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Original Research Article

Congenital cystic adenomatoid malformation (CCAM): antenatal and postnatal management

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ABSTRACT

Background: Congenital cystic adenomatoid malformation (CCAM) is a rare abnormality of lung development. The estimated incidence ranges from 1: 10,000 to 1.35,000 live births. It is diagnosed by prenatal screening at 18-20 weeks of gestation. Surgical excision of symptomatic lesions is relatively straight forward, but management of asymptomatic lesions is controversial.
Methods: Among women who delivered at St. Johns medical college and hospital, Bangalore between Jan 2011 to Dec 2016, those with the diagnosis of CCAM during anomaly scan were included in the study. Antenatal and Post-natal period and their outcomes were evaluated. Follow up was extend up to the childhood in the affected foetus.
Results: There were 5 cases of CCAM in 13057 deliveries during 5-year study. Incidence was 1:2611. Mean gestational age at diagnosis was 21.6±2.5weeks. All foetus had CVR (CCAM volume) ratio more than 1.6 and there was no compromise on lung volume. Mean lung volume was 62.8±8.6 cc. and mean Apgar score at 1minute was 6.8±2.7 and at 5 minutes was 8.0±2.2. Among 5 foetuses, 2 foetuses had regression of cyst by birth and 3 underwent surgery for resection after birth.
Conclusions: CCAM remains a challenge for obstetricians, neonatologists and paediatric surgeons. The combination of prenatal MRI and serial ultrasound studies optimize foetal surveillance and postnatal care. In asymptomatic CCAM, babies should be followed up to adolescence and adulthood, as they can manifest with malignant changes.

Keywords: CCAM, CTM, Non-immune hydrops

INTRODUCTION

Congenital Cysticadenomatoid malformation (CCAM) is a rare abnormality of lung development. It is characterized by cystic intrathoracic masses caused by proliferative terminal respiratory bronchioles and by a reduction in the number of normal alveoli. It usually affects a single pulmonary lobe; multi- lobular or bilateral involvement is rare.[1] CCAM was first reported in 1949 by ch'in and Tang.[2]

The estimated incidence of CCAM ranges from 1:10,000 to 1: 35,000 live births, with male and female neonates equally affected. Most available data regarding accuracy of prenataldiagnosis, prevalence and outcomeof CCAM are derived largely from tertiary referral centres and may not reflect general population rates.[3]

CCAM accounts for 95% of congenital cystic lung diseases and is the most common cystic lung lesion diagnosed by prenatal screening at 18-20 weeks of gestation.[4] However, with the advent of prenatal ultrasound (USG), it is likely that the true incidence may have been underestimated because previously undiagnosed lesions are now being detected. Serial ultrasound study of foetuses with lung lesions has helped

to define the natural history of these lesions, determine the patho-physiologic features that affect clinical outcome and formulate management on the basis of prognosis. The overall prognosis depends on the size of the lung mass and the secondary patho-physiological effects; a large mass causes mediastinal shift, hypoplasia of normal lung tissue, polyhydramnios, and cardiovascular compromise leading to foetal hydrops and death.[5] Large foetal lung tumours may partially disappear on serial prenatal ultrasound, illustrating that improvement can occur during foetal life.

The management of symptomatic CCAMs is consensually agreed, whereas the management of asymptomatic CCAMs is still contentious.[6]

Only a few CCAMs cause foetal problems, with foetal hydrops being the best predictor of foetal death. Although many CCAMs regress during pregnancy, most remain detectable postnatally by CT scans. Surgical excision of symptomatic lesions is relatively straight forward, but management of asymptomatic lesions is controversial. Some surgeons adopt a "wait and watch" approach, operating only on those patients who develop symptoms, but other operate on asymptomatic patient usually within the first year of life. Due to the potential of malignant transformation5, children should have long term follow up. There is an urgent needto delineate the natural history of antenatally detected CCAMs to guide future management.[5]

Classification of CCAMs

The description and classification of congenital lung cyst has evolved over time.

Several classifications have been proposed. A great controversy exists regarding the correlation between clinical behaviour, prognosis and the CCAM type. Stocker's classification was based upon 38 cases. It reflects the pattern of the lesions that were characterised from autopsied infants with a predominance of type II and type III lesions.[1] Later studies showed that the prognosis of prenatally diagnosed lesions depends on the presence or absence of hydrops.[7]

Other prognostic factors include: the size of the lesions and its secondary effects namely mediastinal shift, the extent of pulmonary hypoplasia, polyhydramnios, cardiovascular compromise, the degree of development of the unaffected lung, and the presence or absence of other congenital anomalies such as extra lobar sequestration, diaphragmatic hernia, pulmonary hypoplasia, cardiovascular malformation, hydrocephalus, skeletal malformation, jejunal atresia, bilateral renal agenesis/dysgenesis and Pierre Robin syndrome.[8]

Types of CCAM[1] are:

- Type O: Acinar atresia
- Type 1: Cysts up to 10 cm. The cysts are lined by pseudo-stratified ciliated cells that are often interspersed with rows of mucous cells
- Type 2: Sponge like multiple small cysts resemble dilated bronchioles separated by normal alveoli. Striated muscle seen in 5%
- Type 3: Solid. Excess of bronchiolar structures separated by small air spaces with cuboidal lining (foetal lung)
- Type 4: Cysts up to 10 cm, the cysts are lined by flattened epithelium resting upon loose mesenchymal tissue.

