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ORIGINAL ARTICLE

Lung Malformations: Prenatal Ultrasound Diagnosis and Obstetrical Management

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ABSTRACT

Purpose: We present our experience in prenatal diagnosis and obstetrical management of congenital lung malformations (CLM).

Materials and methods: The diagnosis of CLM was performed during routine second and third trimester fetal morphology assessment. The extent of the disease was established according to the type, localization and size of the pulmonary lesion and the presence of fetal complications (mediastinal shift, fetal hydrops, hydramnios). Termination of pregnancy (TOP) was indicated in cases associated with extrapulmonary anomalies, untreatable cases and fetal hydrops. After delivery a pulmonary X-ray and surgical examination was performed in all newborns.

Results: We diagnosed 15 cases with congenital lung malformations. Of these, 9 had congenital cystic adenomatoid malformation (CCAM). TOP was performed in 6 cases with CCAM. Three cases had a favorable pre/postnatal evolution. Bronchopulmonary sequestration (BPS) was diagnosed in 3 cases, all with favorable perinatal evolution. Right pulmonary agenesis was diagnosed in one case and the outcome was neonatal death. One case of congenital high airway obstruction syndrome was followed by TOP. One case of severe bilateral pulmonary hypoplasia (secondary to a severe bilateral hydrothorax) resulted in neonatal death.

Conclusion: Obstetrical management is established individually depending on the severity of the cases.

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INTRODUCTION

Prenatal diagnosis of congenital fetal lung malformations relies mainly on the visualization of a hyperechoic fetal lung. This feature is common for cystic congenital adenomatous lung malformation (CCAM), bronchopulmonary sequester (BPS), congenital high airway obstruction syndrome (CHAOS) and congenital lobar emphysema. The natural evolution of these malformations involves intrauterine or postnatal complications.[1] Another congenital lung malformation which can be diagnosed prenatally is unilateral or bilateral pulmonary agenesis. The unilateral agenesis has a higher incidence than the bilateral form. When present as an isolated malformation, left pulmonary agenesis is compatible with long time survival. Unfortunately, right lung agenesis may have a reserved prognosis due to mediastinal displacement and compression on the great vessels and trachea.[2,3] Fetal hydrops, characterized by generalized cutaneous edema in association with pericardial effusion, hydrothorax or ascites is a nonspecific ultrasonography finding and may be caused by a large variety of fetal or maternal conditions.[4] Hydrothorax can favor the apparition of lung hypoplasia.[5]

This study aimed to present the authors' experience in prenatal diagnosis of congenital lung malformations and establish the obstetrical attitude when these malformations are diagnosed.

MATERIALS AND METHODS

The diagnosis of fetal lung malformations was established during the routine examination of fetal morphology in second and third pregnancy trimesters. The fetal lung was examined on the four chambers view, in left and right sagittal

paravertebral sections. We analyzed the two lung areas, pulmonary echogenity, mediastinum position (cardiac axis).

Unilateral hyperechoic lung lesions with or without cystic lesions and without collateral vessels emerging from descending aorta were interpreted as congenital cystic adenomatous malformation of the lung (CCAM). Unilateral hyperechoic lung lesions without cystic lesions situated usually in the basal lung lobes and irrigated by vessels emerging from the descending aorta were interpreted as bronchopulmonary sequestration (SBP). Bilateral homogenous hyperechoic lung areas, significantly increased lung volume, diaphragmatic inversion, dilatation of trachea and both main bronchi, associated with a decreased cardiothoracic index were interpreted as congenital high airway obstruction syndrome (CHAOS). The absence of a lung area and of its ipsilateral pulmonary artery branch with a normal contralateral lung image, ipsilateral heart displacement and its position near the thoracic wall was interpreted as unilateral lung agenesis. Significantly decreased lung areas and decreased cardiothoracic index in a case with fetal hydrops with massive hydrothorax during the third pregnancy trimester was interpreted as bilateral lung hypoplasia.

For ultrasonography description of CCAM, we used the classification proposed by Adzick et al which divides CCAM in macrocystic (one or more cysts ≥5 mm) and microcystic or solid (cysts less than 5 mm).[6] In all CCAM cases we calculated the ratio between cystic volume and head circumference (cystic volume ratio—CVR).[7] A CVR > 1.6 at the time of prenatal diagnosis and the presence of one or more associated fetal complications (hydrops, mediastinal deviation, diaphragmatic inversion, ascitis) were considered indicators of a reserved prognosis. We did not perform invasive fetal treatment techniques (aspiration of a dominant cyst or thoraco-amniotic shunt). In cases with solid CCAM, starting with 2012, we indicated prenatal maternal treatment with intramuscular Betamethasone 12 mg/day for two consecutive days.[8,9] The severity of pulmonary pathology was established according to the type, localization and size of the pulmonary lesion and the presence of fetal complications (mediastinal deviation, diaphragmatic inversion, hydrops, ascitis, hydramnios). Amniotic fluid volume was determined by calculating the amniotic fluid index (AFI) acording to the method described by Moore.[10] In fetal hydrops cases, we measured placental thickness and the systolic velocity on the middle cerebral artery; the systolic velocity was compared with the Mari diagram.[11] In case of fetal hydrops associated with severe hydrothorax we measured both lung areas, calculated the right and left lung area to head circumference ratio (LHR) and compared the results with the existing diagrams.[12] We performed an ultrasonographic follow-up of the tumoral lung volume and fetal complications. We recommended termination of pregnancy (TOP) in cases with lung malformations which were either untreatable or associated with extrapulmonary anomalies or fetal complications at the time of diagnosis. A pulmonary X-ray and a surgical examination was performed in all newborns. Fetal necropsy was done in cases with TOP or neonatal death. We used the classification of Stocker et al for pathological description of CCAM.[13]

