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Congenital Cystic Adenomatoid Malformation Diagnosed During First-Trimester Ultrasound Scan

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 26
Final Diagnosis: Congenital cystic adenomatoid malformation (CCAM)
Symptoms: Inconveniently • polyhydramnios
Medication: —
Clinical Procedure: Termination of pregnancy
Specialty: Obstetrics and Gynecology

Objective: Congenital defects/diseases
Background: Congenital cystic adenomatoid malformation (CCAM) is mostly reported from the second trimester of pregnancy. We report a case of a microcystic type of CCAM that was suggested by routine ultrasound examination at a gestational age of 12 weeks.
Case Report: First-trimester ultrasound screening revealed the presence of a hyperechoic image that occupied the whole of the right lung, without no other any associated complications. The cardiac and aorta deviations with diaphragmatic eversion associated with a poly-hydramnios had subsequently appeared. The diagnosis of CCAM was confirmed histologically after termination of the pregnancy at 25 weeks of gestation.
Conclusions: CCAM may occur at a very early stage of fetal lung development.

MeSH Keywords: Congenital Abnormalities • Cystic Adenomatoid Malformation of Lung, Congenital • Fetus • Prenatal Diagnosis

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Background

Congenital cystic adenomatoid malformation (CCAM) is a benign hamartomatous malformation inducing proliferation of pseudo-glandular bronchial structures and multiple cysts formation in the terminal bronchioles, without alveolar development [1]. This pulmonary parenchyma dysplasia can emerge at an early stage of bronchiolar development, during the pseudoglandular stage, which corresponds to the formation of the airways, until the bronchiolar stage, from the fifth to the seventeenth week of gestation. The bronchoalveolar differentiation occurs before the eighth week of gestation, even though some authors justify the absence of reported cases during the first trimester by locating bronchoalveolar differentiation around the thirteenth week [2].

The discovery of CCAM is a rare event, with an incidence of 1 in 25 000 to 1 in 35 000 pregnancies [3]. Mostly diagnosed in the second trimester or in the etiological investigation of hydramnios or hydrops [4], this malformation can be complicated in utero by compressive phenomena such as mediastinum deviation, superior vena cava, or esophagus compression, which can lead to hydrops, hydramnios, and pulmonary hypoplasia [3].

We report a case of early CCAM diagnosed during first-trimester ultrasound screening.

