Prenatal diagnosis of congenital cystic adenomatoid lung malformation: Case report and review of the literature

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Summary

Congenital cystic adenomatoid malformation of the fetal lung is an extremely rare developmental abnormality characterized by excessive overgrowth of the terminal respiratory bronchioles at the expense of the saccular spaces. We present a case of a 33-year-old, gravida 2, para 1, woman with congenital cystic adenomatoid lung malformation-type II diagnosed by ultrasound at the 20th week of gestation. On the right side of the chest an area with a maximum diameter of 18.5 mm and with small cystic lesions was recognized. The maximum diameter of the cysts was 0.5 cm. There were no other fetal abnormalities. The pregnancy was terminated and the postmortem examination confirmed the ultrasonographic findings. The cysts had the appearance of bronchiolus-like structures and were lined with cuboidal and columar epithelium. Distended alveoli were present, while the airways were normal in structure. No other congenital anomalies were found. In conclusion, in this study we describe the ultrasonographic and pathologic findings of an unusual case of congenital cystic adenomatoid malformation of the fetal lung.

Key words: Congenital cystic adenomatoid lung malformation; Type II; Ultrasound; Prenatal diagnosis.

Introduction

Congenital cystic adenomatoid malformation of the lung is an extremely rare developmental abnormality characterized by an excessive overgrowth of the terminal respiratory bronchioles at the expense of the saccular spaces [1, 2]. Chin and Tang, first described it in 1949 [3].

Congenital cystic adenomatoid malformation of the lung is usually unilateral involving only one lobe or segment [1, 4]. There is a broad spectrum of clinical associations such as polyhydramnios, fetal hydrops and hypoplasia of the contralateral lung due to the compression of the pulmonary mass [1, 5]. However, the prognosis is variable ranging from spontaneous *in utero* regression or perinatal death to no neonatal morbidity [2].

Sonography is important for the prenatal diagnosis. The objective of this paper was to report the diagnosis of a congenital cystic malformation of the lung *in utero* and to present the ultrasonographic findings and the postmortem pathology. The aetiology of this entity is also discussed and the international literature is reviewed.

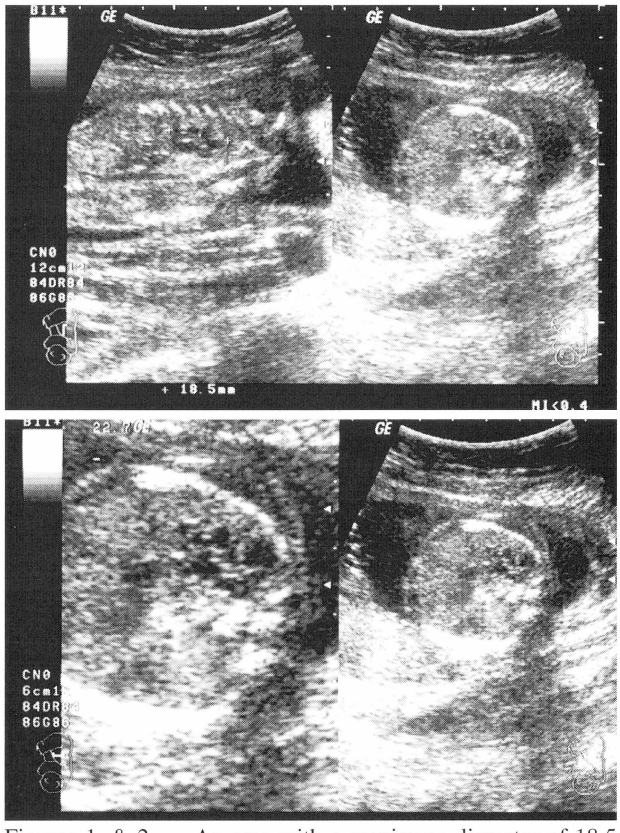
Case report

Our patient was a 33-year-old, gravida 2, para 1, rhesus positive woman who had had a previous normal pregnancy. She presented to the Obstetrics and Gynecology Department of "G. Chatzikosta" General Hospital, Ioannina, Greece for a routine sonographic examination at the 20th week of gestation. Initially this pregnancy was uneventful and maternal serum alpha-fetoprotein was normal. Her sickle test and haemoglobin electrophoresis were normal. Serological testing of the mother showed no IgM antibodies against toxoplasma, cytomegalovirus and rubella. There was no familial nor maternal history of congenital cystic malformation of the lung.