RESULTS

Between 03.01.2005 and 31.03.2013, 15 cases with lung malformation were diagnosed: nine with CCAM, three with BPS, one with right lung agenesia, one with CHAOS and one with pulmonary hypoplasia secondary to a severe hydrothorax.

Congenital Cystic Adenomatous Malformation of the Lung

We diagnosed nine cases of CCAM (Table 1 and Fig. 1). The average maternal age was 28.6 years (24-32 years). The average pregnancy age when the prenatal diagnosis was performed was 22.5 weeks (18-33 weeks). Six cases (66.7%) presented with macrocystic CCAM and three cases had the microcystic form. In seven cases (77.7%), the lesion was localized on the left side. All nine cases were associated with mediastinal shift. By correlating the CVR value (CVR ≥1.6) with fetal complications at the moment of prenatal diagnosis (mediastinal shift, hydrops, ascitis, diaphragmatic inversion, hydramnios) or other associated malformations, we established in six cases a severe prognosis of CCAM (Table 1; cases 2,3,5,6,8; Fig. 2).

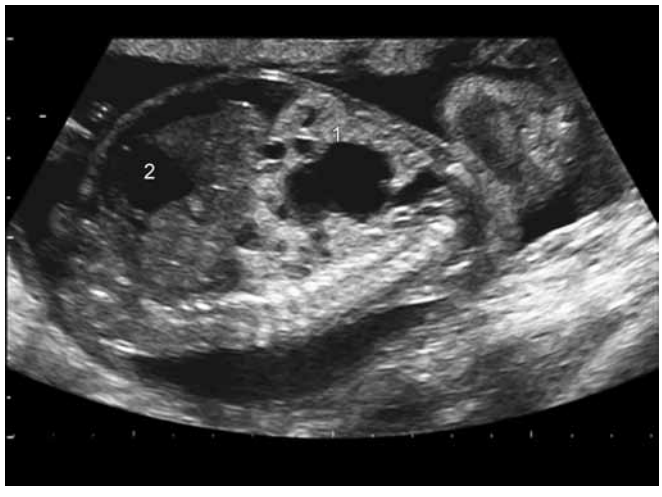

Fig. 1: Case 8 (Table 1). Sonographic views of a 20^{+4} week gestation fetus with a left congenital cystic adenomatoid malformation (macrocystic type). Left sagittal paravertebral view: 1—macrocystic left CCAM; 2—diaphragmatic inversion and fetal ascitis

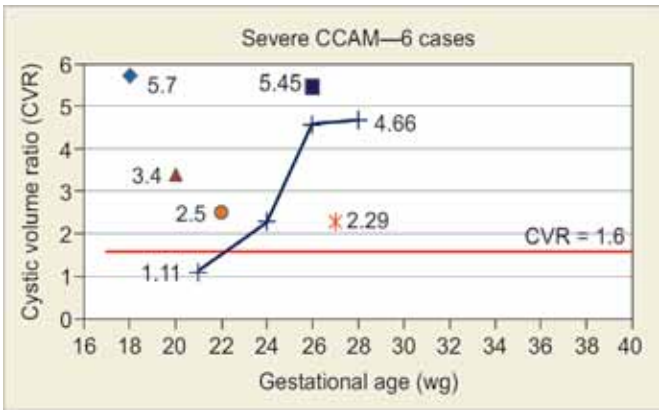

Fig. 2: Severe congenital cystic adenomatoid malformation (Table 1). CVR index at the diagnosis time and CVR evolution. Case 2—CVR: 5.45; Case 3—CVR: 2.45; Case 5—CVR: 5.7; Case 6—CVR: 2.29; Case 7—CVR: 1.11-4.66; Case 8—CVR: 3.4

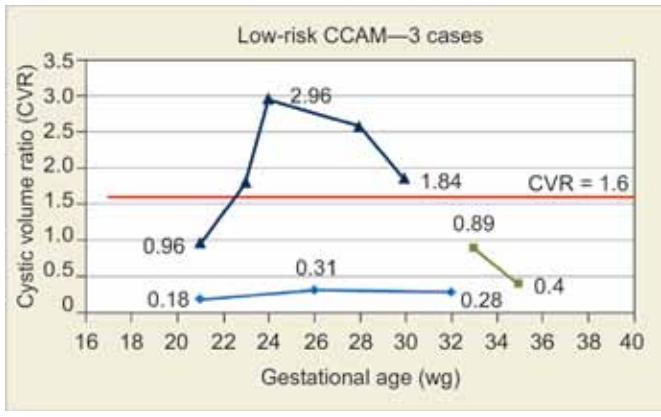

Fig. 3: Low-risk congenital cystic adenomatoid malformation (Table 1). CVR index evolution. Case 1—CVR: 0.89-0.4; Case 4—CVR: 0.18-0.28; Case 9—CVR: 0.96-1.84

A Description of the Patients' Evolution is Presented

Case 2 was diagnosed at 26 weeks, with a CVR = 5.45, developed an evolutive hydramnios (AFI = 359 mm) and delivered prematurely at 29 weeks a newborn which died immediately after birth. The patient chose not to have a necropsy for this baby.

