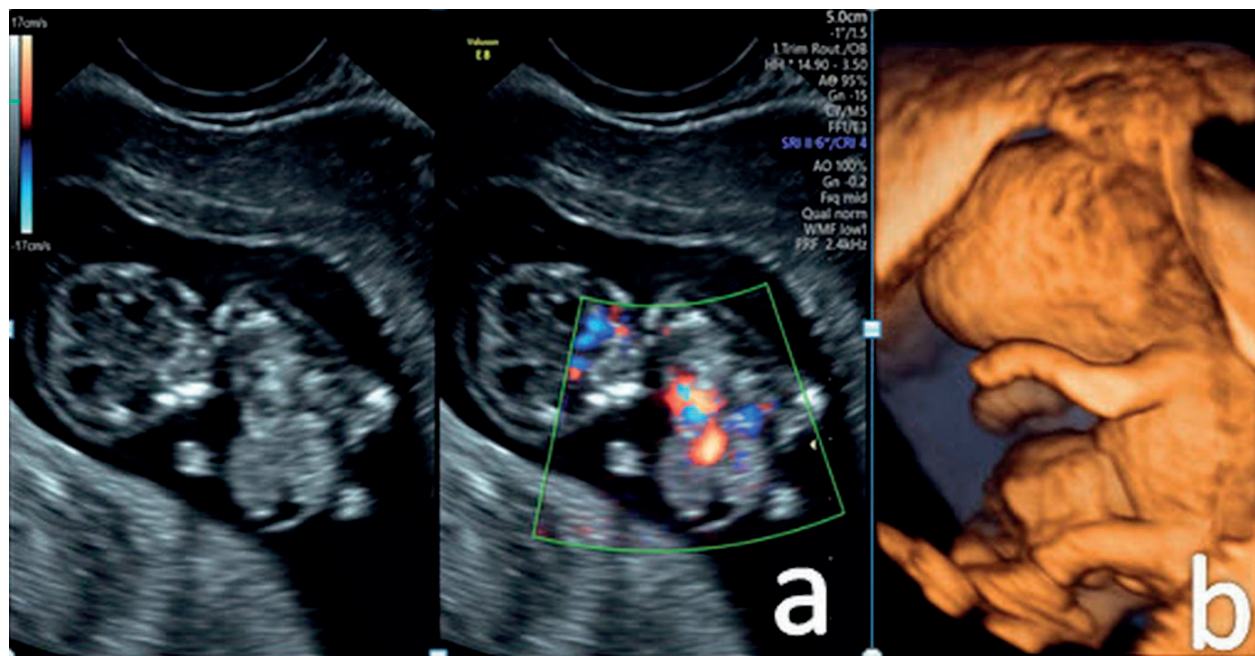
Figure 4. Ultrasound image of a BSS diagnosed in the first trimester: a. Gray scale and color image of the fetus with BSS; b. 3D image of the fetus with BSS.

abnormally caudal position of the body stalk and failure of mesenchymal ingrowth [83]. In the past, the estimated prevalence was reported higher as 1 case in 20,000 births [84], while more current studies describe a rate of 1 case per 200,000–400,000 live births [85]. Female fetuses are more likely to be affected by the anomaly. Prenatal US findings of CE include an absent normal bladder, with a lower abdominal wall defect, with herniated segments of the intestinal tract and a cystic pelvic mass in case of intact cloacal membrane. In fact, the first initial feature is often the omphalocele (in 70–90% of cases), but in a cranial part. Generally, the amniotic fluid index is normal, as the upper urinary tract has no obstruction to flow. Color Doppler examination of both umbilical arteries can help in accurate localization of the bladder [86]. Other associated anomalies may include spinal defects such as sacralization of L5, congenital scoliosis, sacral agenesis [87] and interpedicular widening, or cardiovascular and central nervous system anomalies or single umbilical artery. Also, is reported the association with gastrointestinal malformations such as malrotation (30%), double appendix (30%), absent appendix (21%), short small bowel (19%), small bowel atresia (5%) or abdominal musculature deficiency (1%) [88]. Also, upper urinary tract anomalies can be seen in 60% of cases as pelvic kidney, horseshoe kidney, hypoplastic kidney and solitary kidney, with subsequent hydronephrosis and oligohydramnios [89]. The US diagnosis can also describe "the elephant trunk sign", which is the protrusion of the ileum in the amniotic fluid, resembling the trunk of an elephant [90]. Typically, CE does not associate aneuploidies, but invasive diagnosis can be offered. The survival rates of this type of AWD are approaching 100% these days, because of important operative techniques and perioperative management progress [91]. Still, the reconstructive staged surgical management of patients with CE remains the most challenging for pediatric surgeons and urologists [92]. Early US detection is important, as termination of pregnancy can be offered to the couple before viability, after intense multidisciplinary counseling,

especially in cases where a wide range of disorders is associated with CE. If the couple decides to continue with the pregnancy, US assessment can help in correct planning of surgical intervention with minimal damage to the exposed organs.