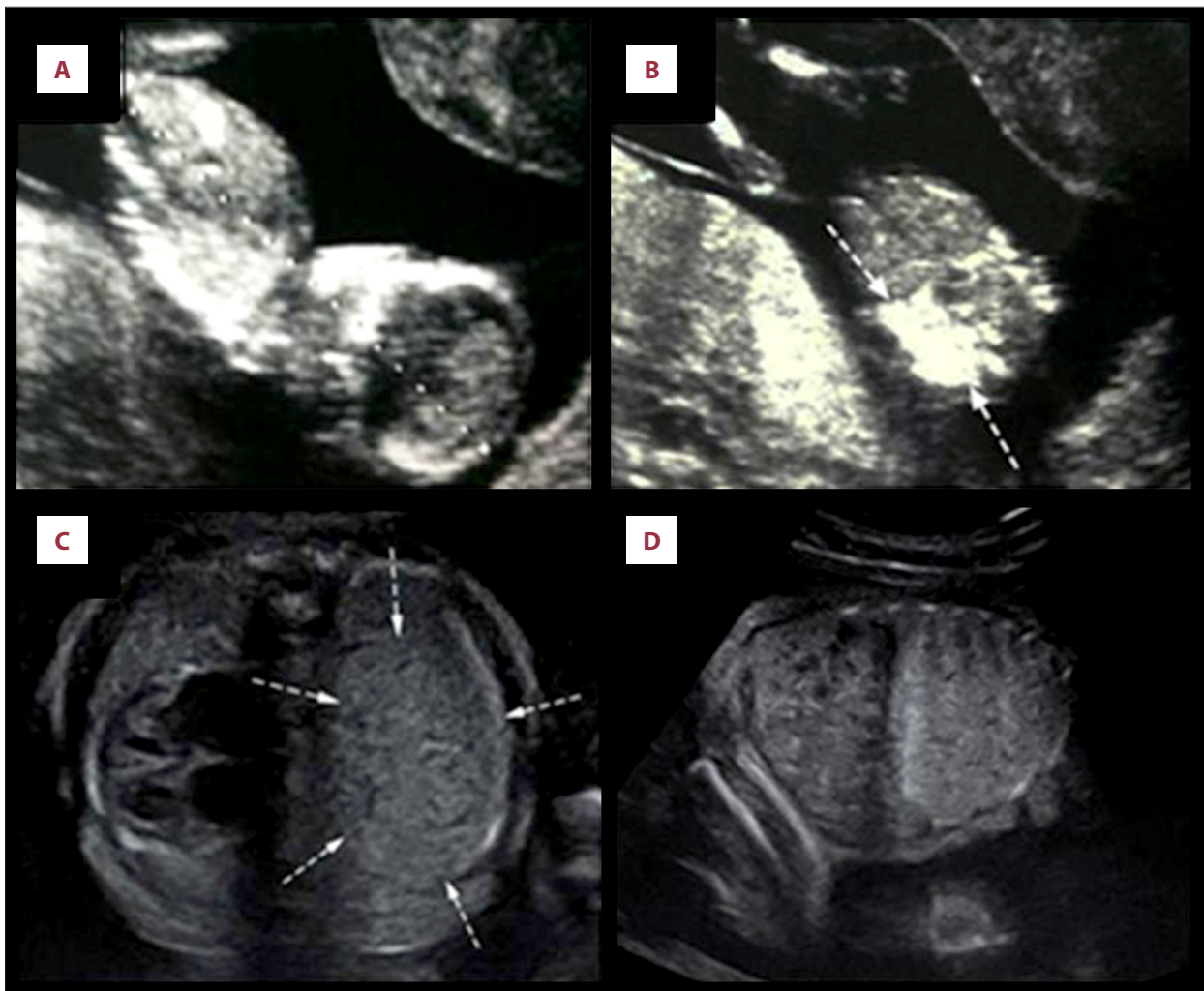


Figure 1. (A, B) Frontal chest section at 12 weeks of gestation: hyperechoic aspect of the right lung. (C) Axial chest section at 25 weeks of gestation: hyperechoic image of the right lung parenchyma. Left lung of usual appearance and heart deviation to the left. (D) Longitudinal section at 25 weeks of gestation: hyperechoic aspect of the lung with inversion of the right diaphragmatic dome.

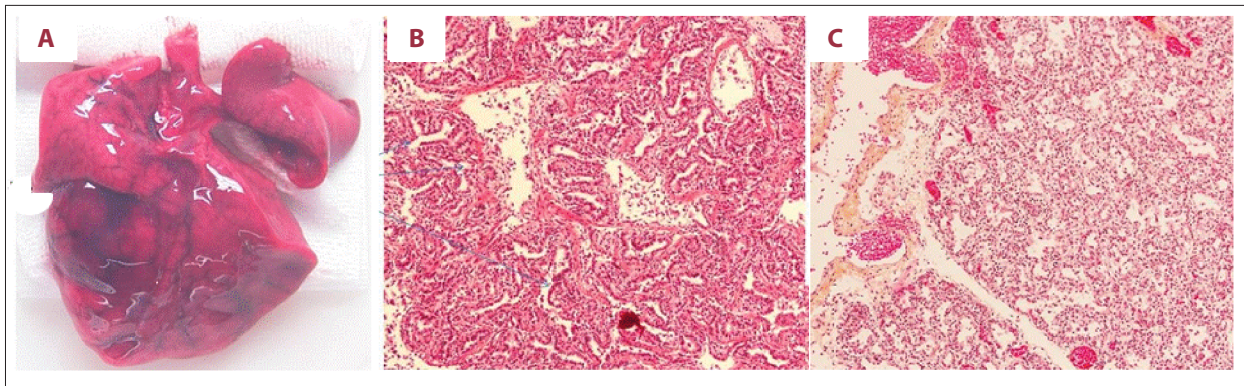


Figure 2. (A) Right lung (49 g) with hypertrophic lower lobe and normal left lung. (B) Histological appearance of right lung tissue with microcystic lesions. (C) Histological appearance of normal left lung tissue.

Case Report

A primiparous 26-year-old patient, with unremarkable personal medical history, was referred to our center. In her family history, we noted that her sister has esophagus atresia associated with situs inversus and primary ciliary dyskinesia.

The first-trimester ultrasound screening at 12 weeks and 4 days of gestation revealed a hyperechoic aspect of the entire right lung, which led us to suspect a unilateral pulmonary pathology (Figure 1A, 1B). Nuchal translucency was measured at 0.9 mm for a cranio-caudal length at 62.5 mm. Regarding the precocity of this abnormality, the retained hypothesis was bronchial atresia, pulmonary sequestration, or CCAM.