A single fetus was found and the placenta was adhered in the posterior uterine wall. The fetal biparietal diameter (BPD) was 45 mm, fetal abdominal circumference 144 mm and fetal femur length (FL) 30 mm. Ultrasonographically, the gestational age was calculated to be 19 weeks and three days. The gestational weight was estimated to be 322 g. Amniotic fluid volume was within normal levels. Fetal movements were normal. On the right side of the chest an area with a maximum diameter of 18.5 mm and with small cystic lesions was recognized (Figures 1, 2). The maximum diameter of the cysts was found to be 0.5 cm (Figure 3) and the lesion was classified as congenital cystic adenomatoid malformations of the fetal lung-type II. There were no fetal ascites, mediastium shift, pericardial effusion, pleural effusion, congenital diaphragmatic hernia or other fetal abnormalities. The most likely diagnosis was thought to be a cystic lesion of the fetal lung. The couple decided to terminate the pregnancy, which was carried out by means of Cytotec®. A female fetus was delivered, weighing 330 g.

The postmortem examination showed a congenital cystic adenomatoid malformation of the right middle lobe of the lung, which was histopathologically classified as type II. No other congenital anomalies were found. The left lung measured 3 x 2.5 x 1 cm and weighed 3.67 g; no gross abnormalities were found. The right lung measured 3 x 1.9 x 1 cm and weighed 5.6 g. The cross section revealed an area which contained cysts of 0.4 to 0.6 cm in diameter, surrounded by normal pulmonary parenchyma at the middle lobe of the right lung (Figure 4). The cysts had the appearance of bronchiolus-like structures and were lined with cuboidal and focally columnar epithelium; distended alveoli were present (Figures 5, 6, 7). The airways were normal in structure. The fetal karyotype was 46, XX.

Revised manuscript accepted for publication March 22, 2003



Figures 1. & 2. — An area with a maximum diameter of 18.5 mm on the right side of the fetal chest with small cystic lesions is demonstrated by ultrasound scans.

Discussion

Intrathoracic extracardiac malformations are usually extrinsic, such as congenital diaphagmatic hernia, which occurs in approximately one in 2,000 births. Intrinsic intrathoracic lesions are rare. They include bronchogenic cysts, congenital cystic adenomatoid malformations of the lung, bronchopulmonary sequestration, primary pulmonary hypoplasia, chylothorax, idiopathic hydrothorax and mediastinal masses [6]. Congenital cystic adenomatoid malformations of the fetal lung are almost always unilateral and may occur in any lobe, involving part of a lung lobe or a whole lobe [7], although bilateral cases have been reported [8]. In our case the lesion involved a field with a maximum diameter of 2 cm in the right lung.

The exact mechanism causing congenital cystic adenomatoid lung malformations is not known, although an arrest in the connecting mechanism between the ectodermal component (conductive airways) and the mesenchymal, i.e., respiratory component with subsequent overgrowth of the terminal bronchioli at the beginning of the sixth week of gestation has been attributed to the development of congenital cystic adenomatoid malformation of the fetal lung [1]. Risk of recurrence of congential cystic adenomatoid lung malformations in future pregnancies appears minimal [9]. A congenital cystic adenomatoid malformation of the fetal lung represents in most instances a sporadic non-hereditary lesion. In addition to that, this malformation can occur in certain genetic syndromes such as trisomy 18 [7].

Stocker *et al.,* in 1977 classified congenital cystic malformations of the lung into three types based on several criteria but mainly on the size of the cysts [10]. All three are characterized by a proliferation of structures resembling terminal bronchioles, increased elastic tissue and polypoid columnar or cuboidal epithelial proliferation: (A) Congenital cystic adenomatoid malformations of the fetal lung-type I: They consist of multiple large cysts more than 2 cm and up to 7 cm in diameter. The cysts are lined by ciliated pseudo-stratified columnar epithelium. The wall of the cysts is thick and contains prominent smooth muscle and elastic tissue [10, 11]. Mucous producing cells are present in approximately one-third of the cases and cartilage in the wall is rarely seen [10]. Relatively normal alveoli may be seen between the cysts [10]. Communications between the cysts and the normal bronchial tree can usually be demonstrated. These lesions frequently result in mediastinal herniation [10]; (B) Con-

Fig. 3

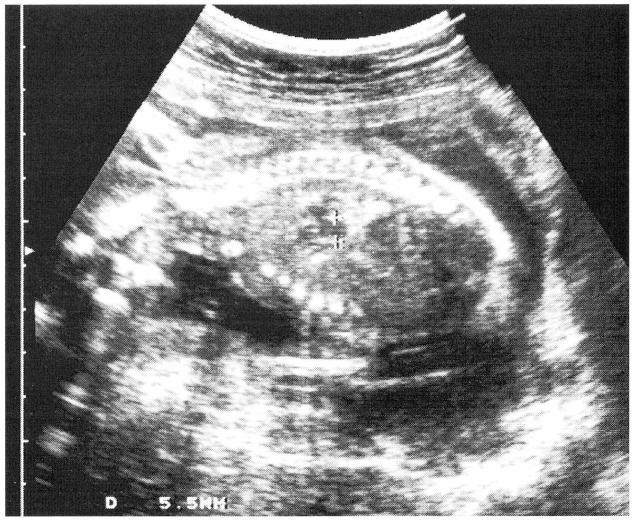


Fig.

