

Prenatally detected congenital cystic adenomatoid malformation and postnatally diagnosed trisomy 13: case report and review of the literature

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SUMMARY: Turan Ö, Hirfanoğlu İM, Beken S, Biri A, Efetürk T, Atalay Y. Prenatally detected congenital cystic adenomatoid malformation and postnatally diagnosed trisomy 13: case report and review of the literature. Turk J Pediatr 2011; 53: 337-341.

Congenital cystic adenomatoid malformation (CCAM) is a rare bronchopulmonary malformation characterized by loss of the normal pulmonary tissue. CCAM may be frequently associated with cardiac and renal anomalies. Rarely, CCAM may be seen with chromosome abnormalities. This is the first reported neonatal case of prenatally detected CCAM and postnatally diagnosed trisomy 13.

Key words: congenital cystic adenomatoid malformation, trisomy.

Congenital cystic adenomatoid malformation (CCAM) is a rare bronchopulmonary malformation characterized by loss of the normal pulmonary tissue, suppression of alveolar development and formation of cysts^{1,2}. The precise etiology of the abnormal cell proliferation is unknown. The true incidence and prevalence of CCAM in the fetal and neonatal period are not yet determined.

Congenital cystic adenomatoid malformation (CCAM) may be rarely associated with chromosome abnormalities and other malformations^{3,4}. This is the first reported neonatal case of prenatally detected CCAM and postnatally diagnosed trisomy 13.

Case Report

The female infant was the 2245 g product of a 37-week gestation born by vaginal delivery to a gravida 2, para 1, 28-year-old woman. Her head circumference was 31 cm (10-25 percentile). Apgar scores were 6 at 1 minute and 8 at 5 minutes. There was no history of maternal disease, drug ingestion or exposure to smoke. The patient's second trimester triple test concluded low risks for trisomy 21 and 18. Amniocentesis was not performed. A multilocular anechogenic cystic mass of

14 x 16 x 19 mm was detected in the upper lobe of the left lung at the 26th week on the prenatal ultrasound at another center. A scan performed upon her referral to our center showed presence of a large anechogenic cystic lesion located in the upper left hemithorax, polydactyly on the hands and single umbilical artery. This anechogenic cystic lesion showed no signs of peristalsis and the fetal stomach and intestines were normal, ruling out a possible diaphragmatic hernia. Fetal biometry was in accordance; amniotic fluid volume was in the normal range, and there were no signs suggestive of hydrops. Her biparietal diameter and head circumference were 8.03 cm and 28.5 cm, respectively. The cystic mass was measured as 48 x 77 x 26 mm (volume 96.0 ml) and the cystic adenomatoid malformation (CAM) volume ratio (CVR) as 1.75 at 32 weeks in our center. She received antenatal betamethasone at the 32nd week. The fetus had a CVR of 1.85 at 37 weeks gestation (Fig. 1). The fetus had mediastinal shift to the right and developed polyhydramnios. No fetal hydrops or pleural effusion was produced. Fetal echocardiography was performed, which showed that the cystic lesion had displaced the fetal heart, causing a mediastinal shift; intracardiac structure was normal.



Fig. 1. Prenatal ultrasound scan of the lung mass.

On physical examination, she was noted to have microphthalmia, aniridia, hypotelorism, low-set ear, postaxial polydactyly on the hands, rocker bottom feet, and single umbilical artery (Figs. 2, 3). The neonate, who had tachypnea, nasal flaring, cyanosis, and retractions, was intubated. She was administered dopamine, as the filling period of the capillary was long and she suffered hypotension. Echocardiography revealed secundum atrial septal defect (ASD), tricuspid deficiency and increased pulmonary artery pressure. She was normal except for TORCHES serology, toxoplasmosis, cytomegalovirus, and rubella Ig G positivity.

On the first day of life, cranial ultrasound demonstrated a large left lateral ventricle occipital horn and mega cisterna magna. Abdominal ultrasound showed bilateral multiple cystic kidneys. Thorax tomography revealed parenchyma being ventilated on the upper lobe anterior segment of the left lung, paracardiac region and lingular inferior segment, while a large cystic lesion, with septae that filled the left hemithorax and included air-fluid levels, was observed. It was also seen that a part of the mediastinal structures, the upper lobe anterior sections of the left lung and heart were shifted to the right. Thorax tomography confirmed the diagnosis of a CCAM type I (Fig. 4). Perfusion scintigraphy showed hypoperfusion on the upper and central lobes of the right lung and lower lobe of the left lung. Follow-up examinations did not report development of pneumothorax. She died on the 7th day of life due to respiratory and cardiac failure. Autopsy was recommended

but declined. Chromosome analysis showed a trisomy 13 (47,XX,+13).

Discussion

Wider use of prenatal ultrasound has allowed detection of CCAMs at earlier stages and realization of diagnosis in increasing numbers. In addition, serial ultrasonography is required for the detection of increase in the size of the mass and the development of hydrops, as well as for monitoring the spontaneous regression. These lung lesions are usually diagnosed within 20 weeks of gestation, even as early as 12 weeks^{2,5}. If there is no increase in the size of the mass during a three-week follow up, *in utero* intervention may not be necessary⁶.

The clinical course of antenatally detected CCAM is variable and related to the size of lesions. In the prenatal period, the cystic mass may spontaneously regress in size or clinical manifestations vary between hydrops fetalis to *in utero* death^{2,4}. Large lesions can result in polyhydramnios, mediastinal shift, hydrops fetalis, and relative pulmonary hypoplasia in the contralateral lung^{2,4,5}. During the perinatal period, CCAMs can cause early respiratory failure because of respiratory distress or air trapping within the cysts. In addition, some CCAMs remain asymptomatic until childhood age or bring about various complications such as recurrent lung infection, pneumothorax and malignant transformation^{2,7}.

