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SHORT COMMUNICATION

Laryngeal Atresia Presenting as Fetal Ascites, Olygohydramnios and Lung Appearance Mimicking Cystic Adenomatoid Malformation in a 25-week-old Fetus With Fraser Syndrome

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We describe a 25-week-old female fetus of consanguineous parents with ultrasonographic findings of increased echogenicity of lungs mimicking CAM (cystic adenomatoid malformation) type III, olygohydramnios and fetal ascites. A therapeutic abortion was performed and unilateral cryptophthalmos, laryngeal atresia and bilateral syndactyly of the hands and feet were observed at post-mortem. These findings confirmed the diagnosis of Fraser syndrome after abortion. Copyright © 1999 John Wiley & Sons, Ltd.

KEY WORDS: Fraser syndrome; laryngeal atresia; cystic adenomatoid malformation type III; fetal ascites; olygohydramnios; prenatal diagnosis

INTRODUCTION

Serville *et al.* (1989), Meagher *et al.* (1993) and Kalache *et al.* (1997) suggested that the diagnosis of laryngeal abnormalities in the fetus is difficult even when prenatal ultrasonography shows increased echogenicity of the lungs and fetal ascites. The prenatal ultrasonography should be examined by a clinical geneticist and post-mortem examination should be performed by a fetal pathologist. Moerman *et al.* (1992) and Labbe *et al.* (1992) demonstrated the importance of lung histopathology in the differential diagnosis of a fetus with laryngeal atresia or CAM. Recently, Morrison *et al.* (1998) reported three independent cases with laryngeal atresia or stenosis presenting as second-trimester fetal ascites. However, there were no other internal malformations. We describe a 25-week-old female fetus of consanguineous parents in whom hyperechogenic lungs, similar to CAM type III, olygohydramnios and fetal ascites were detected by ultrasonography and suggested a possible diagnosis of Fraser syndrome. After therapeutic abortion the diagnosis of Fraser syndrome was confirmed by the findings of cryptophthalmos, and bilateral syndactyly of hands and feet. Laryngeal, renal, ureter and vaginal atresia were also observed in autopsy.

CASE REPORT

Ultrasonography at first admission demonstrated lungs similar to CAM type III, olygohydramnios and fetal ascites in a 25-week-old female fetus of consanguineous parents (Fig. 1). After therapeutic abortion, Fraser syndrome was diagnosed by the findings of cryptophthalmos and bilateral syndactyly of hands and feet (Fig. 2). The length and weight of the fetus were 32 cm and 1500 g, respectively. Low-set ears, narrow external acoustic meatus, protuberant abdomen, and extremely low insertion of umbilical cord were also noted (Fig. 3). At autopsy, laryngeal atresia with hypoplastic epiglottis was observed (Fig. 4). Both lungs were diffusely hard, swollen and heavier than those of a normal fetus at the same gestational age. Complete atresia of the larynx was confirmed by histopathologic examination (Fig. 5). Lung histology showed dilated alveoli including extravasation of erythrocytes and a variety of lining epithelium in many bronchioles with low cuboidal epithelium besides normal ciliated columnar epithelium (Fig. 6). The post-mortem chromosomal analysis was normal, 46,XX. Following the abortion the mother became pregnant again. Ultrasonography showed a normal fetus at 14 weeks of gestation. A normal baby was subsequently born.

DISCUSSION

In 1962, Fraser (1962) described a new autosomal recessive syndrome in two sisters with various combinations of cryptophthalmos, syndactyly, laryngeal atresia or stenosis, renal agenesis, and ambiguous genitalia. Lurie and Cherstvoy (1984) reported four families with the cryptophthalmos syndactyly syndrome. Nine affected fetuses died in the perinatal period; autopsy, in six cases, revealed unilateral renal

