Early Human Development 111 (2017) 16–19

Contents lists available at ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

Prenatal diagnosis of biliary atresia: A case series

O. Shen[a,*], H.Y. Sela[a], H. Nagar[b], R. Rabinowitz[a], E. Jacobovich[c], D. Chen[d], E. Granot[c,e]

[a] Department of Ob/Gyn, Shaare Zedek Medical Center, Jerusalem, Israel
[b] Department of Pediatric Surgery, Shaare Zedek Medical Center, Jerusalem, Israel
[c] Department of Pediatrics, Kaplan Medical Center, Rehovot, Israel
[d] Tel-Aviv Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel
[e] Department of Pediatrics, Shaare Zedek Medical Center, Jerusalem, Israel

ARTICLE INFO

Keywords:
Biliary atresia
Prenatal diagnosis
Ultrasound
Gallbladder
Triangular cord sign
Prenatal nonvisualization of the gallbladder
Amniotic fluid
Digestive enzymes
Biliary cystic malformation
Choledochal cyst

ABSTRACT

Background: Biliary atresia is a progressive disease presenting with jaundice, and is the most common indication for liver transplantation in the pediatric population. Prenatal series have yielded conflicting results concerning a possible association between BA and prenatal nonvisualization of the gallbladder.
Aims: This retrospective case series was performed to assess the association between biliary atresia, prenatal nonvisualization of the gallbladder and other sonographic signs.
Study design/subjects: We identified biliary atresia patients who underwent a Kasai procedure by a single pediatric surgeon and/or follow up by a single pediatric gastroenterologist. Axial plane images and/or video recordings were scrutinized for sonographic signs of biliary atresia on the second trimester anomaly scan.
Outcome measures: Proportion of biliary atresia cases with prenatal sonographic signs.
Results: Twenty five charts of children with biliary and high quality prenatal images were retrieved. 6/25 (24%) of cases analyzed had prenatal nonvisualization of the gallbladder or a small gallbladder on the prenatal scan. Two cases had biliary atresia splenic malformation syndrome. None of the cases had additional sonographic markers of biliary atresia.
Conclusions: Our study suggests that in addition to the well-established embryonic and cystic forms, an additional type can be suspected prenatally, which is characterized by prenatal nonvisualization of the gallbladder in the second trimester. This provides additional evidence that some cases of BA are of fetal rather than perinatal onset and may have important implications for prenatal diagnosis, for counseling and for research of the disease's etiology and pathophysiology.

1. Introduction

Biliary atresia (BA) is a severe condition, with an incidence of approximately 1:14,000–1:16,000 live births [1,2] frequently resulting in severe morbidity or death. It is the leading indication for liver transplantation in children [3,4]. Prenatal diagnosis is important, as it allows parents to make informed decisions concerning continuation of the pregnancy, as well as facilitating early neonatal diagnosis when pregnancy is continued. Signs of BA on prenatal ultrasound are largely unknown. The aim of this study was to identify possible signs of BA on prenatal ultrasonography. This is the first attempt to assess the presence of midtrimester sonographic markers, other than biliary cystic malformations, in a cohort of children with BA.

2. Patients and methods

This was a retrospective study of infants with biliary atresia. Patients entered into the study were either operated by one of the authors (HN) in the period between January 2004 and June 2014 at Tel Aviv medical center or at Shaare Zedek medical center Jerusalem, or had pediatric follow up by one of the authors (EG) during the same period. All patients underwent hepatoportoenterostomy (Kasai procedure). Some, subsequently, had liver transplantation.

Prenatal records were collected from the participating institutions' databases. Electronic images and video recordings were collected from the sonographers or from the patients. Postnatal charts and ultrasound reports were reviewed in all cases. Second trimester fetal anomaly scan reports and axial plane images/video recordings of the portal area were reviewed by two experienced sonographers (OS and RR), who were blinded to the reports. Cases lacking good quality prenatal electronic

* Corresponding author at: Dep't. Ob/Gyn, Shaare Zedek Medical Center, P.O. Box 3235, Jerusalem 91031, Israel.
E-mail address: orishen@netvision.net.il (O. Shen).

http://dx.doi.org/10.1016/j.earlhumdev.2017.05.005
Received 9 December 2016; Received in revised form 8 May 2017; Accepted 13 May 2017

images and/or video recordings were excluded.

The following parameters were recorded from the prenatal ultrasound reports and electronic media: presence, size and shape of the fetal gallbladder; gallbladder longitudinal and transverse diameter were measured if it appeared subjectively to be small; presence of triangular cord sign, a thickened *peri* portal echogenicity, as assessed subjectively; hepatic hyperechogenicity; existence of biliary cystic malformations (biliary cystic malformation); liver longitudinal length; presence of echogenic bowel (EB); existence of associated anomalies.

Institutional review board approval was obtained and oral consent given by the patients.

3. Results

We identified 53 cases of children with BA. Twenty eight cases were excluded from the study; 13 were excluded because prenatal anomaly scans were not performed, and in 15 cases the prenatal images were of insufficient quality to be reliably assessed. Twenty five cases had good quality electronic images and/or video recordings for review, and these constituted the study group. Within the study group there was complete agreement between the two reviewing sonographers concerning the presence or absence of potential signs of BA.

Median gestational age at prenatal sonography was 22 weeks (range 19–24).

