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MATERNAL-FETAL MEDICINE

Prenatal ultrasound diagnosis of duplication gallbladder: a multicenter study

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Abstract

Background Gallbladder duplication is a rare anatomic anomaly characterized by the presence of an accessory gallbladder.
Objective To appraise the prevalence and significance of prenatal diagnosis of duplication of gallbladder in a multicenter study.
Methods This was a multicenter case series with literature review. Clinical records of all consecutive pregnant women with a prenatal diagnosis of duplication of gallbladder, who were referred to our Centers were included in this study. The diagnosis of duplication of gallbladder was based on the evidence of double gallbladder in the standard abdominal circumference plane using grey scale. Postnatal magnetic resonance cholangiopancreatography (MRCP) 3D and postnatal neonatal abdominal ultrasound scan were offered soon after birth to confirm the diagnosis of double gallbladder. The systematic review was conducted using electronic databases from inception of each database through December 2019.
Results Five studies, including a total of seven cases, were identified as relevant and included in the systematic review. Gestational age at diagnosis ranged from 20 to 32 weeks of gestation. Associated findings were reported in only one case, where the fetus presented with a left-sided gallbladder, and bilateral renal agenesis with Potter sequence. None of the included cases reported abnormal karyotype. Our cases series included nine cases (0.03%) of double gallbladder with postnatal confirmation, with an overall incidence of this anomaly of 0.03%.Associated findings were reported in only two cases, one with IUGR and omphalocele, that opted for I-TOP, and one with single umbilical artery. Except for the I-TOP, neonatal outcome was favorable in all cases.
Conclusions Duplication of the gallbladder is a very rare malformation with only seven cases reported in the literature diagnosed prenatally. This anomaly is not associated with abnormal karyotype, and the neonatal outcome is favorable if there are no other associated abnormalities.

Keywords Malformation · Neonatal intensive care unit · Abortion · Genetic · Gallbladder

Introduction

Gallbladder duplication is a rare anatomic anomaly characterized by the presence of an accessory gallbladder, with an incidence reported in literature of about 1:3800 [1–4].

It is usually diagnosed accidentally later in life, with only few cases of in utero prenatal diagnosis reported so far. At prenatally ultrasound scan gallbladder duplication can be observed as two fluid-containing cystic structures in the right upper quadrant of the fetal abdomen laying on the same plane [5]. Differential diagnosis includes folds, septum, and diverticulum of the gallbladder, hepatic or mesenteric cysts, persistence of a right umbilical vein, and lymphangioma of the abdomen [5–7].

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Objective

The aim of this study was to appraise the prevalence and significance of prenatal diagnosis of duplication of gallbladder in a retrospective multicenter study.

Material and methods

Literature review

The search for the systematic review was conducted using MEDLINE, EMBASE, Scopus, ClinicalTrials.gov, OVID and Cochrane Library as electronic databases. The citations were identified with the use of a combination of the following text words: "double gallbladder," "duplication of gallbladder" "congenital anomalies of gallbladder," from inception of each database through December 2019. Review of articles also included the abstracts of all references retrieved from the search. No restrictions for language or geographic location were applied.

Case series

This was a multicenter retrospective case series. Clinical records of all consecutive pregnant women with a prenatal diagnosis of duplication of gallbladder, who were referred to our Centers (DiagnosticaEcografica e Prenatale di A. DiMeglio, Naples, Italy; University of Naples Federico II, Naples, Italy), were included in this study. The inclusion criteria were pregnant women with gestational age greater than 13 weeks of gestation.

The diagnosis of duplication of gallbladder was based on the evidence of double gallbladder in the standard abdominal circumference plane using grey scale (Fig. 1). The gallbladder duplication was defined by the presence of two saccular/tubular fluid-full structures oriented in the same plane in the right upper lobe without any color flow on Doppler. In all cases of double gallbladder, a detailed fetal anatomy scan was performed, and a postnatal neonatal abdominal ultrasound scan was offered to confirm the diagnosis of double gallbladder and exclude choledochal cysts. Postnatal magnetic resonance cholangiopancreatography (MRCP) 3D was also offered to confirm the type of the gallbladder duplication. The primary outcome of the study was the incidence of double gallbladder in our cohort. The secondary outcomes were the rate of associated malformations.