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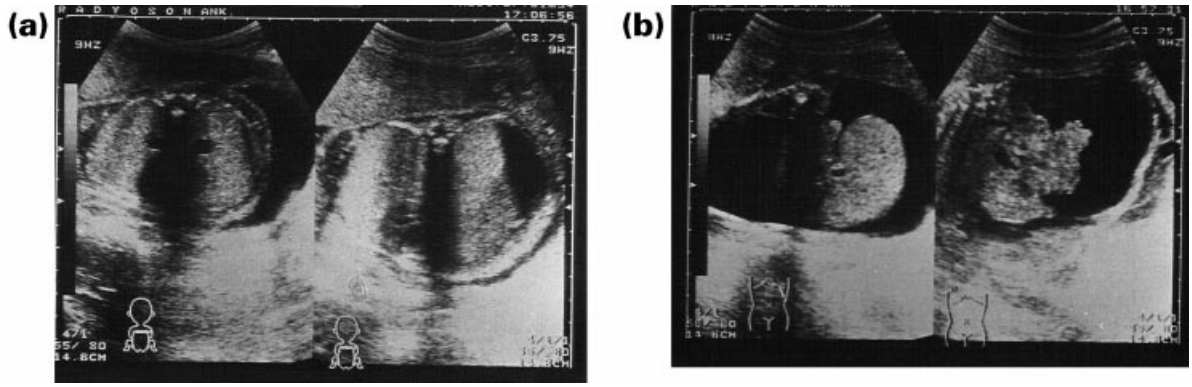

Fig. 1—(a) Bilateral hyperechogenic lung fields, similar in appearance to type III CAM, were noted on 25-week-old fetal ultrasonography. (b) Fetal ascites and olygohydramnios were detected on 25-week-old fetal ultrasonography

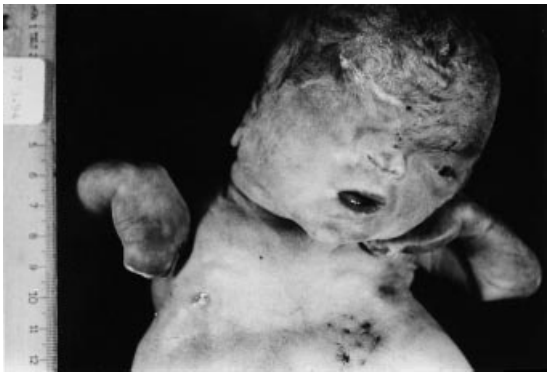

Fig. 2—Right complete and the left partial cryptophthalmos, hair growth on lateral forehead extending to the lateral eyebrow, broad nose with depressed bridge and hypoplastic notched nares, bilateral syndactyly of the hands and feet, unilateral absence of the right nostril, low-set ears, underdeveloped helix and antihelix, and the narrow external acustic meatus

Fig. 4—Laryngeal atresia with hypoplastic epiglottis was observed macroscopically

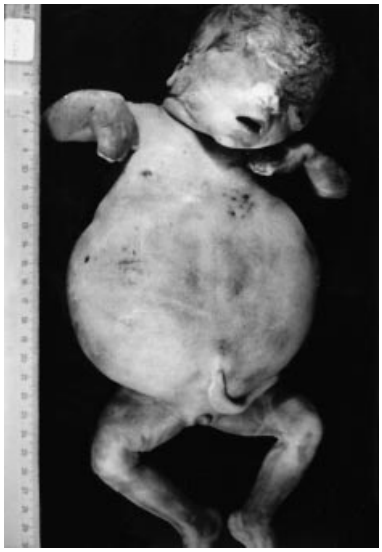

Fig. 3—The abdomen was prominent. The umbilical cord was extremely low set and was inserting 0.5 cm above the symphisis. The external genitalia were hypoplastic with non-identifiable labia major but prominent clitoris

