Congenital high airway obstruction syndrome (CHAOS): discussing the role and limits of prenatal diagnosis starting from a single-center case series

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Abstract

Objectives: we aimed to report our experience about congenital high airway obstruction syndrome (CHAOS) that is a rare and fatal congenital anomaly; laryngeal atresia is the most frequent cause. Sonographic findings are enlarged echogenic lungs, dilated trachea, and ascites.

Methods: we performed a single-center case series analysis collecting antenatally through ultrasound examination, and some of them confirmed by autopsy.

Results: we report six cases of CHAOS diagnosed by antenatal ultrasonography between 2007 and 2013.

Conclusion: to date literature provides very few individual case reports. This work describes typical sonographic findings of this syndrome and it underlines the importance of early prenatal diagnosis to improve prognosis thought an ex utero intrapartum treatment, that seems to be the only chance of survival for the affected fetus.

Key words: congenital high airway obstruction, prenatal diagnosis, diagnosis, prognosis.

Introduction

Congenital high airway obstruction syndrome (CHAOS) is an extremely rare congenital anomaly, caused by laryngeal or tracheal atresia, tracheal stenosis, obstructing laryngeal cysts and obstructing tumors of the oropharynx and the cervical region, or rarely by compression from a double aortic arch (1). Laryngeal atresia seems to be the most frequent cause (2). In these cases, an outflow obstruction of the fetal lung fluid leads to pulmonary hyperplasia. Prenatal ultrasound findings are very characteristic and include lungs symmetrically enlarged and highly echogenic, dilated and fluid-filled trachea and bronchi, inverted hemidiaphragms (3). The heart appears small compared with the enlarged lungs and positioned towards the midline of the thorax due to compression by the lungs. Fetal ascites is often present and sometimes hydrops.

Methods

We report our experience of six cases of CHAOS, diagnosed antenatally through ultrasound examination, and some of them confirmed by autopsy.
Results

Case 1
A 37-year-old woman, gravida 1, parity 0, was referred at 22 weeks of gestation for evaluating fetal ascites. She and her family had both unremarkable medical histories. Ultrasonography showed enlarged and highly echogenic lungs, absence of unscathed pulmonary parenchyma, thoracic effusion and fetal ascites. The ultrasonographer was not able to observe bladder, left kidney; furthermore, both feet showed altered axis, cerebellum was hypoplastic. The couple was referred to a genetics specialist and amniocentesis procedure was performed. Fetal karyotype study found a trisomy 18. The pregnancy was stopped as requested by parents, who did not request fetal autopsy.

Case 2
A 30-year-old woman, gravida 2, parity 1, was referred to our center at 21 weeks of gestation for suspicious fetal anomaly. Ultrasonography showed enlarged and highly echogenic lungs, an avascular anechoic formation in the chest compatible with ectatic trachea (Figure 1) and single umbilical artery. The most probably diagnosis was CHAOS, so the possibility of unfavorable outcome was discussed. A genetic counseling and amniocentesis procedure were proposed to the couple. The couple refused amniocentesis and decided to interrupt the pregnancy. Postmortem examination was not allowed for choice of relatives.

Case 3
A 33-year-old woman, gravida 4, parity 3, was referred to our center at 19 weeks of gestation for evaluating fetal ascites. Ultrasonography showed enlarged and highly echogenic lungs, absence of unscathed pulmonary parenchyma, thoracic effusion and fetal ascites. Fetal biometry and amniotic fluid was normal. No other anomalies were observed. The tentative diagnosis was more likely CHAOS and the possible unfavorable outcome of pregnancy was discussed with the couple. The couple was referred to a genetics specialist and amniocentesis procedure was offered. Parents refused, pregnancy was stopped as they requested and autopsy was declined.

Case 4
A 33-year-old woman, gravida 1, parity 0, was referred to our ultrasound diagnostic center at 13 weeks of gestation for evaluating fetal neck. Ultrasonography showed echogenic lungs, retronuchal edema that stretched the neck and the thorax, suggesting cystic hygroma; ductus venosus showed reverse flow, nasal bone was hypoplastic. Two possibility were discussed with the couple: on one side the high risk of chromosomal anomaly, on the other side the suspect of CHAOS due to pulmonary hyperchogenicity. The high possibility of unfavorable outcome was also discussed. A genetics counseling and fetal karyotype study was proposed. A case of aneuploidy was found. The pregnancy was interrupted for choice of the parents and autopsy confirmed CHAOS.

Case 5
A 39-year-old woman, gravida 1, parity 0, was referred to our center at 16 weeks of gestation for evaluating gastric bubble. Ultrasonography showed highly echogenic lungs bilaterally, an avascular anechoic formation in the chest (compatible with ectasic trachea), fetal ascites. Cardiac anatomy was regular, although the heart was compressed by the lungs. There was single umbilical artery. The ultrasonographer was not able to observe the gastric bubble, the bowel was hyperchoic and there was ierplacento-sis with placenta previa. The possibility of unfavorable outcome was discussed with the couple, a ge-
nentic counseling and amniocentesis procedure was offered. The couple refused fetal karyotyping and chose an expectant management. Caesarean section was performed at 8 months gestation for placenta previa and the baby died a few minutes after birth. Diagnosis of CHAOS was confirmed by autopsy.

