

Nonvisualization of fetal gallbladder: a case report and review of the literature

Annamaria Giacobbe¹
 Elsa Giorgio¹
 Angela Dinatale¹
 Maria Antonietta De Oronzo²
 Irene Iozza³
 Giovanna Garofalo³
 Salvatore Politi⁴

¹Department of Obstetrics and Gynecology, G.Martino, Messina, Italy

²Campus Biomedico, Rome, Italy

³Bambino Hospital. Department of Microbiological and Gynecological Sciences. University of Catania, Italy

⁴Department of Gynaecology and Obstetrics Policlinico Universitario Gaspare Rodolico, Catania, Italy

Corresponding author:

Annamaria Giacobbe, MD
 Department of Obstetrics and Gynecology,
 G.Martino, Messina, Italy.
 Via Consolare Valeria, Messina, Italy
 Phone:+39 090 336988/3471973495
 E-mail:annamaria_8119@yaho. Com

Summary

Failure to visualize prenatally the gallbladder at ultrasound scan may indicate different fetal malformations with a highly variable prognosis, but also a simple anatomic variable. An adequate prenatal management could help in defining diagnosis and prognosis.

Key words: gallbladder, cystic fibrosis, ultrasound scan, prenatal diagnosis, karyotype.

Case report

A 32-years-old secondipara Caucasian woman was referred to Artemisia Fetal Maternal Medical Centre at 22 weeks of gestation because of nonvisualization of gallbladder at second-trimester US. Both parents were healthy and non-consanguineous. The previous pregnancy ended in spontaneous abortion (blighted ovum) at 10 weeks.

The current pregnancy was defined "regular". The first ultrasound scan, performed at 12 weeks of gestation, was normal and nuchal translucency measured 1.5 mm. The anomaly scan, performed at 20 weeks + 4 days was unremarkable excepting for gallbladder that was not visualized. A second scan, performed 1 week later, confirmed this finding and the patient was referred to our

centre. We saw the patient at 22 weeks + 0 days of gestation for the first time. Gallbladder was not visualized, no major malformation were seen but only a soft degree of gut hyperechogenicity was revealed. In genetic counseling, parents were informed about the possibility of additional examinations such as second-trimester genetic amniocentesis for fetal karyotyping, viral screening, screening for cystic fibrosis mutations and assay of amniotic fluid digestive enzymes. They decided to undergo them. Amniocentesis indicated a normal fetal karyotype (46,XY) and viral screening resulted negative. Screening for cystic fibrosis revealed the presence of two rare mutations, G542X and R1174, indicating cystic fibrosis. Levels of amniotic fluid digestive enzymes were below the first percentile, a profile compatible with this pathology. The parents decided to carry out the pregnancy.

Discussion

Gallbladder can be visible at prenatal ultrasound from 14th week of gestation as a pear-shaped structure with echogenic walls visualized in the right anterosuperior quadrant of the fetal abdomen and its description is mandatory as part of fetal morphological evaluation. Prenatal diagnosis of gallbladder's abnormalities is very difficult because of nonvisualization of fetal gallbladder is a rare event that occurs in 0,1% to 0,15% of pregnancies (1) and this is underlined by very few articles that have been reported in literature. When gallbladder is not visualized at ultrasound examination, it's necessary to confirm this finding by a second US scan, performed 7 to 15 days later. Differential diagnosis about nonvisualization of fetal gallbladder must take into consideration fetal diseases of highly variable prognosis such as biliary agenesis, biliary ducts atresia, cystic fibrosis but also it may consider the case of postnatal visualization in a child free of any disease (2). The gallbladder's anomalies could be either isolated, 12 to 28% of nonvisualization of fetal gallbladder, (3) or syndromic: cases in association with situs inversus, cardiac defects, hydronephrosis, renal agenesis, cerebral ventricular dilatation, intestinal malrotation are reported in literature. There are sporadic cases of associated chromosome aberrations in cases of absent gallbladder, particularly trisomies (17%) (1,4). Likewise in a recent case report Ochshorn confirmed the relationship between fetal gallbladder's anomalies and chromosome aberrations but he also reported a lower rate of association (2,8%) (5). Anywhere, etiology should be investigated because of association with various abnormalities and multiple malformations aggravates prognosis. However, an isolated non visualized gallbladder, does not exclude severe pathologies as biliary duct atresia and cystic fibrosis that usually no present specific sonographic signs.

Management depends on the presence of associated malformations evidenced by US scan, parental screening for cystic fibrosis, fetal karyotyping, and assays of amniotic fluid digestive enzymes. The assays of digestive enzymes in amniotic fluid (GGTP gamma-glutamyl-transpeptidase; LAP leucine-aminopeptidase) represents a precious aid and it is actually the only test that allows to point to a diagnosis. These digestive enzymes, synthesized by biliary epithelium and by enterocytes, are present in amniotic fluid from 12-13 weeks of gestation and gradually decreased to 24 weeks for the progressive maturation of anal membrane that became impermeable to digestive secretions. Every obstacle to intestinal transit impairs flow of digestive secretions to amniotic fluid. After 24 weeks of gestation these enzymes are present in amniotic fluid in low concentrations but it is very difficult to differentiate between abnormally low or physiologically low levels, although high values permits to excluding biliary atresia and cystic fibrosis. In particular, in biliary atresia amniotic levels of GGTP drop dramatically after 16 weeks of gestation (6) whereas in cystic fibrosis and intestinal atresia levels of all digestive enzymes fall sharply (3) Prenatal diagnosis of gallbladder's anomalies is very difficult because of their low incidence and because of amniotic fluid is rarely sampled to give information on digestive enzymes. In summary, nonvisualization of fetal gallbladder should be confirmed as soon as possible in order to perform an adequate management including serial ultrasound examinations and eventually amniocentesis for CFTR mutation screening, digestive enzymes assays and fetal karyotyping.

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Conflict of Interest Statement

The authors declare no conflict of interest.