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Review Article

Prenatal diagnosis of abdominal lymphatic malformations

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ABSTRACT

Abdominal lymphatic malformations (LM) are rare congenital malformations of the lymphatic system, representing only 2% of all LM in newborns. They may arise from intra-abdominal solid organs (such as the liver, pancreas, kidneys, spleen, adrenal glands, and gastrointestinal tract), mesentery, omentum, and retroperitoneum. Mesenteric LM are the most commonly seen, with retroperitoneal LM being the second most common. Fetal abdominal LM could be associated with karyotypic or other abnormalities, including skin edema, hydrops fetalis, and polyhydramnios, and prenatal diagnosis and perinatal counseling for these LM are important. Prenatal ultrasound (US) and magnetic resonance imaging (MRI) have led to an increased diagnosis of abdominal LM and improved monitoring and intervention postnatally. This article provides an overview of fetal abdominal LM, including the prenatal diagnoses, differential diagnoses, comprehensive illustrations of the imaging findings, treatments, and fetal outcomes.

Introduction

Lymphatic malformations (LM) can occur in a variety of anatomical locations. They are most commonly seen in the nuchal area (75%), followed by the axillary region (20%); in 5% of the patients, LM may be detected in other locations of the body, such as the mediastinum, intra-abdominal organs, retroperitoneum, limbs, and bones [1–9]. They can be detected prenatally in the first trimester of pregnancy [1,2,10–14], and nuchal LM are frequently (50–80% of cases) associated with karyotypic abnormalities and various malformation syndromes causing a poor fetal outcome, such as Turner syndrome, Down syndrome, Noonan syndrome, hydrops fetalis, chromosomal aneuploidy, other trisomies, fetal alcohol syndrome, and even intrauterine fetal demise [1,2,9,11,15,16]. In contrast to the fetal neck LM, lesions in other locations carry a more variable prognosis depending on their growth rate and infiltration of the surrounding organs or tissue. Because of the paucity of available data, karyotype evaluation of the parents of an affected fetus is still recommended [1,9,15–22]. Ultrasound (US) is the primary imaging modality used for the prenatal evaluation of LM [9,16,22,23]. Magnetic resonance imaging (MRI) is necessary when these cystic lesions are equivocal or inconclusive on US findings because MRI images the fetus in a large field of view with excellent tissue contrast and provides the exact delineation, detection of associated and/or concomitant pathologies, and differential diagnoses among other cystic pathologies [24,25]. In summary, fetal abdominal LM have the same US and MRI

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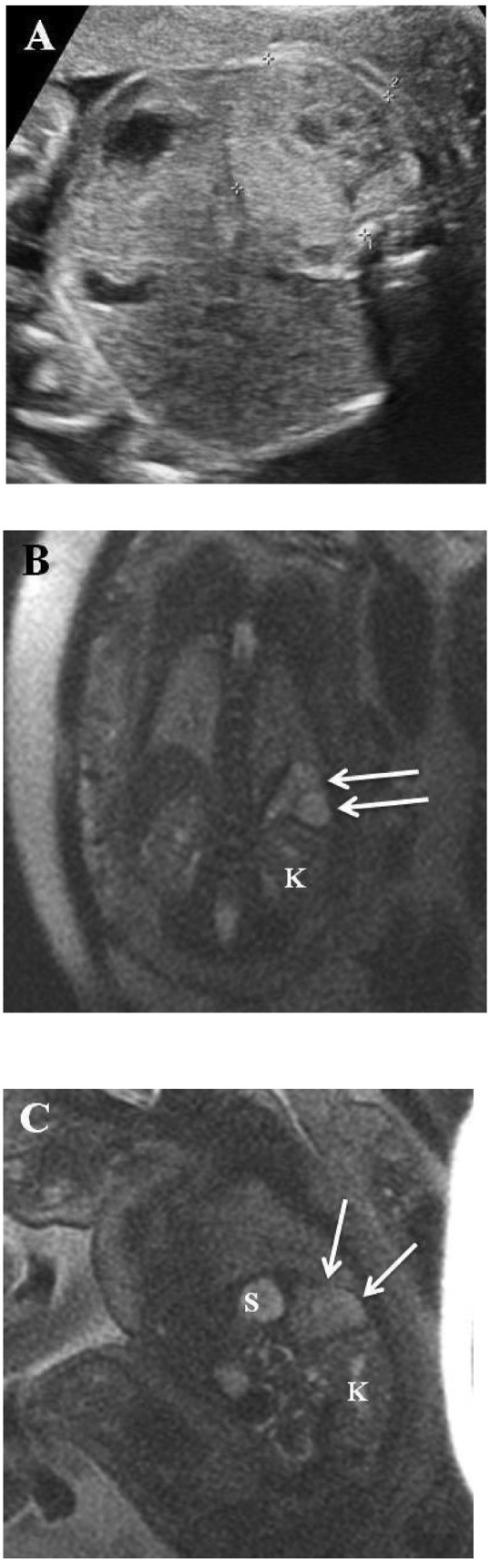