Bladder exstrophy represents an AWD with a failure of the anterior bladder wall to close normally, due to the lack of muscular or connective tissue [93]. The reported incidence is 0.25–0.5 in 10,000 births, more common in males in the ratio of 2:1 [94]. The main US finding described for prenatal diagnosis is the absence or non-visualization of the bladder, as the bladder is open to the abdominal wall, and urine is released directly into the amniotic fluid. According to the American Institute of Ultrasound in Medicine guidelines, a normal bladder must be demonstrated from the first trimester as a midline fluid-filled structure flanked by the umbilical arteries in color Doppler examination [95]. Other US findings include: lower abdominal protruding mass, formed by the exstrophied bladder, lower umbilical insertion and an umbilical cord cyst and external genitalia malformation, represented by a small penis with anteriorly displaced scrotum. Also, in females, a bifid clitoris and uterine and vaginal anomalies can be identified [93], besides a widening of the iliac crests [96]. The accuracy and sensitivity of the US can be relatively low, as not all signs are always present, and an urachal cyst may mimic the presence of the bladder [97]. Bladder exstrophy should be considered if no urinary bladder is visualized, and there is no oligohydramnios associated or other renal abnormalities. Still, for the differential diagnosis with an empty bladder, the scan of the lower abdomen should be repeated in 15 minutes interval. Also, the exclusion of CE should be made, as the management is more complicated and the prognosis poorer. Prenatal US correct detection of the anomaly helps in parental counseling and recommendation for delivery in the tertiary center, as the prognosis is quite favorable. The postnatal management includes early surgical procedure to close the anterior wall defect within the first 3 days after birth. If the surgical repair is performed later, there is a higher risk of urinary incontinence or uterine prolapsed, infertility and increased risk of bladder adenocarcinoma [86]. Besides the bladder closure, pediatric surgeons must repair also the epispadias simultaneously, or in staged intervention, to offer an acceptable appearance and function of the external genitalia [98].

3.6. Urachal cyst

The urachus is a primitive structure between the umbilical cord and the bladder, in developing fetus. It disappears normally prior to delivery, but in rare cases, parts can persist. The urachal cyst is a sinus considered a congenital urachal remnant abnormalities [99]. It is diagnosed in children, by means of ultrasound and MRI. It usually suspected if there is bleeding in the cyst or infection. The infected urachal cyst can rupture into the peritoneal cavity, leading to peritonitis. The first line treatment is the surgical procedure of complete primary excision with excellent prognosis.

3.7. Omphalocele-exstrophy of bladder-imperforate anus-spinal deformities complex (OIES complex)

OIES complex represents the most severe expression of the abnormal development of the cloaca with the arrest of the urorectal septum in the 7th–8th week of gestation. The reported

incidence is rare, of only 0.025–0.04 in 10,000 live births [100, 101]. The diagnosis is accessible early in pregnancy, at the end of the first trimester. The imagistic findings include the presence of omphalocele and bladder exstrophy, associated with anomalies of the spine. The imperforated anus is often found postnatally, even if it can be detected antenatally, but with high suspicion by specialized observer. Other anomalies evaluated with OIES complex are spina bifida, genital anomalies, fistulas, renal anomalies, limb hypoplasia, craniofacial anomalies and single umbilical artery [86]. As the prognosis is poor when multiple structural defects are associated, termination of pregnancy is offered as an option to the couple, after multidisciplinary prenatal counseling. If desire to continue the pregnancy, there is a high risk of preterm delivery, low birth weight or intrauterine death. The proper treatment of OIES complex includes a series of surgeries depending on the severity of the condition [100, 101].