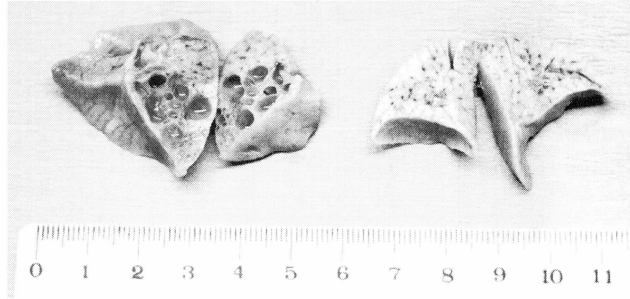


Figure 3. — In a longitudinal scan of the fetus the maximum diameter of the cysts was found to be 0.5 cm; the lesions were classified as congenital cystic adenomatoid malformations of the fetal lung-type II.

Figure 4. — Cross section of the fetal lungs: In the middle lobe of the right lung an area containing cysts with diameters ranging between 0.4 and 0.6 cm is demonstrated. The lesion is surrounded by normal pulmonary parenchyma.

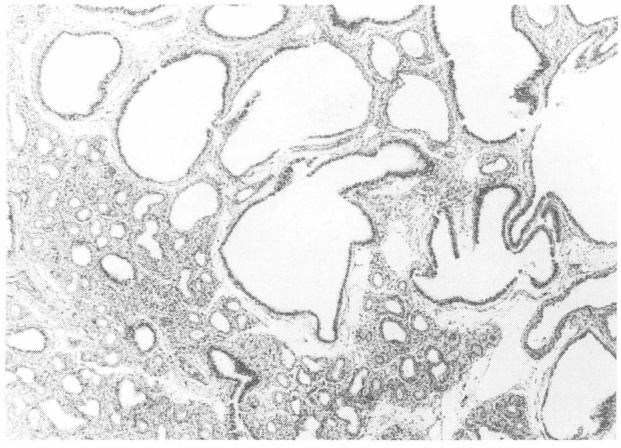


Fig. 5

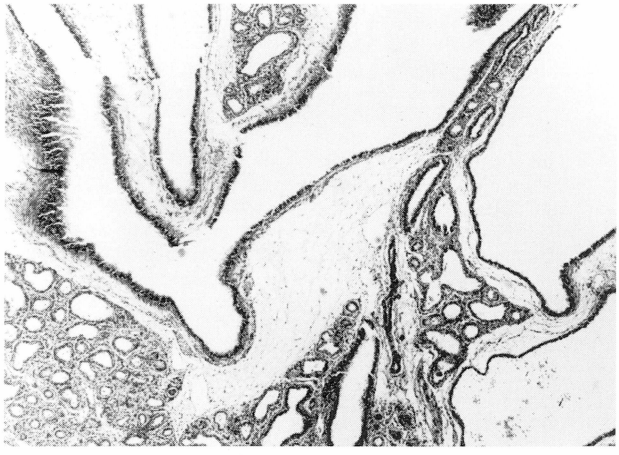


Fig. 6

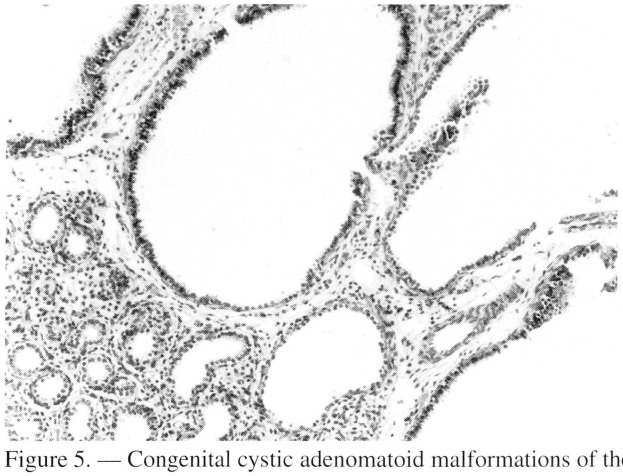


Fig. 7

Figure 5. — Congenital cystic adenomatoid malformations of the fetal lung-type II: The cysts are lined by ciliated cuboidal to columnar epithelium and the wall is thin. These structures resemble respiratory bronchioli. Distended alveoli are present between the cysts. (Haematoxylin and eosin x 40).
Figure 6. — The same as Figure 5. (Haematoxylin and eosin x 40).
Figure 7. — The same as Figure 5. (Haematoxylin and eosin x 100).