Crombleholme et al.⁸ demonstrated that the development of hydrops correlated with the volume of the CCAM. The CAM volume (length



Fig 2. Facial appearance with microphthalmia is seen.



Fig 3. Postaxial polydactyly on the hand is seen.

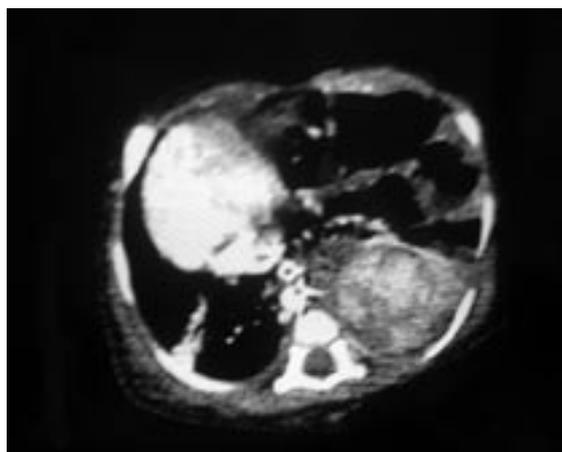


Fig. 4. Postnatal computed tomography scan showing congenital cystic adenomatoid malformation of the lung.

x width x height x 0.52) was divided by the head circumference to yield the CVR. Fetuses with a CVR of 1.6 or higher were at very high risk for hydrops⁸. Our patient's CVR was higher than 1.6 but no hydrops developed.

Cardiac defects (tetralogy of Fallot, transposition of the great vessels) and renal abnormalities (renal agenesis) are frequently associated with CCAM^{1,2,9}. Less frequently, it may accompany gastrointestinal tract (agenesis of the gallbladder, imperforate anus), central nervous system (CNS) (hydrocephalus, arrhinencephaly) and multiple structural anomalies (cleft palate, clubfeet)^{3,10}.

Trisomy 13 is an autosomal trisomy caused by the presence of an extra copy of chromosome 13. Anomalies associated with this syndrome are cleft lip, often midline, ocular hypotelorism, low-set malformed ears, small abnormal skull, cerebral malformation, microphthalmia, cardiac malformations, hypoplastic or absent ribs, omphalocele, and polydactyly. Pulmonary malformations in trisomy 13 cases are described as very rare, such as pleural effusion, diaphragmatic hernia and CCAM^{3,11,12}. As chromosome anomalies rarely underlie fetal pulmonary lesions, routine fetal karyotyping for isolated pulmonary lesions is not recommended. To date, less than 15 fetal and neonatal cases with chromosomal anomalies have been published in the literature. Nine cases with trisomy detected in combination with CCAM were reported^{1,3,4,9,13-16}. Table I shows the demographic features of these cases. Only one

of them was trisomy 13, and this case is a fetus concluded in termination of the pregnancy. Heling et al.³ reported that the incidence of chromosomal anomaly in CCAM patients is 1.2%, while Pressey et al.¹³ reported this incidence to be 1.6%. Our case was the first CCAM neonatal case with trisomy 13.

The prognosis in intrauterine diagnosis is variable. If hydrops develops in the fetus before the 32nd week, the neonatal prognosis would be expected to be poor. In our case, there was no bilateral disease or hydrops fetalis, which are known as having a worse outcome^{4,17}. Early detection of lesion, mediastinal shift and polyhydramnios are not poor prognostic factors.

Consequently, CCAM may cause fetal or neonatal death, in combination with fetal hydrops, prematurity, and other system and chromosome anomalies. Interestingly, most prenatally diagnosed CCAMs have a better prognosis. Diagnosis in the early days of the prenatal period offers the chance of treatment and makes it easier to make postnatal diagnosis and treatment. With the detection of chromosome anomaly, *in utero* treatment may not be necessary. Although the incidence of karyotypic abnormalities in CCAM is low, clinicians should consider the possibility of chromosomal abnormalities when additional anomalies are revealed by detailed prenatal ultrasonography.

Table I. Prenatally Diagnosed CCAM and Associated Trisomy

Author, year	CCAM location CVR	Associated defects and malformations	Karyotype	Outcome
Moerman et al., 1992 ¹⁵	Right	Potter sequence - pulmonary stenosis - VSD Not done	Trisomy 18	Termination of pregnancy
Thorpe-Beeston et al., 1994 ¹⁶	Left		Trisomy 18	Termination of pregnancy
Adzick et al., 1998 ⁹	No detailed information		Trisomy 21	
Laberge et al., 2001 ¹⁴	No detailed information		Trisomy 18	Died postnatally
Heling et al., 2003 ³	Left	VSD, holoprosencephaly, arhinencephaly, cleft palate	Trisomy 13	Termination of pregnancy at 23 weeks
Calvert et al., 2006 ⁴	No detailed information		Trisomy 21	
Hüsler et al., 2007 ¹	Left 2.17	Conoventricular ventricular septal defect	Mosaic trisomy 18	37 weeks delivery
Hüsler et al., 2007 ¹	Right 0.49	Transposition of the great vessels	Mosaic trisomy 16	Termination of pregnancy at 20 weeks
Pressey et al., 2007 ¹³	Right 0.78	-	Trisomy 1q monosomy X	Termination of pregnancy at 22 weeks
Current patient	Left 1.85	Aniridia, polydactyly, single umbilical artery, mega cisterna magna, multiple cystic kidneys	Trisomy 13	37 weeks delivery

CCAM: Congenital cystic adenomatoid malformation. CVR: CAM volume ratio. VSD: Ventricular septal defect.

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