Acta Obstet Gynecol Scand 1997; 76: 378–379
Printed in Denmark – all rights reserved

Acta Obstetricia et Gynecologica Scandinavica
ISSN 0001-6349

CASE REPORT

Type III congenital cystic adenomatoid malformation of the lung detected through maternal serum screening positive for Down's syndrome

CHIH-PING CHEN[1], CHUN-YU CHUANG[2], YI-CHIN CHANG[3] AND CHI-YUAN TZEN[3]
From the Departments of [1]Obstetrics & Gynecology, [2]Medical Research and [3]Pathology, Mackay Memorial Hospital, Taipei, Taiwan, R.O.C.

Acta Obstet Gynecol Scand 1997; 76: 378–379. © Acta Obstet Gynecol Scand 1997
Key words: alpha-fetoprotein; cystic adenomatoid malformation of the lung; human chorionic gonadotrophin; maternal serum screening
Submitted 7 October, 1996
Accepted 12 November, 1996

A 24 year old primigravida was referred for genetic counseling because of an abnormal maternal serum result which indicated a Down's syndrome risk of 1:59 calculated from the gestational age, maternal age, a maternal serum alpha-fetoprotein (AFP) value of 32.50 ng/ml or 0.64 multiples of the median (MoM), and a human chorionic gonadotrophin (hCG) value of 130.30 IU/ml or 3.84 MoM (EIA, AFP, hCG; Abbott Laboratories, Inc., North Chicago, IL, USA) at 17 weeks' gestation. The gestational age was confirmed by ultrasonography. The estimated risk of Down's syndrome during the second trimester at a maternal age of 24 years is 1:942. A maternal serum screening result with a calculated risk of greater than 1:270 is deemed 'screen-positive' and a recommendation for diagnostic amniocentesis is initiated. Ultrasonographic examination at 19 weeks' gestation during genetic amniocentesis revealed a single fetus with an estimated gestational age of 19 weeks, and a large echogenic mass within the left hemi-thorax. The mediastinum was displaced to the right. No polyhydramnios, fetal hydrops, fetal ascites, or associated structural abnormalities were noted. A tentative diagnosis of Type III congenital cystic adenomatoid malformation of the lung (CCAML) was made. Cytogenetic analysis revealed a 46,XY karyotype. The amniotic fluid AFP level was 7316 ng/ml, 1.37 MoM at 19 weeks' gestation. The parents were nonconsanguineous and healthy. There was no family history of congenital malformations. The maternal blood group was O, Rh-positive and the maternal thalassemia, syphilis, and hepatitis B screen results were negative. The mother was followed up by serial obstetric ultrasonography which confirmed the persistent appearance of an echogenic fetal lung. At 23 weeks' gestation, the fetal thoracic circumference measured 17.9 cm, the echogenic mass circumference measured 11.0 cm, the area of the fetal thorax 24.6 cm^2, and the area of the echogenic mass 10.2 cm^2. The echogenic mass occupied 42% of and the area of fetal thorax. The unilateral echogenic mass in the fetal thorax was felt to be consistent with type III CCAML. There were lateral displacement of the fetal heart, the tumor involvement of the left lung, and compression of the right lung but without coexistent polyhydramnios or fetal hydrops (Fig. 1). The parents opted to terminate the pregnancy at 24 weeks' gestation. A male fetus weighing 706 g was delivered with no external morphological abnormalities. Necropsy revealed that the entire left hemi-thorax was occupied by a greatly enlarged left lung which displaced the heart and compressed the right lung. Microscopically, the upper and lower lobes of the left lung showed the characteristic histological appearance of type III CCAML. The parenchyma comprised small cysts resembling expanded terminal bronchioles lined with cuboidal epithelium. No cartilage plates or mucogenic cells could be identified. Examination of the placenta revealed neither hydatidiform mole nor hydropic degeneration.

Abbreviations:
CCAML: congenital cystic adenomatoid malformation of the lung; AFP: alpha-fetoprotein; MoM: multiples of the median; hCG: human chorionic gonadotrophin.