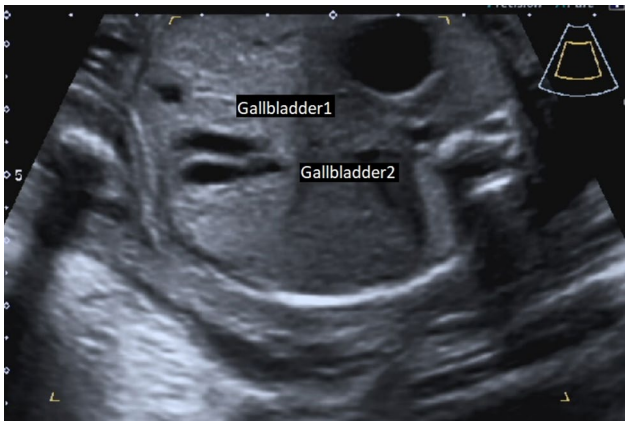

Fig. 1 Sonographic appearance of fetal gallbladder duplication: two adjacent fluid-filled structures in the gallbladder fossa (case 4)

Results

Literature review

Five studies [1, 5, 8–10], including a total of seven cases, were identified as relevant and included in the systematic review (Table 1). Three studies were case reports [5, 9, 10], and the other two studies [1, 8] included two cases each.

Gestational age at diagnosis ranged from 20 to 32 weeks of gestation (Table 2). Associated findings were reported in only two cases. In one case of Kinoshita et al. [8] the fetus was diagnosed with mild intrauterine growth restriction (IUGR). In one case of Bronshtein et al. [1] the fetus presented with a left-sided gallbladder, and bilateral renal agenesis with Potter sequence. None of the included cases reported abnormal karyotype.

In all the cases, except the one of the left-sided gallbladder, the double gallbladder was described as the presence of two saccular\tubular fluid-full structures oriented in the same plane in the right upper lobe without any color flow on Doppler. Only in one case of Kinoshita et al. [8] the authors reported the evidence of two cystic ducts. In the other cases, assessing the cystic duct was not feasible.

Out of the seven included case, six women delivered a live baby, while the one with bilateral renal genesis decided for induced termination of pregnancy (I-TOP). Out of the six women who delivered a live baby, only one experienced cesarean delivery.

The diagnosis was confirmed postnatally by ultrasound in four cases, while in two cases also a MRCP was performed. The abortion had the confirmed diagnosis by autopsy.

Table 1 Studies included in the systematic review

	Study location	Maternal age (years)	GA at diagnosis (weeks)	Ultrasound characteristics of gallbladder	Associated abnormalities	Timing of delivery	Neonatal outcome	Postnatal confirmation
Bronshtein [1] Case 1	Israel	Not reported	20	Left sided and separated	Bilateral renal agenesis, Potter sequence	I-TOP at 22 weeks	–	By autopsy
Bronshtein [1] Case 2	Israel	Not reported	29	Bilobate, septate gallbladder in the right upper lobe	None	At 40 weeks	Regular	Not reported
Kinoshita [8] Case 1	USA	33	30	Two saccular fluid contains structures in the right upper lobe with 2 separate cystic ducts	Mild IUGR	Scheduled cesarean delivery at 36 2/7 weeks	Regular	By postnatal ultrasound, as two partially separate cystic duct
Kinoshita [8] Case 2	USA	Not reported	32	Two saccular fluid contains structures oriented in the same plane in the right upper lobe	None	At 40 weeks	Regular	By postnatal ultrasound
Sifakis [5]	Greece	26	32	Two saccular fluid contains structures in the right upper lobe	None	At 38 weeks	Regular	By postnatal ultrasound
Gerscovich [9]	USA	29	20	Two parallel tubular fluid contains structures in the right upper lobe	None	At 40 weeks	Regular	By postnatal ultrasound and by postnatal RMCP, as two separate cystic ducts joining a common bile duct
Maggi [10]	Italy	38	21	Double gallbladder	None	At 40 weeks	Regular	By postnatal ultrasound and by postnatal RMCP, as type 2 H duplicated gallbladder