The second-trimester test was based on the level of the maternal serum free-beta-hCG (1.04 multiples of the median [MoM]) and on alpha-fetoprotein (AFP) (0.90 MoM).

An ultrasound scan at 21 weeks described the same hyperechoic aspect of the entire right lung associated with discrete mediastinal and heart deviations with hydramnios. The patient was then referred to our department at 25 weeks of gestation. A hyperechoic right intra-pulmonary image, with left heart and aorta deviations, a right diaphragmatic dome eversion, and hydramnios, were confirmed. The color Doppler imaging showed homolateral pulmonary vessels vascularization. There was no Doppler flow evidence of a systemic arterial supply to the lesion. The left lung was compressed by mass effect (27×14 mm) (Figure 1C, 1D).

An amnio-drainage of 2500 ml of amniotic fluid and a karyotype were performed the same day. A few hours after puncture, a premature rupture of membranes was observed and the patient requested a medical pregnancy interruption. The biochemical analysis of amniotic fluid and the karyotype were normal (46 XY). Medical pregnancy interruption was accepted in accordance with the French laws and was performed uneventfully.

On autopsy, the fetus was discovered to be a male weighing 1550 g. The external examination revealed abdominal distension. On internal examination, all organs were *in situ*. The pulmonary parenchyma of the right lung lower lobe consisted in microcysts of variable size; most of them were 0.5 cm, inducing a major right lung hypertrophy (49.1 g vs. 5.5 g of the left lung, normal=27±7 g). This tumor compressed and latero-deviated to the left the mediastinum (heart, thymus, left lung) and caused an eversion of the right diaphragmatic dome. On histology, right lungs showed multiple cysts relatively uniform in size, lined by stratified columnar epithelium, and having thin fibromuscular septa. All other visceral organs were congested but well-developed and revealed no anomalies. Based on these features, a pathological diagnosis of CCAM Stocker type 3 was confirmed (Figure 2A–2C).

Discussion

CCAM is a bronchopulmonary malformation characterized by the presence of intraparenchymal cysts of variable size, ranging from a few millimeters to several centimeters. Currently, the etiology of this malformation is not completely known. Several theories have been proposed to explain the pathophysiology. Its sporadic incidence, associated to a highly-localized character surrounded by healthy pulmonary parenchyma, could suggest a non-genetic and more likely obstructive abnormality during fetal lung development.

However, a localized genetic origin cannot be completely ruled out [5]. A second, but highly controversial, hypothesis is that this malformation may be the result of a pulmonary bronchi obstruction during fetal development, with dilated airways and pseudocyst formation [6]. Another hypothesis involves the association of airway obstruction and local molecular phenomena [7]. Expressions of early pulmonary development markers within the lesion, such as thyroid transcription factor-1 (TTF-1) or Hoxb5, evoked an abnormality occurring during the

pseudo-glandular (6–16 weeks of gestation) [8] or canalicular (17–26 weeks of gestation) stage [9].

Marshall et al. suggested that this phenomenon occurred during the second trimester of pregnancy and this may be why no cases have been described during the first trimester [10]. The second trimester routine morphology ultrasound is performed in the middle part of the pregnancy; thus, CCAM is more often detected in the second trimester. Furthermore, sensitivity to detected morphological abnormalities is higher with the advancement of pregnancy and fetal development. In our case, the lesion was present at 12 weeks, and at 21 weeks the voluminous mass had already displaced the mediastinum and the diaphragm. We suggest that in certain cases the CCAM may be a missed diagnosis of the first trimester and could be detected at an early stage of fetal development.

The fetal lung development has been divided into 5 stages: embryonic (3–7 weeks), pseudoglandular (7–17 weeks), saccular

(24–36 weeks), and alveolar (36 weeks to maturity) [11]. Cha et al. [12], in a previous review, described 11 fetuses carrying this malformation, at between 21 and 27 weeks of gestation. Histological analysis showed that in 7 fetuses, the malformation could have the aspect of pseudoglandular fetal lung period development, anterior to chronological age, and 4 had canalicular-stage lung characteristics.

Conclusions

CCAM in certain cases may be sonographically detectable as early as 12 weeks. First-trimester ultrasound screening may be helpful to suggest early fetal lung development abnormalities.

Conflict of interest

None.

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