3.8. Prune belly syndrome

The prune belly syndrome is another rare congenital syndrome, characterized by deficient abdominal muscles, urinary tract abnormalities and cryptorchidism in male fetuses. The pathophysiology has not been completely elucidated, as some consider the syndrome as a consequence of severe bladder outlet obstruction and others consider an abdominal muscle deficiency, secondary to a migration defect of the lateral mesoblast between weeks 6 and 7 of pregnancy [102]. The incidence is estimated to be 1 in 35,000 to 1 in 50,000 live births. The antenatal diagnosis is obtained during the second trimester scan, when megacystis is noticed, and an abnormally distended abdomen, in the absence of keyhole sign. However, there are reports in regards to the early US diagnosis [103, 104]. In the most severe form of Prune belly syndrome, a high incidence of oligohydramnios, pulmonary hypoplasia and ultimately stillbirth is reported [105]. Often, termination of pregnancy is the couple's option in early pregnancy. The postnatal management may include a single comprehensive surgical approach or a multiple step one, with good long-term results, but with a considerable incidence of iterative surgery and progression of the disease [106].

3.9. Cantrell pentalogy

With an incidence of 5.5 cases per 1 million live births and a male predominance [107], pentalogy of Cantrell is characterized by a midline, supraumbilical AWD, with a defect of the lower sternum, deficiency of the anterior diaphragm, defect in the diaphragmatic pericardium and cardiac anomalies such as septal defects and tetralogy of Fallot [108]. The main event during embryogenesis, thought to be the cause of this rare anomaly, is an abnormal differentiation of the intraembryonic mesoderm, at approximately 14–18 days after conception [108]. Chromosomal anomalies, such as trisomy 13, 18 and Turner syndrome, are often associated, so the invasive diagnosis is mandatory. Other anomalies observed with pentalogy of Cantrell include craniofacial and vertebral anomalies. US diagnosis of Cantrell's pentalogy is possible early, at 10 weeks' gestation, using 2D and 3D scans [109]. The combination of omphalocele and ectopia cords highly indicates a case of pentalogy of Cantrell [110]. The pentalogy is "complete" if four or all five defects are present, and is "incomplete" when various combination of defects are observed, if a sternal abnormality is present [86]. The AWD may contain stomach, liver,

Abnormality	Covering membrane	Site of defect	Umbilical cord insertion	Additional findings
Omphalocele	Yes	Umbilical insertion	Omphalocele membrane	
Gastroschisis	No	Right of umbilical insertion	Normal insertion	
Umbilical hernia	Yes	No umbilical ring defect	Normal insertion	
Pentalogy of Cantrell	Yes	Above umbilical insertion	Omphalocele membrane	Anterior diaphragmatic hernia, sternal clefting, ectopia cordis, and intracardiac defect.
OEIS complex	Yes	Umbilical insertion	Omphalocele membrane	Bladder exstrophy, imperforate anus, and spina bifida.
Body-stalk anomaly	Herniated organs in extraembryonic coelom	Whole anterior abdominal wall	Cord absent or shortened	Kyphoscoliosis, cranial defects, and limb defects.
Bladder exstrophy	Not applicable	Below umbilical insertion	Low insertion	Non-visualisation of bladder, lower abdominal bulge (exstrophied bladder), small penis with anteriorly displaced scrotum (if male), and widening of the iliac crests.
Cloacal exstrophy	Not applicable	Below umbilical insertion	Low insertion	Renal anomalies, neural tube defect, omphalocele, vertebral anomalies, non-visualisation of the bladder, distended bladder, hydrocolpos, dilated or echogenic bowel, umbilical cord cyst, separated pubic bones, and 'elephant trunk' sign.

OEIS, omphalocele, bladder exstrophy, imperforate anus, spina bifida complex.

Figure 5. Ultrasound findings in fetal abdominal wall defects [26].

bowel or total abdominal contents, evisceration. There is a pleural and pericardial effusion and the fetal heart is completely external or just partially. The prognosis is fatal and the survival is uncommon. Prenatal diagnosis is important as termination of pregnancy is the only option for the couple.

The ultrasound features that best characterize fetal AWDs are presented in **Figure 5** [26].