Case 7 were bichorial twins, where the first fetus had an evolutive macrocystic CCAM. Cystic volume ratio increased from 1.1 at 21 weeks to 4.66 at 28 weeks. A C-section was performed at 29 weeks for progressive selective intrauterine growth retardation (IUGR) with Doppler flow modified on the umbilical and middle cerebral arteries and ductus venosus for the second twin. The first twin with CCAM had 2450 gm and died immediately after birth. The second twin, with selective IUGR, had 1050 gm, was admitted in neonatal intensive care unit and had a normal development.

Termination of pregnancy (TOP) was required in cases 3,5,6,8. Necropsy was performed in five cases (cases 3,5,6,7,8) and the diagnosis of type II CCAM was established.

In three of the nine cases with CCAM (Table 1, cases 1,4,9), the evolution was good (Fig. 3).

Cases 1 and 4 had a normal pregnancy progression with CVR ≤ 1.6 and delivered at term. Case 4 had associated hydramnios. Case 9 was diagnosed at 21 weeks with microcystic CCAM (CVR = 0.96). At 23 weeks the mother was prescribed Betamethasone because the cystic lung volume increased and CVR increased to 1.8. Cystic volume ratio reached a peak of 2.96 at 24 weeks and then decreased. The case was followed by our team up to 30 weeks (CVR = 1.84), then the patient was transferred to another center. All three CCAM cases with good evolution delivered at term. Newborns' thoracic X-ray showed a small-sized lung tumor which did not require postnatal surgery and the patients were monitored by the pediatric surgeon.

Bronchopulmonary Sequestration

Bronchopulmonary sequestration (BPS) was identified in three cases. The average age was 33.3 years (25-41 years). The average pregnancy age when BPS was diagnosed was

Table 1: Outcome of 9 fetuses with congenital cystic adenomatoid malformation

Case no.	*GA*	*Type*	*CVR*	*Mediastinal shift*	*Eversion of diaphragm*	*Hidrops*	*Ascites*	*Hydramnios*	*Other defects*	*Outcome*
1	33	Mac	0.89	+	–	–	–	–	–	FTB
2	26	Mac	5.45	+	–	–	+	+	–	PTB; NND
3	22	Mic	2.45	+	–	–	–	+	–	TOP
4	21	Mac	0.18	+	–	–	–	+	–	FTB
5	18	Mac	5.7	+	+	+	+	–	–	TOP
6	21	Mic	2.29	+	–	–	–	–	CIC	TOP
7*	21	Mac	1.1	+	±	+	+	+	–	PTB; NND of the first fetus
8	20	Mac	3.4	+	+	–	+	–	–	TOP
9	21	Mic	0.96	+	–	–	–	–	–	FTB

CIC: Cerebral interhemispheric cyst; FTB: Full term birth; Mac: Macrocystic type; Mic: Microcystic type; NND: Neonatal death; PTB: Preterm birth; TOP: Termination of pregnancy; *Twin pregnancy, first fetus with CCAM

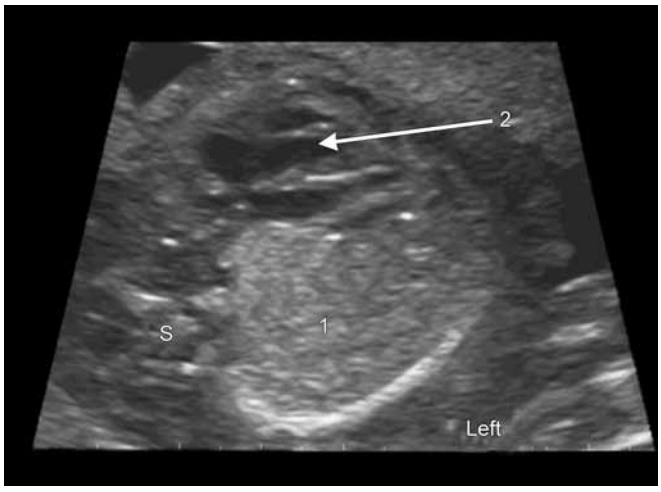

Fig. 4: Sonographic views of a 21^{+4} week gestation fetus with a bronchopulmonary sequestration (BPS). Transverse view through the fetal chest (four-chamber view): 1—BPS; 2—heart (right ventricle), dextrocardia and right mediastinal shift; S—spine