The natural history of prenatal cystic lung lesions varies from complete regression in utero to life threatening hydrops foetalis. The timing of regression is variable but tends to be in the mid-third trimester usually at 32034 weeks of gestation.[8] Hydrops is the strongest prognostic factor and it may be an indication for prenatal intervention. A Survival rate is more than 95% in CCAMs without hydrops. The development of hydrops typically limited to those foetuses with very large chest masses with mediastinal shift and venacaval obstruction. Ultrasound measurement of the CCAM volume ratio (CVR) is an index estimated as the CCAM volume divided by the head circumference. A CVR is >1.6, the risk for hydrops ranges between 15-75%.[9] Proposed antenatal and perinatal interventions include steroid administration, intrauterine puncture or shunting of macrocytic masses, alcohol embolization or lasering of the feeding vessel or lobectomy. The evidence for these interventions is currently poor.[6]

Primary objective was to assess the maternal complications and outcome of the neonate of antenatally diagnosed congenital cystic adenomatoid malformation for the foetus. Secondary objectives were to assess the need for the surgery in the neonate and rate of respiratory infections in the childhood.

METHODS

Among pregnant women who delivered at St. John's medical college and Hospital, Bangalore, India between Jan 2011 to Dec 2016, who had prenatal diagnosis of congenital cystic adenomatoid malformation of the lung in the foetus. Foetuses with other chest or lung abnormalities were excluded from the study.

All the cases with CCAM was observed for antenatal and Postnatal complications and neonatal outcome. Data on maternal age, obstetric history, gestational age at diagnosis, maternal complication, gestational age at delivery, mode of delivery antenatal administration of steroids, size of the cyst at diagnosis, change in the size of cyst with progression of the pregnancy, CVR ratio, lung volume, sex of the baby, birth weight, APGAR score, need for resuscitation, need for ventilator support, course in NICU, need for surgery, rate of respiratory

infection in the child was collected. The diagnosis of CCAM was determined based on the anomaly scan or ultrasound study at any gestational age and management was planned accordingly. Antenatal mothers presenting with the diagnosis of CCAM were evaluated by a protocol which included screening for obstetric complications in the mother like preeclampsia, Gestational Diabetes Mellitus (GDM) and polyhydramnios. Antenatal steroids were given only in case of preterm delivery. Size of the cyst was analysed by serial ultrasound. Lung volume and CVR ratios were analysed for all the cases.

RESULTS

During the study period 6 years, 13057 women delivered and among them 5 foetuses had CCAM. Incidence of CCAM in our centre was 1 in 2611. The demographic and clinical features of the cares are shown in Table 1.

Table 1: Maternal characteristics.

Maternal age in years	Parity	Risk factors	Gestational age at delivery in weeks +Days	Mode of delivery
30	G_2 P_1L_1	GDM	39	FTVD
25	Primi	PPROM	32+4	PTVD
25	$G_3P_1L_0$ A_1	Hypothyroid	38	FTVD
27	$G_3P_1L_1A_1$	GDM, mild preeclampsia	38+4	Caesarean delivery for MSL grade II
19	Primi	Nil	40+1	FTVD

*G- Gravida, P- para, L- Live baby, A- abortion, PPROM- preterm premature rupture of membranes, GDM Gestational diabetes mellitus. FTVD- Full term vaginal delivery PTVD – Preterm Vaginal delivery, MSL – Meconium stained liquor

The age of the pregnant woman, ranged between 19 to30 years with a mean of 25.2 ±4.0. Two of them were primigravidae and three were multigravidae. Out of 5 of them, two had GDM, one had mild preeclampsia, and one had hypothyroidism. One case presented with preterm premature rupture of membranes (PPROM) and one had no obstetric complication. Four of them had vaginal deliveries and one underwent emergency Caesarean delivery for grade 2 meconium stained liquor (Table 1).

Table 2: Foetal characteristics.

Gestational age at diagnosis in weeks + days	Size of the cyst at diagnosis (in cm)	Increase in the size of cyst	Regression of cyst	CVR *	Lung volume (in cc)
21+2	4 x 3	No	No	1.9	67
26 +3	4 x 3	No	No	1.6	49
21+1	3x2	No	Yes	1.9	60
19+3	1x1	Yes	No	1.7	70
21+1	2x2	No	Yes	1.6	68

*CVR - CCAM volume ratio

The mean gestational age at diagnosis was 21 weeks and 6 days (±2 weeks and 6 days). Four of them were diagnosed during anomaly ultrasound scan. Only one case was diagnosed at gestational age 26 weeks and 3 days of gestation when she presented with polyhydramnios.