agenesis (three) and bilateral renal agenesis (three). Thomas *et al.* (1986) reviewed the literature on 124 cases; 27 had isolated cryptophthalmos, 11 were unclassified, and 93 cases showed a pattern of multiple congenital malformations similar to the Fraser syndrome. Boyd *et al.* (1988) also reported detailed postmortem findings of 11 cases of probable Fraser syndrome. These authors concluded that prenatal diagnosis was possible by ultrasound examination of the eyes, digits and kidneys. Schauer *et al.* (1990) reported a case diagnosed prenatally by ultrasonography at 18.5 weeks of gestation. The cause of the laryngeal stenosis has not been fully elucidated. Laryngeal atresia has been defined in Fraser syndrome due to abnormal mid-line fusion of the arytenoid cartilages at their vocal processes and to occlusion of the glottis. However, Ramsing *et al.* (1990) suggested that neurocristopathy may be a factor. Defective neural crest cell migration, differentiation and deficient preprogrammed cell death could be an explanation for otic, ocular, facial and laryngeal abnormalities. Increased echogenicity of lungs detected by prenatal ultrasonography is due to an increase in lung size as a result of the upper airway obstruction. Histopathologic changes in the lung are

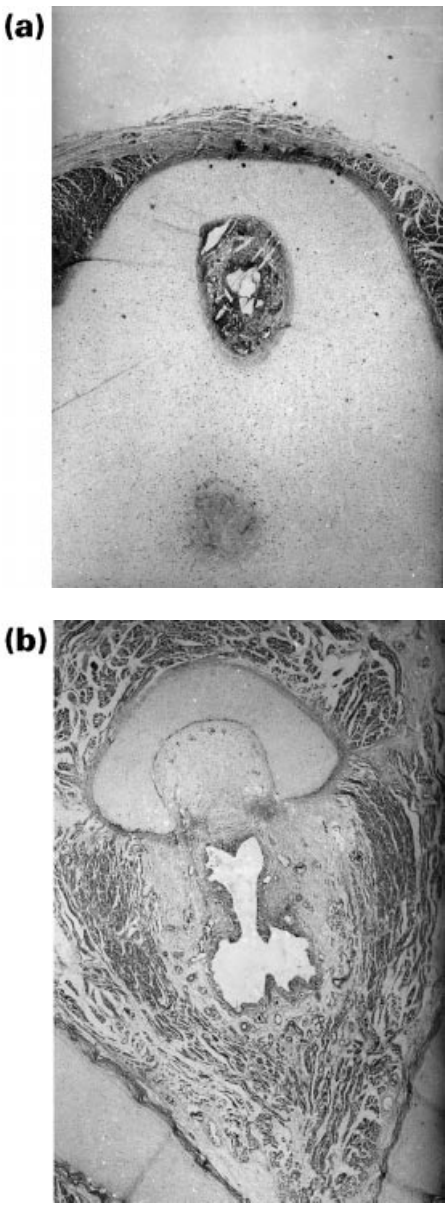

Fig. 5—(a) Transverse section of the larynx showing abortive channels in the level of laryngeal stenosis (HE × 28). (b) Laryngeal aperture, lined by pseudo-stratified epithelium (HE × 28)

also related to upper airway obstruction. Ascites is probably due to compression of the great veins and right atrium, due to increased lung mass. Pressure on the eosophagus may result in decreased fetal swallowing of amniotic fluid and polyhydramnios. However, olygohydramnios was observed in our case due to bilateral renal agenesis. Laryngeal atresia is a feature of Fraser syndrome and when present may be suggested on prenatal ultrasound by increased echogenicity of lungs, with olygohydramnios and fetal ascites.

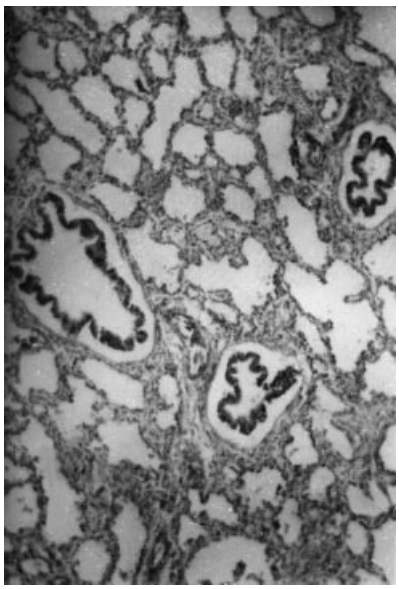

Fig. 6—Normal alveolar spaces and bronchioles which are compatible with gestational age with minimal expansion of alveoli (HE × 115)

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