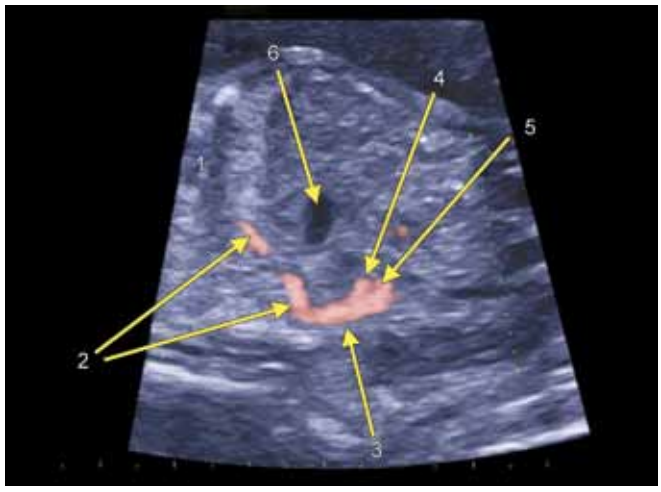

Fig. 5: Same case as figure 4. Sonographic views of a 21^{+4} week gestation fetus with a bronchopulmonary sequestration (BPS). Left sagittal paravertebral view: 1—BPS; 2—collateral vessels from thoracic aorta; 3—abdominal aorta; 4—celiac truncus; 5—superior mesenteric artery; 6—stomach

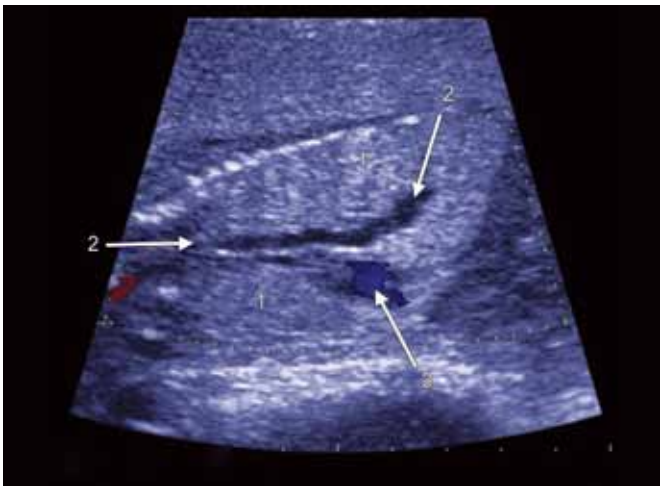

Fig. 6: Sonographic views of a 20-week gestation fetus with a congenital high airway obstruction syndrome. Color Doppler. Left sagittal paravertebral view: 1—right hyperechoic lung; 2—dilated trachea and main bronchiae; 3—heart and diaphragmatic inversion

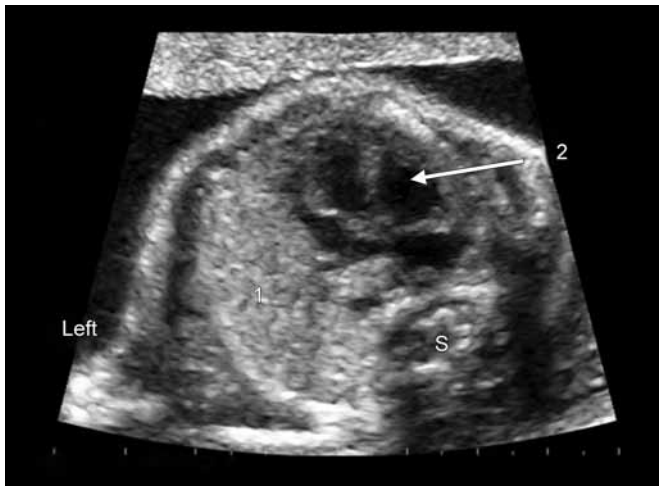

Fig. 7: Sonographic views of a 24-week gestation fetus with a right lung agenesis. Transverse view through the fetal chest (four-chamber view). Absence of right lung, normal cardiac situs, dextrocardia: 1—left lung; 2—heart, right ventricle; S—spine

20.7 weeks (19-22 weeks). In all cases, BPS was localized in the basal lobe of the left lung, dextrocardia was present due to mediastinal shift, color Doppler showed collateral vessels rising from thoracic aorta, amniotic fluid index was normal and the size of the BPS decreased prenatally (Figs 4 and 5). Two cases delivered at term. In these cases, lung X-ray did not show any tumor, the newborns developped normally and are followed-up by the pediatric surgeon. The third case is a still on-going pregnancy.

Congenital High Airway Obstruction Syndrome

We diagnosed a case of CHAOS at 20 weeks (Fig. 6). The maternal age was 26 years. The fetus had a very small cardiothoracic index (6.4%), a congenital heart malformation (ventricular septal defect and truncus arteriosus), bilateral kidney dysplasia (hypoechogenic small kidneys), hydrops