GA gestational age, *I-TOP* induced termination of pregnancy, *IUGR* intrauterine growth restriction, *RMCP* magnetic resonance cholangiopancreatography

Table 2 Cases included in the case series

	Maternal age (years)	GA at diagnosis (weeks)	Characteristics of gallbladder	Abnormal karyotype	Associated abnormalities	Timing of delivery	Neonatal outcome	Postnatal confirmation
Case 1[a]	24	19	Two saccular fluid contains structures in the right upper lobe	No	None	At 41 weeks	Regular	By postnatal ultrasound
Case 2[a]	28	21	Two saccular fluid contains structures in the right upper lobe	No	None	At 40 weeks	Regular	By postnatal ultrasound and by postnatal RMCP, as type 2 H duplicated gallbladder
Case 3[b]	27	16	Two saccular fluid contains structures in the right upper lobe	No	IUGR, omphalocele	I-TOP at 20 weeks	–	By autopsy
Case 4[a]	31	15	Two saccular fluid contains structures in the right upper lobe	No	None	Scheduled cesarean delivery at 394/7 weeks	Regular	By postnatal ultrasound
Case 5[b]	30	33	Two saccular fluid contains structures in the right upper lobe	No	None	Scheduled cesarean delivery at 35 0/7 weeks	Regular	By postnatal ultrasound and by postnatal RMCP, as type 2 H duplicated gallbladder
Case 6[b]	29	19	Two saccular fluid contains structures in the right upper lobe	No	None	At 35 weeks	Regular	By postnatal ultrasound
Case 7[b]	38	15	Two saccular fluid contains structures in the right upper lobe	No	None	At 37 weeks	Regular	By postnatal ultrasound
Case 8[b]	39	26	Two saccular fluid contains structures in the right upper lobe	No	Single umbilical artery	Emergency cesarean delivery at 34 0/4 weeks	Regular	By postnatal ultrasound
Case 9[b]	19	20	Two saccular fluid contains structures in the right upper lobe	No	None	At 40 weeks	Regular	By postnatal ultrasound

GA gestational age, *I-TOP* induced termination of pregnancy, *IUGR* intrauterine growth restriction, *RMCP* magnetic resonance cholangiopancreatography

[a]Cases at University of Naples Federico II

[b]Cases at Diagnosi Ecografica e Prenatale di A. Di Meglio

Case series

From January 2010 to January 2019, out of the 31,539 ultrasound scans performed, nine cases (0.03%) of double gallbladder with postnatal confirmation were identified.

Gestational age at diagnosis ranged from 15 to 33 weeks, with the vast majority diagnosed at the time of the routine anatomy scan. Associated findings were reported in only two cases (2/8, 25%), one with IUGR and omphalocele, that opted for I-TOP, and one with single umbilical artery. Except for the I-TOP, neonatal outcome was favorable in all cases. None of the included cases reported abnormal karyotype at amniocentesis. All cases were confirmed postnatally with ultrasound (Fig. 2).

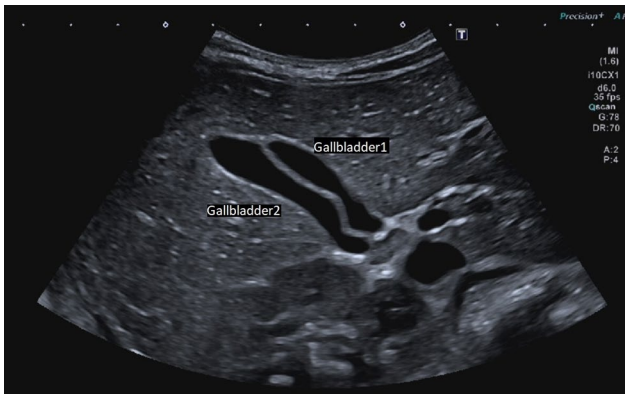

Fig. 2 Postnatal ultrasound confirmation of double gallbladder at 21 months of age (case 9)