6/25 (24%) cases had an absent or abnormal gallbladder. Five of these had PNVGB and one had an abnormally small gallbladder, < 2 standard deviations below the median longitudinal and transverse diameters [5]. In all but one of these cases (PNVGB) the report issued by the sonographer confirmed PNVGB. There were no cases with biliary cystic malformation, defined as a cyst in the portal region assessed as being part of the biliary system, and no cases of an abnormally thick wall of the left or right portal vein branch, representing a triangular cord sign [6]. All cases had normal liver echogenicity and length between the 5th and 95th percentile [7]. None had echogenic bowel (EB). Biliary atresia splenic malformation syndrome was present in 2/25 (8%) cases in the study group. One case with an absent gallbladder had polysplenia, centrally positioned liver, preduodenal portal vein, annular pancreas, gut malrotation, horseshoe kidney and interrupted inferior vena cava with azygous continuation. A second case with a normally appearing gallbladder had gut malrotation and interrupted inferior vena cava with azygous continuation. 3/28 (10.7%) of the excluded cases had biliary atresia splenic malformation (Fig. 1) bringing the total no. of cases with biliary atresia splenic malformation to 5/53 (9.4%).

In all 6 cases with prenatal absent/small gallbladder (Fig. 2), the gallbladder was not visualized on post-natal sonography. 10/19 (52.6%) of the cases with a normally visualized fetal gallbladder, had non visualization of the gallbladder on the postnatal sonogram, 5/19 (26.3%) had a small gallbladder and 4/19 (21.1%) had normal appearance and size of the gallbladder on postnatal sonography.

Mean age at surgery was 54 days (range 49–90) and 50 days (range 38–68) for infants with and without PNVGB respectively (p = 0.401).

In the excluded group a post-natal sonogram was not available in three cases, demonstrated a normally appearing gallbladder in 4/25 (16%) cases and was absent or of abnormal shape or size in 21/25 (84%) cases. Average age at surgery in the excluded group was 53 days (range 44–78).

After completing data collection, a case of PNVGB associated with presumably triangular cord sign (Fig. 3) was observed outside the participating centers (courtesy CG). The postnatal diagnosis was isolated gallbladder agenesis.

4. Discussion

There are few reports of prenatal diagnosis of BA [8]. Most cases are diagnosed post-natally following the appearance of jaundice or acholic

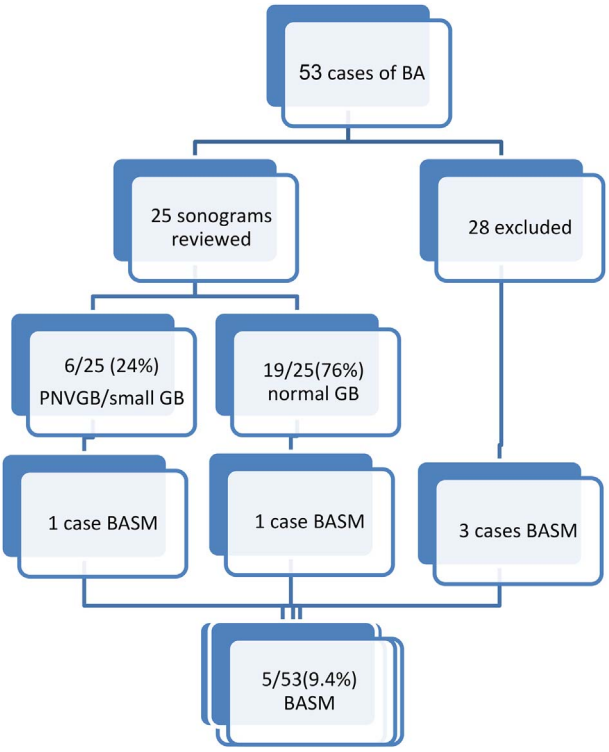

Fig. 1. Features of BA cases
BA, biliary atresia; PNVGB, prenatal nonvisualization of gallbladder; BASM (biliary atresia splenic malformation).

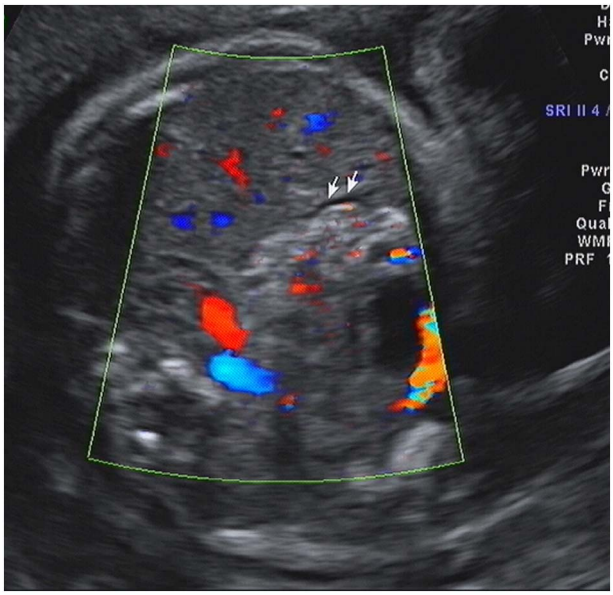

Fig. 2. Abnormally small gallbladder in case of BA at mid trimester. Arrow pointing to gallbladder.

stools. The purpose of this study was to assess whether established postnatal sonographic signs are present on prenatal scans of infants with BA.

Specific postnatal sonographic signs of BA include a small or absent gallbladder and triangular cord sign [9–13]. Triangular cord sign [6], present in most infants with BA is the sonographic depiction of a fibrous thickening in the peri-portal area. An abnormal triangular or cone shaped echogenicity is depicted as an abnormally thick (> 4 mm) echogenic anterior wall of the right portal vein. It is a specific sign, and present in 73%–85% of infants [9–12]. Although not used by all