Discussion

The unique aspect of our case is the association between an abnormal maternal serum result, particularly an elevated hCG level, and type III CCAML. This finding is significant and, in addition to ultrasonography, may be useful in helping detected prenatally a fetus with type III CCAML. Sherer et al. (1992) (1) documented an abnormal maternal serum screening result for Down's syndrome with an elevated hCG level of 3.87 MoM and a normal AFP level of 1.83 MoM at 17 weeks' gestation in a pregnancy of bilateral type III CCAML with nonimmune fetal hydrops and oligohydramnios. The 28 year old mother was counseled due to the increased risk of Down's syndrome calculated at 1:228 (vs 1:755 for age 28). She elected to undergo genetic amniocentesis. Ultrasonography before amniocentesis disclosed type III CCAML, fetal hydrops, and oligohydramnios. Petit et al. (1987) (2) reported the observation of highly elevated AFP levels in the amniotic fluid of a 23-week-gestation fetus with type III CCAML, oligohydramnios, fetal ascites, renal agenesis, and imperforate anus. Albright and Katz (1989) (3) demonstrated an elevated maternal serum AFP level of 3.34 MoM at 17 weeks' gestation and a normal amniotic fluid AFP level of 1.7 MoM at 19 weeks' gestation in a type III CCAML pregnancy with fetal ascites, hepatomegaly and anomalous pulmonary venous return on the right side. However, Journel et al. (1988) (4) described a case of CCAML without increase in maternal serum AFP. Journel et al. (1988) (4) further concluded that elevated AFP in CCAML could have resulted from the associated malformations and AFP may not be a reliable indicator or diagnostic sign of the presence of CCAML. Our case of type III CCAML showed normal levels of maternal serum AFP and amniotic fluid AFP, whereas there was an elevated maternal hCG level of 3.84 MoM at 17 weeks' gestation without other coexistent structural or chromosomal abnormalities. Low maternal serum AFP, low maternal serum uE_3, and high maternal serum hCG during the second trimester are associated with Down's syndrome. High levels of hCG in the second trimester have been reported in cases of fetal monoparental disomy of chromosome 16, sex chromosome aneuplodies, Turner syndrome, marker chromosomes, hydrops fetalis, abdominal wall defects, complete molar pregnancies and partial