Fig. 1. Retroperitoneal LM of case 1. (A) Transverse US at 25 weeks' gestation demonstrates LM with cystic and solid components. (B) Coronal and (C) sagittal MRIs at 26 weeks' gestation show a heterogeneously hyperintense LM over the left adrenal region (arrows). K: left kidney; S: stomach.

features; both US and MRI can detect the exact cystic components, US can monitor the growth profiles conveniently and MRI can evaluate the extent of the lesions and their relation to adjacent structures [3,21–23,26–28] (Figs. 1–2, cases 1 and 2).

Abdominal LM on US and MRI

Abdominal LM can be detected prenatally in the first trimester of pregnancy. Oliver et al. [22] observed a higher frequency of intra-abdominal/retroperitoneal lesions than previously reported frequency, of approximately 6.8% in their respective series, and provided a new US classification system, which may help guide physicians with respect to the treatment and prediction of the postnatal treatment outcomes. The system categorizes all LM by cyst size and conveys the overall internal architecture and complexity of the lesion. Type I lesions (multiseptate lesions with multiple thin and/or thick internal septations) are of intermediate complexity, type II (predominantly cystic with no more than three septations) and III lesions (purely cystic) are the simplest type; and type IV lesions (mixed cystic and solid with at least a 30% solid component) are the most complex. The majority of cases (type I and II; approximately 80%) showed the classic appearance of LM; however, the remaining 20% of the cases (type III and IV) did not show these classic features, making accurate diagnoses challenging. For example, the purely cystic type III LM may mimic pleural effusions, localized ascites, or abnormal dilated colon segments. Type IV LM presenting as cystic and solid lesions with areas of internal vascularity and punctate echogenic foci (pathologically proven internal dystrophic calcifications) can be incorrectly diagnosed as teratomas [22]. There was no evidence of blood flow in the wall of the cysts; however, areas of internal flow were found in the atypical mixed cystic and solid (type IV) lesions [22,23]. The absence of solid components, calcifications, and internal vascularity has been suggested to help distinguish LM from other congenital lesions such as teratoma [22,42]. However, these findings may not be as reliable as previously reported.

Up to the present time, at least 34 cases of fetal abdominal LM have been reported in the English literatures (Table 1). They essentially have the same imaging features in both prenatal [21–23,27–41] and postnatal [3–6] US and MRI. Both US and MRI can convey the overall internal architecture and complexity of the lesions [22,26,27]. Among these, 10 cases underwent prenatal MRI evaluation in addition to US. The location was classified as retroperitoneum (47.1%, 16/34 cases), mesentery (23.5%, 8/34 cases), omentum (2.9%, 1/34 case), colon (2.9%, 1/34 case), and intra-abdomen locations (23.5%, 8/34 cases). The US and/or MRI texture of the solitary LM was 29.4% (10/34) multiseptate/cystic (type I); 23.5% (8/34) predominantly cystic with only a few septations (type II), 14.7% (5/34) purely cystic (type III), 8.8% (3/34) mixed with cystic and solid components (type IV), and 23.5% (8/34) without the aforementioned types. More than half of the fetal abdominal LM have the classic appearance (type I and II), and retroperitoneal LM are most commonly seen than mesenteric LM. No definite fetal chromosome or structural abnormality was found in the above collected cases, although 16 cases without mention. Notably, in five cases, pregnancy termination was performed due to the rapid growth of the tumor and expectation of a poor prognosis.

US can monitor the growth profiles of fetal abdominal LM conveniently. Peranteau et al. [26] reported that LMs have variable prenatal growth profiles in their serial US measurements between 19 and 39 weeks of gestation. The lesion volume ratio increased in 53%, decreased in 23%, and remained stable in 23% of fetuses from the initial to the final US. Unlike abdominal or other site LM, which demonstrated both positive and negative growth profiles, the axillary lesions only revealed increased growth until the end of