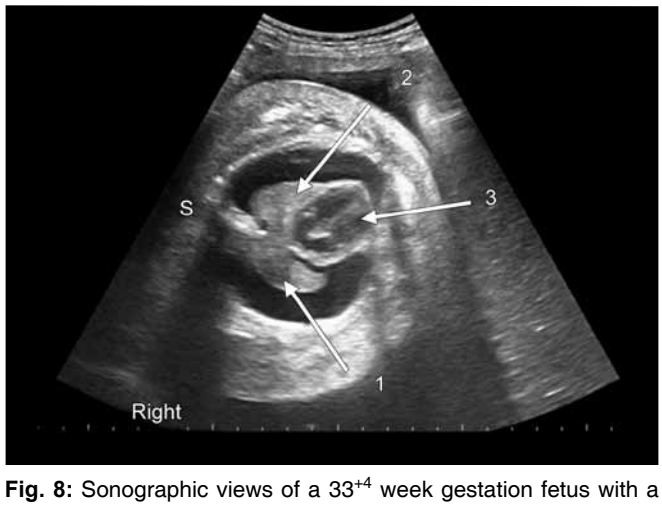

Fig. 8: Sonographic views of a 33^{+4} week gestation fetus with a fetal hydrops and severe bilateral hydrothorax. Transverse view through the fetal chest (four-chamber view): 1—right lung; 2—left lung; 3—heart, right ventricle; S—spine

with ascitis and severe oligohydramnios (AFI = 50 mm). Termination of pregnancy was required. The patient denied permission for a necropsy.

Right Lung Agenesis

We diagnosed a case with right lung agenesis at 24 weeks (Fig. 7). Maternal age was 39 years. The patient delivered at 35 weeks (spontaneous premature rupture of membranes) a living 2350 gm newborn who died after 2 months because of respiratory complications. Postnatal X-ray and echocardiography confirmed the diagnostic and trisomy 21 was found. The family denied permission for a necropsy.

Secondary Bilateral Pulmonary Hypoplasia

A 23 years old patient was referred at 33 weeks of gestation for a fetal morphologic examination. Fetal hydrops with severe bilateral hydrothorax and ascitis and associated with severe hydramnios (AFI = 372 mm) were diagnosed (Fig. 8). Placental thickness was normal. Thoracic examination showed small pulmonary areas (318 mm^2 left and 394 mm^2 right) and a small cardiothoracic index (17%). Fetal heart was normal. Fetal echocardiography showed an increased diameter of inferior vena cava (6.2 mm) compared to abdominal aorta diameter (4.2 mm). The left LHR was 1.02 and the right LHR was 1.27. At 33 weeks of pregnancy, the normal left LHR is greater than 2.0 and right LHR is greater than 3.05. Systolic velocity for the middle cerebral artery was normal for the gestational age (59.9 cm/s). Rhesus incompatibility was excluded. TORCH test indicated the presence of a chronic toxoplasmosis. The patient delivered at 34 weeks a baby which died immediately postpartum. Necroptic examination confirmed hydrops, severe bilateral hydrothorax and severe bilateral pulmonary hypoplasia.

DISCUSSION

In our study, we present 15 cases with prenatally diagnosed lung malformations. The malformations with echogenic lung appearance represented the majority of the cases [13 cases (86.7%)]. The echogenic lung appearance is present in a wide variety of lesions, both more common abnormalities (CCAM and especially BPS) as well as lesions with a rare incidence (tracheal obstruction, bronchial atresia or congenital lobar emphysema).[14]

Congenital Cystic Adenomatous Malformation of the Lung

Congenital cystic adenomatous malformation (CCAM) is a lung hamartoma.[15] The real incidence of this malformation is unknown. Anatomical pathology studies have shown that CCAM represents 25% of congenital malformations of the lung.[15] In 95% of cases, the malformation is limited to one lobe or segment.[16] In very rare cases the disease can be bilateral[17] or it can affect more than one lung lobe. There have been reports of mixed malformations of the lung, CCAM and BPS in one single tumor form[18] or even three histopathological entities in one single lung tumor (CCAM, SBP and bronchogenic cyst).[19]

On ultrasound, CCAM appears as an uncompressed echogenic tumor mass, solid or mixed (cystic and solid). The prenatal diagnosis is made in the weeks 16 to 22. The large tumor sizes and the presence of macro cysts enable an early diagnosis. There is an anatomical and pathological CCAM classification proposed by Stocker et al,[13] but its use in the fetal sonographic practice is more difficult. More practical for the prenatal ultrasonography is the simplified classification proposed by Adzick et al, that divides the lung disease in macrocystic CCAM, with cysts ≥5 mm, and microcystic CCAM (or solid), with cysts <5 mm.[6] The evolution of the cases with CCAM is variable and depends on the size of the lesion and of the secondary modifications induced by this.[6] The prognostic factors were re-evaluated over time. The initial studies have shown that microcystic CCAM (solid) has a poorer prognostic than macrocystic CCAM. The experience showed that the prognostic factors are represented by the size of the tumor (regardless of the sonographic texture),[7] the degree of mediastinal shift[20] and the presence or absence of hydrops and of hydramnios.[1,19,7] There is a direct correlation between tumor sizes and the presence of hydrops and degree of the mediastinal shift. Serial ultrasonography has shown that the lung lesions may regress in 53% of the cases. The survival rate in cases of tumor regression is 100%.[20] Gaining knowledge regarding the relatively benign evolution of CCAM simplified the counseling of the patients and contributed to the decrease of the therapeutic abortion from 33% at the beginning of the '90s to 1.49% in 2000.[1,21]