Ultrasound was done for the evaluation of increased liquor, which detected the presence of CCAM in the foetus. All the cases were Type I CCAM. When the cases were monitored with serial ultrasound studies, only one case had an increase in size of the cyst by 1x 1 cm. Two cases showed regression of the cyst. In other two, the size in serial ultrasound remained the same. CVR ratio for all of them was more than 1.6.

There was not much of reduction in lung volume because of the cyst at the time of delivery (Table 2).

Among the 5 pregnancies, one received antenatal steroids for prematurity. Average birth weight of term babies was 3400 grams, one preterm baby weighed 1500 grams at 32 weeks and 4 days of gestations age. The preterm delivery was due to preterm premature rupture of membranes (PPROM). Apgar score of term babies was good as it was 8/10 for 1 minute and 9/10 for 5 minutes. Only one preterm baby had low Apgar score and needed invasive

ventilation along with surfactant therapy. Out of four term babies, one baby had CPAP made of ventilation for 48 hours. Three babies underwent surgical resection and all of them had an uneventful post-operative course (Table 3).

Table 3: Neonatal outcomes and follow up.

Antenatal steroids	Birth Weight (in grams)	Apgar score (Out of 10)		Sex of the baby	Resuscitation	Ventilation	Course in NICU	Surgery
		1min	5min					
No	3600	8	9	Girl	BMV	CPAP	48 hours on ventilation	Yes
Yes	1570	2	4	Boy	BMV	CPAP	Surfactant, Pneumothorax	Yes
No	2940	8	9	Boy	Nil	No	Monitoring	No
No	3770	8	9	Girl	Nil	No	Monitoring	Yes
No	3280	8	9	Girl	Nil	No	Monitoring	No

*BMV-Bag and mask ventilation, CPAP-Continuous positive airway pressure. NICU-Neonatal intensive care unit

DISCUSSION

CCAM is a very rare lung abnormality. CCAM is one of the congenital thoracic malformations (CTM). CCAM is the most common congenital cystic lung diseases. Followed by pulmonary sequestration, bronchogenic cysts, and bronchial atresia.[10] The disease spectrum of CCAM is variable. Lesions with spontaneous regression and complete resolution during third trimester have been reported. On the other side of the spectrum, there have been cases of rapidly growing lung masses with non-immune hydrops and in utero demise have been reported. Very close monitoring during the perinatal period is mandatory to optimize the outcome. The differential diagnosis of congenital thoracic malformations (CTMs) are:

- Congenital cystic adenomatoid malformation (CCAM)
- Congenital diaphragmatic hernia.
- Tracheo-oesophageal fistula
- Pulmonary sequestration
- Cysts
- bronchogenic cysts
- foregut cysts
- Tumours
- neuroblastoma
- mediastinal teratoma
- rhabdomyoma
- Atresia - Bronchial with distal degeneration.
- Congenital lobar emphysema
- Congenitally small lungs
- Lung agenesis
- Vascular abnormalities
- vascular rings
- pulmonary artery slings.

The incidence of CCAM in our centre was 1 in 2611, which is higher compared to the other reports.[3] This could be due to the referral bias as this is a referral centre for high risk cases due to availability of multidisciplinary approach by high risk obstetric management, neonatal intensive care unit and Paediatricsurgeons.

Occurrence of CCAM is sporadic and is not related to genetic predisposition, gender predilection or maternal factors such as race, age or environmental exposures. CCAM is known to cause obstetric complications like pre-eclampsia and polyhydramnios and non-immune hydrops.[6]

In present study, two cases had GDM, one among them also had pre-eclampsia. One had PPROM because of polyhydramnios at 32 weeks and 4 days of pregnancy. All five babies had Type 1 CCAM,which is the most common type without any hydrops changes. They were diagnosed during anomaly scan and were monitored with serial ultrasound.

At the time of birth, the lung volume for all the neonates was normal. CVR ratio ranged between 1.6 to 2.0 which did not show any compromise. Two babies showed spontaneous regression at birth. The size of the cyst remained same for two babies and increased in one baby by 1×1cm. All these three neonates, underwent surgical resection. On regular follow, up of these 5 babies, ranging from 6 months to 5 years of age, there was no increased rate of pulmonary infection. All the 5 babies had normal growth and development.

Limitation of present study was retrospective in nature. The study numbers were also very small due to the rarity of the disease. This study is conducted in a tertiary care centre, which is a referral centre, hence may not be

applicable to general population as such. There is a need for multi-centre study to evaluate the need for surgical intervention in relatively asymptomatic CCAMs after birth.

CONCLUSION

In summary CCAM of the foetal lung remains a challenge for obstetricians, neonatologists, and paediatric surgeons. Improvements in antenatal serial monitoring is necessary and will aid in enhancing the prediction of outcomes.

The combination of prenatal MRI and serial ultrasound studies will optimise foetal surveillance and help postnatal care.

In neonates with asymptomatic CCAM in whom surgical intervention was not performed, they should be followed up to adolescence and to adulthood, as they can manifest with malignant changes.

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