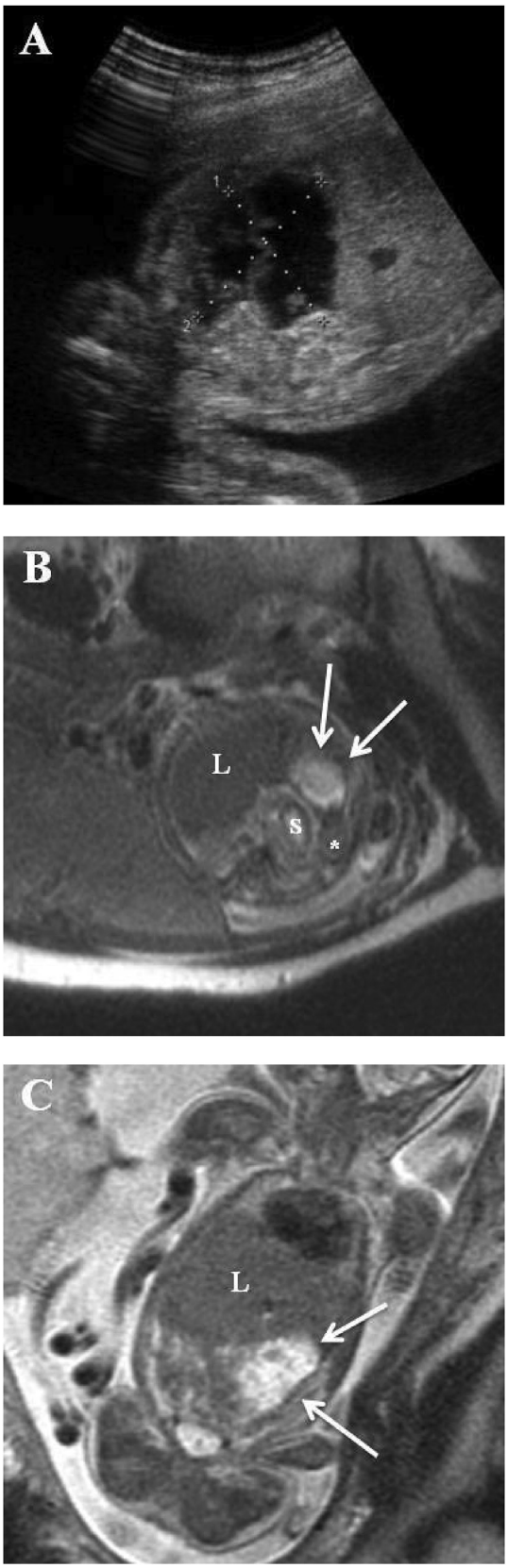

Fig. 2. Mesenteric LM of case 2. (A) US at 24 weeks' gestation demonstrates cystic LM with internal septations. (B) Axial and (C) coronal MRIs at 24 weeks' gestation show a heterogeneously hyperintense LM over the left upper abdomen (arrows). L: liver; S: stomach. *: spleen.

gestation. Thus, the location can influence the growth profile of LM; the significance of lesion growth is also dependent on the location, which is important to be noted during prenatal counseling.

MRI can also monitor the growth profiles of abdominal LM, but inconveniently and cost-expensively [27]. Coronal MRI can evaluate the extent of the lesions and their relation to adjacent structures; thick-slab T2 MRI has the capacity to provide additional information on cystic lesions on global overview [19,21,27,28].

Postnatally, US and MRI of abdominal LM are usually classified as microcystic (echogenic and predominantly solid lesions), macrocystic (multiple loculated, anechoic cysts with thin septations), and mixed type. Occasionally, the cyst may be complicated due to blood, pus, or chyle components, causing different internal echoes and representing fluid–fluid levels. Pure macrocystic lesions are avascular; however, Doppler US can reveal the fine veins and arteries in the capsule and fibrous septations [3–6]. MRI has the same imaging appearance as US. The appearance of MRI T1-and T2-weighted images can be quite heterogeneous owing to the variable contents. The presence of chyle, pus, internal blood products, or fluid–fluid levels are helpful in making the diagnosis of abdominal LM [3]. In the mesenteric LM with chylous contents, signal dropout on fat-saturated and chemical shift artifacts may be presented on opposed-phase MRI [3].

Differential diagnosis

Prenatal differential diagnoses of abdominal LM are varied. The differential diagnosis can be based on the origin and incidence of cystic lesions, including genitourinary origin (simple renal cyst, multicystic dysplastic kidney, hydronephrosis, ovarian cyst, ureterocele, and hydrocolpos), gastrointestinal origin (choledochal cyst, mesenteric or omental cyst, enteric duplication cyst, meconium peritonitis), retroperitoneal cystic teratoma or fetus in fetu, and isolated ascites [3,7,22,23,28,43].