In order to follow the evolution of prenatal cases with CCAM, Crombleholme et al[7] proposed the use of CVR index (cystic adenomatoid malformation of the lung volume ratio). The index is calculated by dividing the tumor volume to the head circumference ($L \times W \times H \times 0.25$/head circumference = CVR). The authors used CVR ≤ 1.6 to define the low-risk group for the development of the fetal complications (hydrops). In this study, 86% of fetuses with CVR ≤ 1.6 and with a dominant cyst did not develop hydrops. In cases without a dominant cyst, 97% of fetuses with CVR ≤ 1.6 did not develop hydrops. The survival rate in this group was 94%. CVR > 1.6 was correlated with a poor prognostic. In this group, 75% of the fetuses developed hydrops, and the survival rate was only 53%. Through serial ultrasonography, the authors determined that the prenatal natural history of

CCAM seems to follow an increasing pattern dependent on the gestational age. Between 20 and 26 weeks, a rapid growth of the tumor takes place. In weeks 26 to 28, the tumor volume reaches a plateau and then decreases. After reaching this plateau, the fetus does not develop hydrops anymore. In 15% of the cases, the tumor can no longer be observed on ultrasonography. This phenomenon occurs between 32 and 34 weeks. The sonographic disappearance of the lesion occurs because the tumor tissue becomes isoechogenic compared to the normal adjacent normal tissue. In these fetuses, the MRI examination confirms that the lesion is still present.[7]

In specialized centers, invasive fetal therapy can be performed. Depending on the severity of the case, this may involve minimally invasive techniques (thoracoamniotic shunting) or fetal open surgery during the pregnancy or at childbirth (the *ex utero* intrapartum therapy—EXIT).[22]

Peranteau et al showed that the maternal prenatal administration of Betamethasone (12.5 mg/day, im, 2 consecutive days) may have beneficial effects on the clinical fetal evolution in the cases with massive CCAM (microcystic), with or without hydrops. In the Betamethasone group, the authors reported a survival rate of 100% in cases with hydrops or those with CVR > 1.6. In the control group, the mortality rate was 100% in the cases with hydrops and 56.2% in those with CVR > 1.6. In the treated group the hydrops resolution occurred in 80% of the cases.[8]

In our study we presented 9 cases of CCAM diagnosed prenatally, of which 6 had a severe evolution (CVR > 1.6 and 1 or 2 associated fetal complications). The cases with severe evolution presented the macrocystic form of CCAM. We did not perform the minimally invasive surgical treatment (thoracentesis or insertion of a thoracoamniotic shunt). In 4 cases with severe CCAM therapeutic abortion was performed, and in two cases the children were delivered prematurely. In all these cases the newborns died soon after birth. Necropsy was performed in five cases and CCAM of type II was diagnosed (Stocker et al classification). Three cases in 9 had a favorable evolution (in one case we performed the prenatal maternal treatment with Bethamethasone), with prenatal regression of the lung lesions. The newborns delivered at term had a good clinical evolution. The lung X-ray examination showed the presence of lesions with reduced dimensions that did not request any neonatal surgical treatment.

Bronchopulmonary Sequestration

Bronchopulmonary sequestration is a lung cyst that does not communicate with the tracheobronchial tree and is supplied through the collateral vessels from the descending aorta. An intralobar form was described, with a normal pulmonary lobe pleura and an extralobar form that has its own pleura and is located intrathoracically or subdiaphragmatically. Most cases of BPS diagnosed in fetuses or newborns are extralobar lesions.

Sonographically, a unilateral echogenic lesion is observed, that is well circumscribed with a lobe or triangular form, with or without pleurisy. In color Doppler mode, collateral vessels coming from the descending aorta are usually identified; this is the pathognomonic sign for BPS.[23] In most cases, prenatally diagnosed BPS is small or medium in size.

The prenatal differentiation between an intralobar and an extralobar BPS is difficult, except the situations where an extralobar BPS is associated with a pleural effusion or is located in the abdomen.[22] The abdominal (or subdiaphragmatic) extralobar BPS appears echogenic, is located on the left side, is identified in the second trimester of pregnancy and may mimic a neuroblastoma or an adrenal bleeding.[24]

The fetal prognostic in cases with BPS is usually favorable. In cases without pleural effusion, the expectative attitude is associated with a survival rate of 100% and without postnatal surgical treatment.[25] Partial or total regression of the lung lesion was observed in 50 to 68.3% of the cases diagnosed prenatally.[26,16] 7.5% of the cases can develop ipsilateral hydrothorax with a tumor mass with the shift of the mediastinum. These complications occur in cases with large lesions[16] which can evolve with fetal hydrops and perinatal death. The fetal prenatal treatment (thoracoamniotic drainage) can improve the prognosis. Usually these cases also require the postnatal excision of the tumor.[16,25]

We diagnosed 3 BPS cases. In all cases, we identified a homogeneous echogenic tumor formation supplied from the aortopulmonary collaterals and mediastinal shift. The lung lesions have regressed spontaneous prenatally in all the cases. Two patients delivered the children at term. The X-ray lung examination did not confirm the existence of the lesions and the newborns had a favorable clinical evolution. One baby with PBS is still under observation.