genital cystic adenomatoid malformations of the fetal lung-type II: They are characterized by multiple small bronchiolus-like cysts, less than 1.0 cm in diameter. The cysts are lined by cuboidal to tall columnar ciliated epithelium that only rarely displays pseudostratification. The wall of the cysts is composed of a thin layer of loose connective tissue containing discontinuous bands of smooth muscle and elastic tissue rarely more than three to four cell layers thick. Sometimes strands of striated muscle fibers are present [10]. Distended alveoli are found between the epithelium-lined cysts [10]. Mucous cells and cartilage are not present [10]; (C) Congenital cystic adenomatoid malformations of the fetal lung - type III: They are characterized by a solid appearance of the lung with multiple microcysts involving the whole lung or even both lungs [10].

Congenital cystic adenomatoid malformations of the fetal lung-type I constitute about 70% of the cases, have the best survival rate and point to their emergence in later stages of fetal development. Also the prognosis of the infant is good after the resection of the lesion [6, 10-12]. Congenital cystic adenomatoid malformations of the fetal lung - type II account for about 20% of the cases, are found in association with other malformations, especially of cardiovascular, urinary and skeletal system in a range of 15% to 42% of congenital cystic adenomatoid malformations of the fetal lung-type II and have a poor prognosis [6, 10-12]. Also, congenital cystic adenomatoid malformation of the fetal lung-type II sometimes coexist with pulmonary sequestration [11]. Congenital cystic adenomatoid malformations of the fetal lung-type III are identified in about 10% of the cases. These lesions have the worst prognosis [6, 10, 12]. Congenital cystic adenomatoid malformations of the fetal lung – when the lung mass reaches large proportions *in utero* – lead to pulmorary hypoplasia, mediastinal shift, polyhydramnios and hydrops [7]. In these cases the prognosis of the fetus is adversely affected [4]. Hydrops is probably the result of decreased venous return following vena cava compression by the pulmonary mass or decreased myocardial contractility due to the extreme mediastinal shift caused by the lesion [7]. However, loss of protein from the congenital cystic adenomatoid malformation of the lung may be a contributing factor because extremely high amniotic fluid protein concentration has been documented in some hydropic cases [7, 13]. Although the precise pathogenesis of polyhydramnios is unknown, it may result from decreased fetal swallowing of amniotic fluid as a result of oesophageal compression by the lung mass or from increased fetal lung fluid production by the abnormal lung tissue [7].

Prenatal sonography demands careful attention to the echogenicity of the lungs to detect fetal lung masses. Disappearance of the lung lesions with spontaneous resolution *in utero* has been reported [14, 15]. The initial impression of the size of the mass may not always be helpful in predicting outcome since shrinkage of the mass due to decompression of fetal lung fluid through abnormal channels to the airway and the gastrointestinal tract has been reported. Another possible explanation is that the pulmonary lesions outgrow their vascular supply and involute [7]. Newborn infants with congenital cyst malformations of the lung present varying degrees of respiratory difficulty [2]. Miller *et al.*, reported that the major-

ity of cases are referred in the neonatal period with respiratory distress, other within hours of birth, and that 14% of fetuses with congenital cystic adenomatoid malformation of lung are stillborn [16]. The neonates develop respiratory distress because of pulmonary compression, pulmonary hypoplasia, prematurity or any combination of these [6]. It is possible that the babies may require major surgery within a few hours or days of birth. For all of these reasons an experienced paediatrician should be present at the birth and delivery should be in a unit with neonate intensive care facilities, ideally close to an infant surgical unit [6]. In addition to that, often 10% of the cases with congenital cystic adenomatoid malformations of the lung present with problems after the first year of life and they do so because of recurrent respiratory tract infections [2].

Surgery has been undertaken to correct such fetal malformations, even on the fetus *in utero* [17, 18]. However, if the abnormality appears major and ultrasound indicates associated problems such as hypoplasia of the remaining lung, then a poor prognosis should be noted when choosing the mode of delivery [9]. In our case although no other abnormalities were detected by the ultrasound scan in the second trimester of pregnancy the couple decided to terminate the pregnancy because of described poor prognoses of congenital cystic adenomatoid malformations of the fetal lung-type II.

In conclusion, we presented a very rare case of congenital cystic adenomatoid malformations of the fetal lung-type II and described the ultrasonographic and pathologic findings of this entity.

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