Discussion

Main findings

In our cohort the prevalence of double gallbladder was 0.03%. In the vast majority of the cases double gallbladder was not associated with other major or minor abnormalities and was an isolated finding. Associated minor or major malformations were presented in the 25% of the cases. Double gallbladder was associated with chromosomal abnormalities in no cases.

The literature review revealed only seven cases of prenatal diagnosis of double gallbladder. The cases were not associated with abnormal karyotype, and only was case was associated with other major malformations. This anomaly was not associated with an increased risk of cesarean delivery.

Implication

Congenital anomalies of the gallbladder are rare and can be accompanied by other malformations of the biliary or vascular tree [11, 12]. They are usually diagnosed accidentally later in life, e.g. during routine preoperative studies or as unusual surprise during laparoscopic surgery [13]. Congenital anomalies of the gallbladder and anatomical variations of their position are associated with an increased risk of complications after laparoscopic cholecystectomy [14–23]. These malformations could also be associated with the development of cholelithiasis, due to inadequate bile drainage.

Gallbladder duplication is one of the possible malformations of the gallbladder. According to Boydens and Harafitis classification, there are two main types of duplication of the gallbladder. The first is the bilobed gallbladder, where a longitudinal septum or invaginating cleft separates the lumen into two chambers. The second is the double gallbladder with two separate gallbladders with their own cystic ducts.

The development of the gallbladder starts between 4 and 5th weeks of gestation, the gallbladder and the cystic duct developed form the gallbladder primodium that budded off from the bile duct. The bile duct developed form a group of cells between the liver bud and the proliferating foregut around the fourth weeks of gestation [3, 25]. The fetal gallbladder has been described as an anechoic, elliptical/tubular/saccular structure laying laterally right of the intrahepatic umbilical vein in the right upper abdomen. Visualization of the gallbladder was described possible starting from the 12 weeks of gestation. Between 16 and 34 weeks of gestation the visualization of the gallbladder could be achieved in more than 90% of the fetus [24, 25].

The diagnosis of double gallbladder during the routine anatomy scan is possible and quite easy, however a postnatal confirmation is highly recommended. In the vast majority of the cases reported in the literature postnatal confirmation were made by ultrasound, with only few cases that required MRCP. At the time of prenatal scan, the fetal gall bladder duplication can be seen as two anechoic structures laying on the same plane laterally right of the intrahepatic umbilical vein in the right upper abdomen. According to our study, this anomaly is not associated with increased risk of fetal or pregnancy complications.

Conclusion

In summary, duplication of the gallbladder is a very rare malformation. This anomaly is not associated with abnormal karyotype, and the neonatal outcome is favorable if there are no other associated abnormalities.

Author contributions LDM: study conception, study design, study methods, data analysis, manuscript preparation, methods supervision. PT: study conception, study design, study methods, data analysis, manuscript preparation, methods supervision. GS: study conception, study design, study methods, data analysis, data collection, manuscript preparation, whole study supervision. LeDM: study conception, study design, data collection, data analysis. LM: study conception, study design, data collection, data analysis. FZ: study conception, data analysis, manuscript preparation, whole study supervision. AR: study design, study methods, manuscript preparation, whole study supervision. AT: study design, study methods, manuscript preparation, whole study supervision. ML: study conception, study design, data analysis, methods supervision, whole study supervision. ADM: study conception, study design, data analysis, methods supervision, whole study supervision.

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Compliance with ethical standards

Conflict of interest The authors report no conflict of interest.

Ethical approval Given the study design (case series with literature review), authors considered ethical approval not necessary.

Informed consent All patients provided a written consent for data publication.

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