Simple renal cyst, multicystic dysplastic kidney, and hydronephrosis

The renal origin of a simple renal cyst, multicystic dysplastic kidney, and hydronephrosis can be determined by their location over the renal fossa close to the fetal vertebral column. A simple renal cyst is a solitary unilocular cyst within the renal parenchyma without communication with the renal pelvis, and the renal architecture is grossly preserved. Multicystic dysplastic kidneys show multiple non-communicating cysts that replace the normal renal parenchyma and grossly distort the reniform shape. In hydronephrosis, the communication between the dilated renal calices and pelvis can be clearly demonstrated, and the surrounding renal parenchyma may be normal and hyperechogenic in the US or complicated with obstructive cystic dysplasia. The majority of cases are mild and will spontaneously resolve in the antenatal or postnatal period.

Ovarian cyst

Ovarian cysts are the most common abdominal cysts observed in the female fetus, typically with anechoic thin-walled cysts and daughter cyst signs, located superior and parasagittal to the urinary bladder. They could be simple or complicated, unilateral or bilateral, and may mimic as a solid mass when complicated with hemorrhage or torsion. Complicated cysts may reveal multiple septations, fluid–fluid levels, or mobile internal echoes.

Table 1
US and/or MRI findings in previous reported cases of fetal abdominal LM.

Authors [Reference]	Location	US findings (GW)	MRI findings (GW)	Classification	Chromosome/ structural abnormality	Perinatal outcome
Ho et al. [1]	Retroperitoneum	Multilocular and hypoechogenic cyst with no blood flow (30)	*	I	–/*	Postoperative recovery was uneventful and discharged 2 weeks later in good condition, although 1 month after, a lymphangioma of the head was found.
Rha et al. [2]	Retroperitoneum	Multiseptated cystic mass at the right side of the abdomen, extending to the right buttock and lower extremity with no blood flow (26)	Large intra-abdominal high-signal-intensity mass with multiple internal locules, displacing the right kidney (26)	I	–/–	Proven by autopsy.
Cozzi et al. [15]	Sigmoid colon	A large anechoic intra-abdominal mass mimicking an isolated ascites (26)	An intra-abdominal circumscribed high signal fluid collection as the amniotic fluid with no septa, compressing the bowel loops to the right side of the abdomen (27)	III	*/*	Postoperative recovery was uneventful. At 24 months' follow-up, the infant was thriving well and remains recurrence-free.
Breysem et al. [21]	Retroperitoneum	Septated cystic lesion in right upper quadrant: origin? (39)	Septated cystic mass surrounding the right kidney (39)	II	*/*	Conservative treatment
Oliver et al. [22]						
Case 1	Intra-abdomen	Purely cystic intra-abdominal LM with no internal septation (*)	*	III	*/*	*
Case 2-5	Intra-abdomen/ pelvis	*	*	*	*/*	*
Li et al. [23]						
Case 1-2	Mesentery	Suspicion of LM (mean, 25)	*	II and III	–/–	*
Case 3-5	Retroperitoneum	Suspicion of LM (mean, 25)	*	One type II and two type III	–/–	*
Peranteau et al. [26]						
Case 1-3	Intra-abdomen	Intra-abdominal LM (27.4 ± 3.6)	*	*	*/*	*
Koelblinger et al. [27]						
Case 1	Retroperitoneum	*	Solid and septated cystic lesions (18)	IV	*/*	*
Case 2	Retroperitoneum	*	Well-defined, septated cystic lesions; 2–5 cysts (24)	II	*/*	*
Flanagan et al. [28]						
Case 1	Retroperitoneum	Hypoechoic cystic lesion with internal septations (22)	A high T2-signal infiltrated mass (22)	II	*/*	Treated by a series of sclerotherapy interventions.
Case 2	Retroperitoneum	Hypoechoic mass with internal septations (31)	A high T2 signal mass infiltrated between the retroperitoneal structures without invading them (31)	II	*/*	Treated by a series of sclerotherapy interventions.
Devesa et al. [29]	Mesentery	An anechogenic lesion behind the abdominal wall with fine septations in the prevesical space (24)	*	II	*/*	Postoperative recovery was uneventful and asymptomatic without evidence of recurrence at 18 months old.
Chew et al. [30]	Mesentery	*	Possible free-fluid within the abdomen and no evidence of bowel obstruction or perforation (*)	I	*/*	Underwent a laparotomy and histopathology confirmed the diagnosis of mesenteric lymphangioma.
Mostofian et al. [31]	Mesentery	Multiloculated cystic mass in the lower portion of the fetal abdomen that crossed the midline (25)	*	I	*/*	Postoperative recovery was uneventful and serial US 2 years after surgery showed no residual or recurrent tumor.
Malpas et al. [32]	Mesentery	Abdominal distension, ascites and an echogenic mass containing dilated loops of bowel (18)	*	*	–/–	The postoperative course was complicated by reaccumulation of chylous ascites and further apparent growth of lymphangioma tissue. Malrotation was identified at laparotomy when the infant was 13 months. Subsequently, a Ladd's procedure was performed.
	Mesentery		*	I	–/–	