4. Pregnancy surveillance

In cases with abdominal wall defects, fetal distress was reported in 43% of cases, with an abnormal neurological outcome in 16% of them [111]. There is also the risk of still birth, reported to be 11% in cases of gastroschisis and 20% in cases of omphalocele [112]. Fetuses with gastroschisis often tend to be small for gestational age and to develop oligohydramnios [113, 114]. In such cases, the assessment of fetal weight can be difficult, as measurements of the fetal abdomen are not valid [115]. Placental insufficiency can be indirectly estimated by umbilical artery Doppler velocimetry, cardiotocography and biophysical profile. Still,

intrauterine growth restriction and oligohydramnios seem not to worsen the prognosis of fetuses with gastroschisis [116]. Fetal bowel features can be also evaluated, to estimate postnatal bowel complications. A cut-off of 1 cm for bowel diameter was considered a far-seeing marker for bowel damage [117, 118]. Overall, there is not yet a consensus regarding how and when fetal monitoring during pregnancy. Because of the associated risk, recommended attitude is a careful monitoring and a monthly interval control scheme, somewhat arbitrarily chosen. In the third trimester, repeated fetal monitoring is indicated [111]. Hospital admittance was proposed at 35 weeks of gestation, as many patients with fetal AWDs deliver prematurely [112, 115].

5. Mode and time of delivery

Even with recent progress in major medical and surgical specialties, the mode and time of delivery of fetuses with antenatal diagnosed abdominal wall defects remains a controversy. Fetal delivery by elective cesarean section is advocated by some centers [119–125], while others consider a vaginal delivery more suitable in cases with diagnosed fetal abdominal wall defect [126–130]. More so, there is no difference in fetal outcome regarding the mode of delivery [131–135]. In cases of omphalocele, delivery by cesarean section is recommended in cases with a large defect, to prevent the sac rupture and the liver damage during labor [136]. However, some researchers found that features such as the size or liver herniation have no importance in establishing the outcome of vaginal delivery [137]. The gestational age for induced delivery or elective cesarean section is another controversy (preterm versus term delivery). Some authors reported more complications and longer hospitalization in preterm deliveries [138, 139]. Others recommend a preterm delivery to optimize the toxic damage of the amniotic fluid to the herniated bowel in gastroschisis [120, 124, 129, 140]. The most recent study presented good results using a protocol for a preterm elective delivery, between 35 and 36 + 6 gestational age for fetuses with gastroschisis. Preterm delivery is not indicated in cases of omphalocele [26]. Still, most studies agree that in utero transport to a specialized pediatric center, where the defect can be corrected, offers an optimal fetal outcome [126, 141].

6. Postnatal prognosis and management

6.1. Gastroschisis

Postpartum, fetuses with gastroschisis must benefit from intravenous fluid resuscitation and wrapped herniated loops in warm saline as there is an increased risk for water and heat losses by evaporation. Specialized management of gastroschisis includes repositioning of the herniated bowel into the abdominal cavity, with closure of the abdominal wall (primary reduction and repair). In such cases, there is a high risk of respiratory complication. The surgical procedure can be also postponed if the patient is unstable [18], but with subsequent longer time

to reach full enteral feeds. In cases of complex gastroschisis, the repair is usually delayed, as anastomosis is impossible immediately after delivery, having an inherent risk of infectious and cholestasis complications [18, 24].

6.2. Omphalocele

In contrast to gastroschisis, there is a low risk of fluid and health losses in neonates with omphalocele, but still a coverage with saline-soaked gauze is required. Postnatal outcome and surgical management depends on the associated anomalies, such as congenital heart disease and pulmonary hypoplasia. Also, fetal gestational age and the size of the defect are relevant [18]. In cases of a small AWD, primary closure is the preferred therapeutic procedure, while in cases of a larger defect, multiple surgeries may be required to repair the considerable defect. Various agents such as povidone-iodine, sulfadiazine, neomycin, silver-impregnated dress-ings, neomycin, polymyxin and bacitracin ointments have been reported to help with the formation of an eschar of the amnion sac. There are different surgical techniques for the cure of omphalocele that include serial reductions or closing the defect gradually after replacing the sac with a mesh [24].

7. Conclusion

Prenatal ultrasound offers a high accuracy in the diagnosis of fetal abdominal wall defects beginning with the first trimester nuchal scan. Most fetal abdominal wall defects have poor prognosis and termination of pregnancy if often offered at the time of the detection after multidisciplinary counseling. Management of gastroschisis can be challenging, and also is the surgical treatment of complex forms. On the other hand, omphalocele, relatively easy to diagnose and treat, is frequently associated with chromosomal and structural anomalies that worsen the prognosis and the final outcome. The importance of ultrasound diagnosis in early pregnancy must be highlighted. This should be available even in under-developed health systems.

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