Congenital High Airway Obstruction Syndrome

The CHAOS is a rare anomaly, usually with an unfavorable vital prognostic. Laryngeal atresia is the most common cause of this poor prognostic. Three types of laryngeal atresia have been described: supraglottic and infraglottic atresia (type 1), intraglottic atresia (type 2) and glottic atresia (type 3).[27] Other etiologies include laryngeal or tracheal membranes, laryngeal cyst, tracheal atresia, stenosis or subglottic atresia and the laryngeal or tracheal agenesis.[28,29] In many cases, the exact diagnosis is established only during necropsy.[30] The first sonographic description of the syndrome was performed in 1994, by Hedrick et al.[31]

The prenatal sonographic diagnosis is based on the identification of secondary signs of the complete obstruction of the airways, including dilated trachea and bronchi, bilateral

echogenic and markedly enlarged lungs, the compression of the heart, the flattened to everted diaphragm.[25,32] The increase of lung volume is the consequence of the parenchymal lung hyperplasia secondary to the pulmonary fluid retention.[33] The large quantity of fluid in the tissue explains the echogenic appearance of the lungs.[30] Fetal ascites is a constant sonographic sign.[34] It occurs due to the compression of the right atrium and the cave veins.[30] Doppler ultrasonography can show the lack of intratracheal flow during fetal breathing movements.[35] Oligoamnios can develop before 20 weeks because of the absence of the lung liquid contribution to the total volume of the amniotic fluid.[28] Hydramnios may be an associated feature, found in 71.4% of cases.[36] It occurs subacutely, usually after 28 weeks, and develops after the compressive obstruction of the esophagus and after stopping of the fetal swallowing.[29,30,35] Nonimmune hydrops and placentomegaly may be the result of the decreased venous return after the increase of the pressure on the heart and on the great veins.[28] Ascites and hydrops may lead to intrauterine fetal death.

The hyperechogenic bilateral lung from CHAOS must be differentiated from CCAM type III, the exceptional version with bilateral pulmonary lesion. The identification of the obstruction, based on the distal expansion of the airways and the absence of intratracheal flow (color Doppler mode) during the fetal breathing movements will support the CHAOS diagnosis.[28,29,37] The prenatal diagnosis of CHAOS becomes a challenge in cases with coexisting laryngo-esophageal fistula. By neutralizing the effect of pressure, there is a gradual regression of ascites, of lung echogenicity and diaphragm inversion. In such situations, the lung is less enlarged or has normal size.[28,37]

The CHAOS cases can present also with associated anomalies that include kidney malformations (renal agenesis, renal ectopia, renal hypoplasia), bone malformations (vertebral anomalies and rib agenesis, scoliosis, long bone syndactyly, frontal and parietal bone abnormalities, agenesis of the radius), intestinal malformations (duodenal atresia, anal imperforation), brain malformations (hydrocephalus, agyria), unique umbilical artery, accessory spleen, hemidiaphragmatic defect.[30,35,38] Typical CHAOS cases are rare. It is important to exclude associated malformations, because airway obstruction may be the expression of various monogenic abnormalities, such as Faser syndrome (renal agenesis, microphthalmia, cryptophthalmos, polydactyly and syndactyly), short rib polydactyly syndrome or chromosomal abnormalities (chromosome 5– 'Cri-du-Chat' syndrome, microdeletion 22q11.2).[39]

In most of the cases, CHAOS is a lethal pathology, even if diagnosed prenatally and treated. The natural prenatal history and the postnatal evolution of CHAOS is influenced by the degree of the airway obstruction. The accuracy of the prenatal diagnosis (the level and the degree of the obstruction) may be useful in cases with planned perinatal surgical assistance. Pulmonary decompression at birth by *ex utero* intrapartum treatment (EXIT) and tracheostoma may improve the prognosis.[37,40,41] There are successful attempts of pulmonary decompression performed during the pregnancy through percutaneous minimally-invasive fetoscopic tracheal decompression using laser, followed by EXIT treatment and tracheostoma at birth, both as experimental therapy[42] and curative attitude.[43]

We diagnosed a case with CHAOS at 20 weeks. The fetus presented sonographic images suggestive for airway obstruction: echogenic and enlarged lungs, dilated trachea and bronchi, compressed heart (cardiothoracic index = 6.4%) and diaphragmatic inversion. Associated malformations (heart and kidney) were diagnosed. We performed therapeutic abortion. Unfortunately, the patient refused fetal necropsy, so we were not able to specify the level of the airway obstruction and did not have the anatomopathological confirmation of the prenatal diagnosis.

Right Pulmonary Agenesis

Pulmonary agenesis is defined by the absence of the parenchyma and pulmonary vessels, as well as the absence of bronchi across the tracheal bifurcation. It can be unilateral or bilateral. Bilateral agenesis is incompatible with life. Unilateral agenesis is compatible with life, and the prognostic depends on the associated pathology.[3,44-46]

Sonographic prenatal diagnosis can be challenging, because it requires a thorough examination of the lung, heart, cardiac outflow ways, venous return and of the diaphragm. In the case of right pulmonary agenesis, a shift of the mediastinum and fetal dextrocardia is identified, without any thoracic tumor mass that moves the mediastinum and the heart.[47] A second fundamental issue is the impossibility of the visualization (in color Doppler mode) of the bifurcation of the pulmonary artery and of the ipsilateral pulmonary veins. Also, the right lung cannot be visualized and the heart, moved to the right, is in a contiguous relation with the right thoracic wall. At the same time, the diaphragm has no discontinuities, and the abdominal organs (stomach, liver) have a normal position.[47,48] The mediastinal shift will bring the problem of a differential diagnosis with the more frequent pathologies, congenital diaphragmatic hernia, CCAM, BPS, or less common malformations, such as pulmonary emphysema, mediastinal teratoma, neuroblastoma, heterotaxy syndrome.[46]

