Prenatal non-visualization of the gallbladder: a diagnostic and prognostic dilemma
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Objective
Non-visualization of the fetal gallbladder has been associated with benign conditions as isolated gallbladder agenesis or severe diseases such as aneuploidies, cystic fibrosis, or biliary atresia (BA). Differential diagnosis is crucial. Amniotic fluid digestive enzymes have been used to distinguish these entities before 22 weeks; but they were useless after this point. Recently GGTP fetal blood levels were reported as useful after 22 weeks. The aim of this study is to determine the contribution of fetal blood GGTP levels in case of non-visualization of the gallbladder past 22 weeks of gestation.

Methods
We described 2 cases in which the gallbladder could not be visualized in ultrasound scan (US) after 22 weeks of gestation.

Results
Case 1: Secundipara of 20+4w, with subcutaneous edema and pleural effusion. No abnormalities on chromosomal microarray-CGH analysis or cystic fibrosis gene mutations were detected. At 24+4w the gallbladder could not be visualized. Progressive hydrops deterioration was observed. MR at 32+2w confirmed non-visualization of gallbladder. BA was suspected and fetal blood sampling for GGTP assay was offered; the patient refused, and decided to terminate the pregnancy. Feticide was performed at 34+2w and fetal blood sample was obtained, GGTP was 573 U/L. Fetal necropsy confirmed BA. Case 2: 32 years old secundipara. At 22+6w and 24+0w US the gallbladder could not be visualized. Amniocentesis for fetal karyotype and prenatal testing for cystic fibrosis mutations was offered, but declined by the patient. MR imaging at 35+0 weeks failed also to visualize it, but no other anomalies were reported. A 2670gr male infant was born by cesarean section at 39+2w. Fetal cord blood sample was obtained, GGTP was 129 IU/L. Clinical and biochemical postnatal examinations were normal. US confirmed gallbladder agenesis with normal extra and intrahepatic bile ducts.

Conclusion
Cases of non-visualized gallbladder after 22 weeks have rarely been reported in literature. Until now, no standard management has been proposed. Our cases support the potential usefulness of fetal blood digestive enzymes.