**Case 6**

A 38-year-old woman, gravida 5, parity 3, 1 ectopic pregnancy was referred to our center at 19 weeks of gestation for evaluating fetal ascites. Ultrasonography showed enlarged and highly echogenic lungs, a stretch avascular anechoic formation in the chest (compatible with ectasic trachea) and severe ascites. Monolateral clubfoot and a growth delay of 8 days detected by fetal biometry were found. The heart anatomy and dynamism were normal. The possible unfavorable outcome was discussed: the couple was addressed for genetic counselling and amniocentesis procedure was proposed. The couple refused any procedures and decided to stop the pregnancy at 20 weeks of gestation. An autopsy confirmed the prenatal diagnosis of laryngeal atresia, clubfoot and ascites.

**Discussion**

Laryngeal atresia is an extremely rare congenital malformation due to deficient recanalization of the upper airways around the 10th week of gestation. Besides laryngeal atresia, the other rare underlying causes of CHAOS are tracheal agenesis, subglottic stenosis or atresia, and laryngeal webs or cysts. However, the obstruction is mostly secondary to laryngeal atresia (4). In case of obstruction in the tracheobronchial tree, the lung fluid cannot be cleared. The accumulation of the fetal lung fluid results in gradual increase of intratracheal pressure leading to enlargement of the lungs; the enlarged lungs cause compression of the heart and great veins. Due to the compression, the heart replaces centrally and becomes small and dysfunctional. Decreased venous return and dysfunctional cardiovascular system may cause ascites and hydrops. The diaphragm flattens or inverts according to the severity of the process (5).

The main diagnostic tool for prenatal diagnosis of CHAOS is sonography. US characteristic findings are bilateral large hypechoic lungs, dilated tracheobronchial tree, small, compressed, and centrally replaced heart, flattened or inverted diaphragm, and ascites (6).

Compression of the esophagus due to dilated trachea may result in polyhydramnios. The typical sonographic findings can also be recognized on MRI, which can be used to localize the exact level of obstruction if a fetal surgical intervention is planned (7). The differential diagnosis include bilateral congenital cystic adenomatoid malformation especially type III (CCAMIII) (4). In order to make a differentiation between CHAOS and CCAM type III, the obstruction site with distal airway dilatation (present in CHAOS) and the systemic arterial supply (present in CCAM type III) must be seen. CHAOS should be also differentiated from extrinsic causes of tracheolaryngeal obstruction. Some of these extrinsic causes are lymphatic malformation, cervical teratoma, and vascular rings like double aortic arch. CHAOS is mostly sporadic, and the exact incidence is not known. The most common associated genetic disorder with CHAOS is Fraser’s syndrome which is inherited by autosomal recessive form and characterized by tracheal or laryngeal atresia, renal agenesis, microptalmia, and syn- or polydactyly (5).

There are some genetic syndromes associated with CHAOS such as Short-Rib Polydactyly Syndrome (SRPS), Shprintzen–Goldberg Omphalocoele syndrome (SGOS) and VATER/VACTERL association. In addition to these syndromes, some chromosomal abnormalities (deletions of 22q11.2, deletion of chromosome 5p, 47, XXX, partial trisomy 9 and partial trisomy 16q) have been reported in association with CHAOS.

The six cases reported were diagnosed by ultrasound examination in our center between 2007 and 2013. The diagnoses were performed between 16 and 22 weeks of gestation and only one case was diagnosed at 13 weeks of gestation. All fetuses had ascites and large highly echogenic lungs and 3 fetuses had tracheal dilatation. Five pregnancies were terminated, as requested by parents. A fetus was born at 8 months gestation by caesarean section for placenta previa but the baby died few minutes after birth. Amniocentesis procedure was performed in two cases and aneuploidy karyotype was found (18 trisomy). In 3 cases CHAOS was confirmed at fetal autopsy.

CHAOS is rare and generally fatal syndrome. Even though some genetic syndromes and chromosome aberrations have been reported in association with CHAOS, the aetiology is still unknown. Antenatal sonographic imaging shows typical findings which can lead to an early diagnosis. This is important especially if any fetal intervention is considered. Although successful intrauterine treatments have been reported, the ex utero intrapartum treatment (EXIT) seems to be the only chance of survival of the affected fetus. The objective of the procedure is to settle an intact airway for the baby before the fetomaternal circulation is stopped (8). Neonatal survival is improved if a well-planned EXIT procedure is performed at the time of a controlled near-term caesarean section (9) therefore prenatal diagnosis has a vital role in these cases.

**Declaration of interest**

All Authors have no proprietary, financial, professional or other personal interest of any nature in any product, service or company. The Authors alone are responsible for the content and writing of the paper. No specific grant/fund was obtained.
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