Associated pathology is more frequent in cases with right pulmonary agenesis and bilateral pulmonary agenesis (80% and 80% respectively) than in the left pulmonary agenesis (50%).[47] It is represented by cardiovascular malformations (interrupted aortic arch, total pathological venous return, scimitar syndrome, hypoplastic left heart syndrome), gastrointestinal malformations (esophagus atresia, pyloric stenosis), genitourinary malformations (horseshoe kidney), facial malformations (palatoschisis, hypoplasia of the maxilla and mandible, ipsilateral microtia, bilateral microtia), bone malformations (bilateral radial ray hypoplasia, ipsilateral radial ray defects and/or hemifacial microsomia).[44,48-50] It is important to note that cardiovascular abnormalities are more frequent in right pulmonary agenesis than in left pulmonary agenesis (76% and 17% respectively).[46]

Pulmonary agenesis is not associated with an increased incidence of the chromosomal abnormalities.[44,47]

The prognostic in right pulmonary agenesis is poorer than in left pulmonary agenesis; this is explained by the important shift of the mediastinum and by a higher frequency of associated pathologies in right pulmonary agenesis.[44,46]

We diagnosed a case with right pulmonary agenesis at 24 weeks. The first sonographic sign was the shift of the mediastinum toward right and the fetal dextrocardia in the absence of a thoracic tumor formation. Then we noticed the absence of the right lung area from right side and the left lung expansion. The Doppler ultrasonography indicated the absence of the right pulmonary artery. Postnatal trisomy 21 was diagnosed. The child died after 2 months of life due to respiratory complications. Permission to perform necropsy was denied.

Bilateral Lung Hypoplasia with Hydrothorax

Unilateral or bilateral hydrothorax may be an isolated pathology or it can be associated with fetal hydrops. There is a wide range of possible causes of fetal hydrothorax, including congenital chylothorax, anemia, cardiac malformations, aneuploidies, viral infections or lung lesions. It may have a favorable evolution, with the reabsorption of the pleural effusion, or it may progress, causing compression on the vena cava, hydrops and ultimately fetal death. Lung compression may lead to lung hypoplasia, and compression of the esophagus may trigger the formation of hydramnios.[51-53] In 72.3 to 81% of cases, the hydrothorax is bilateral and, in 84% of cases, it is diagnosed in the third trimester of pregnancy.[51,54] Compared to the unilateral hydrothorax, the bilateral one is more often associated with malformations (21% *vs* 78.9%) or chromosomal abnormalities (17.4% *vs* 82.6%).[54] Bilateral hydrothorax is more often associated with fetal hydrops (71.4%), compared to unilateral hydrothorax (14.3%).[54]

If we exclude the associated pathologies described by Ruano et al, the negative prognostic factors are: low gestational age at which the diagnosis was performed and at which the baby was delivered, the occurrence of hydrops and a bilateral form of hydrothorax.[51]

A review of the literature showed that after multivariate analysis, hydrops remained the only negative prognostic factor.[52] Estroff et al showed that polyhydramnios is a poor prognostic factor.[55] A gestational age at birth greater than 31 weeks, the absence of hydrops and the minimally invasive treatment (thoracoamniotic shunt) were associated with a favorable evolution.[53]

The treatment option for the moderate or severe pleural effusion is the application of the thoracoamniotic shunt. Thoracentesis proved to be ineffective. By this maneuver, thoracic decompression and lung expansion is performed and the risk for pulmonary hypoplasia is reduced. The evolution after this maneuver is influenced by the initial presence or absence of hydrops and by the gestational age at birth.[56]

We diagnosed a case with severe bilateral hydrothorax at 33 weeks, associated with fetal hydrops at a pregnant woman without Rh incompatibility. The fetus showed low lung areas: on the left side similar to a pregnancy of 23 weeks, and on the right side similar to a pregnancy of 22 weeks,[12] as well as other signs of intrathoracic compression (cardiothoracic index = 17% and dilated inferior vena cava). Doppler examination of the middle cerebral artery excluded the fetal anemia. The TORCH test of the pregnant woman revealed chronic toxoplasmosis. The child was delivered prematurely at 34 weeks because of hydramnios with severe evolution and died immediately after birth. The anatomopathological diagnosis confirmed the diagnosis of secondary lung hypoplasia and severe bilateral hydrothorax.

CONCLUSION

The prenatal lung sonographic examination represents an important evaluation of the fetal morphology and offers the possibility of the prenatal diagnosis for a wide category of fetal lung lesions. The gravity of the lung pathology will be established according to the type, localization and dimensions of the lung lesion, as well as to the presence of fetal complications. Bronchopulmonary sequester and CCAM may improve during intrauterine life. Fetal hydrops associated to CCAM is an indicator of reserved prognosis. The obstetrical management will be established individually. In specialized centers, the prenatal surgical treatment, especially minimally invasive techniques, or the EXIT treatment may improve the fetal and neonatal prognosis.

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