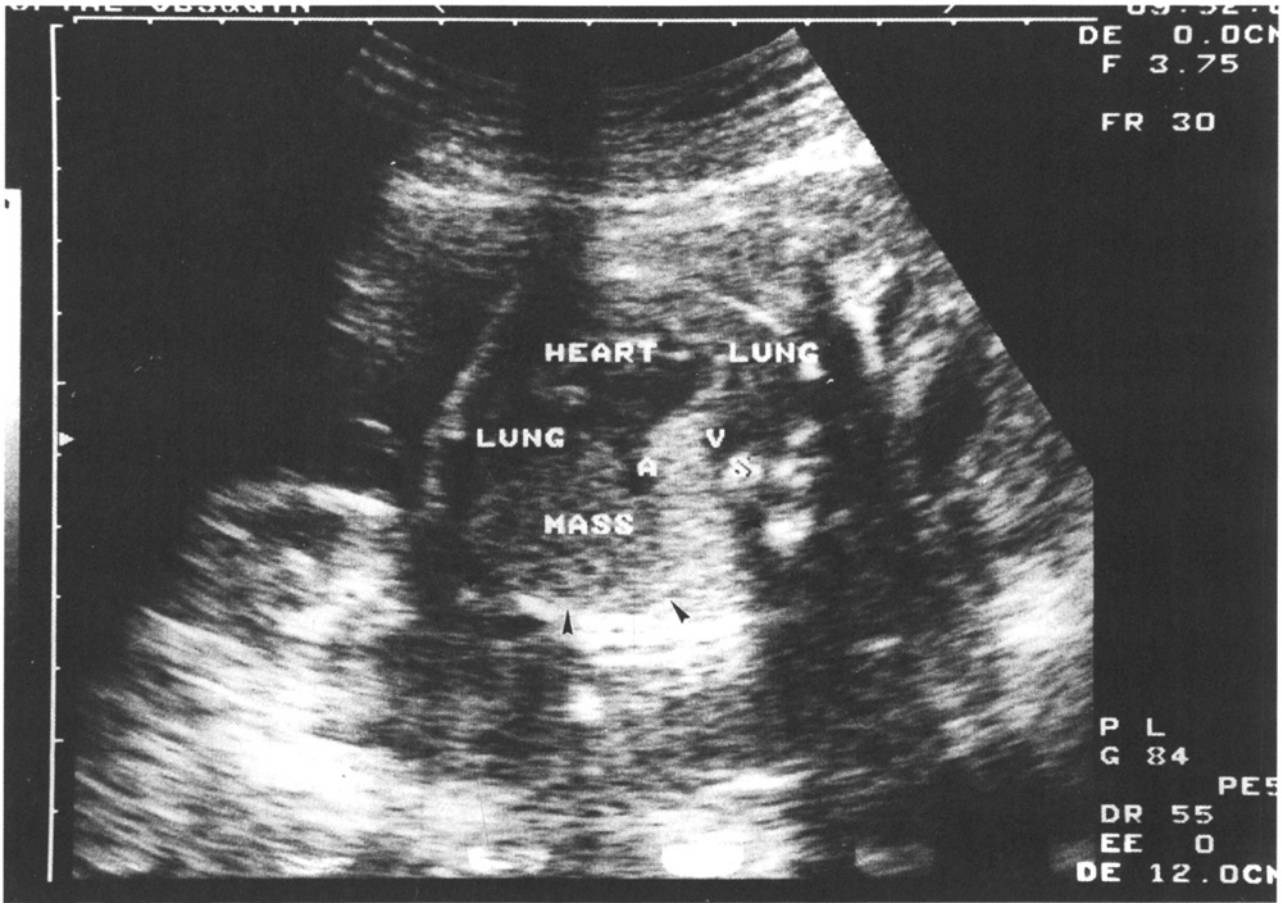

Fig. 1. Prenatal ultrasonography at 23 weeks' gestation. Transverse view of the fetal chest showing fetal heart and the fetal lungs compressed by an echogenic lung mass (arrows).

molar pregnancies (5). Hydrops fetalis, itself, rather than the underlying disorder, can cause the high level of hCG and screen positivity (6). Because hCG is produced by the placenta, an elevation in its level may represent altered placental circulation or function. The maternal serum screening results in the case of bilateral type III CCAML *in utero* reported by Sherer et al. (1) can be explained by the associated fetal hydrops. However, in this case of unilateral type III CCAML *in utero* without concomitant fetal hydrops to affect hCG, the hCG level was significantly elevated. Whether or not the type III CCAML itself causes the elevated level of hCG and screen positivity will require large collaborative studies.

References

1. Sherer DM, Abramowicz JS, Metlay LA, Roberts M, Woods Jr JR. Nonimmune fetal hydrops caused by bilateral type III congenital cystic adenomatoid malformation of the lung at 17 weeks' gestation. Am J Obstet Gynecol 1992; 167: 503–5.
2. Petit P, Bossens M, Thomas D, Moerman PH, Fryns JP, Van den Berghe H. Type III congenital cystic adenomatoid malformation of the lung: another cause of elevated alpha fetoprotein? Clin Genet 1987; 32: 172–4.
3. Albright SG, Katz VL. Alpha-fetoprotein findings in a case of cystic adenomatoid malformation of the lung. Clin Genet 1989; 35: 75–6.
4. Journel H, Le Guern H, Le Goff JL. Congenital cystic adenomatoid malformation of the lung and alpha fetoprotein. Clin Genet 1988; 34: 344.
5. Chard T, Iles R. Measurement of human chorionic gonadotrophin (hCG) as a screening test for Down's syndrome. In: Grudzinskas JG, Chard T, Chapman M, Cuckle H, eds. Screening for Down's Syndrome. Cambridge: Cambridge University Press, 1994: 73–84.
6. Knowles S, Flett P. Multiple marker screen positivity in the presence of hydrops fetalis. Prenat Diagn 1994: 14: 403–5.

Address for correspondence:
Chih-Ping Chen, M.D.
Department of Obstetrics and Gynaecology
Mackay Memorial Hospital
92, Section 2, Chung-Shan North Road
Taipei, Taiwan, R.O.C.