Table 1 (*continued*)

Authors [Reference]	Location	US findings (GW)	MRI findings (GW)	Classification	Chromosome/ structural abnormality	Perinatal outcome
Kozlowski et al. [33]		Multiloculated mass arising from the left pelvis to the left leg (19)				Mesenteric LM confirmed by autopsy.
Groves et al. [34]	Mesentery	Multiple septate cystic abdominal lesion (19)	*	I	−/−	Postoperative recovery was uneventful and the US examination 4 weeks and 5 months postoperatively were normal.
Signorelli et al. [35]	Greater omentum	A hyperechoic mass with heterogeneous tubular structures was detected on the posterior aspect of the abdominal cavity (21)	*	I	*/*	Postoperative recovery was uneventful and the infant was 4 months old and completely asymptomatic at present.
Kaminopetros et al. [36]	Retroperitoneum	A septated cystic mass behind and lateral to the right kidney (28)	Lesion with high signal on T2 weighting and extended into the posterior buttock and thigh (29)	II	−/−	Termination of pregnancy because of the rapid growth of the tumor and anticipation of a poor outcome.
Giacalone et al. [37]	Retroperitoneum	A large heterogenous cystic and solid multiloculated mass within the lower side of the posterior abdominal wall and extended to the right lumbar region (27)	*	IV	−/−	Cavernous hemangiolymphangioma proven by autopsy.
Hachisuga et al. [38]	Retroperitoneum	Thin-walled, multiseptate hypoechogenic masses over the retroperitoneum (27)	Heterogeneous mass with high signal intensity over the left retroperitoneum (38)	I	−/−	At the time of this report, the infant was over 4 months old and doing well and had not experienced any complications. The size of the mass was unchanged.
Malnofski et al. [39]	Retroperitoneum	A cystic septated mass in the left lower quadrant of abdomen displacing the bladder to the right (36.5)	*	I	−/−	Underwent a laparotomy and histopathology confirmed the diagnosis was retroperitoneal LM.
York et al. [40]	Retroperitoneum	Large multicystic abdomino-pelvic mass and the mass was primarily cystic, with solid components in the cyst walls (27)	*	IV	*/*	Postoperative recovery was uneventful with no progression of the residual mass.
Deshpande et al. [41]	Retroperitoneum	Multicystic and multiseptate hypoechogenic lesions over the left-sided retroperitoneal abdomino-pelvic region causing anterior displacement of the ipsilateral kidney (20)	*	I	−/−	Termination of pregnancy because of the rapid growth of the tumor.

LM: Lymphatic malformations.
GW: Gestational age.
US: Ultrasound.
MRI: Magnetic resonance imaging.
Classification: type I-IV [22].
*: Not available.
−: Negative finding.

Ureterocele

Ureterocele is a thin-walled cystic lesion in the pelvic cavity abutting the urinary bladder. It represents as the “bladder in bladder” sign and is usually associated with hydroureter. Visualization of the cystic lesion with a direct extension to the ureter confirms the diagnosis.

Hydrocolpos

Hydrocolpos is a fluid-filled midline pelvic mass posterior to the urinary bladder due to vaginal dilatation caused by an outlet obstruction. If both the uterus and vagina are dilated, the condition is called hydrometrocolpos.

Choledochal cyst

Choledochal cysts are rare congenital cystic dilations of the bile duct presenting as unilocular cysts with communication to the bile ducts and located in the right upper abdomen. The cysts observed with direct communication with the gallbladder or cystic duct are also more suggestive of choledochal cysts, especially in the thick-slab T2-MRI. Choledochal cysts appeared to enlarge during

pregnancy, which would aid the diagnosis of choledochal cysts over biliary atresia.

Mesenteric or omental cyst

Mesenteric or omental cysts are benign abdominal cysts with an unknown etiology. The fluid contents may be serous, chylous, or hemorrhagic. Prenatal diagnosis is suggested by the findings of a multiseptate or unilocular, usually mid-line, cystic lesion of variable size, and with solid appearance if complicated by hemorrhage.

Enteric duplication cyst

Enteric duplication cysts are thick-walled cysts of the gastrointestinal tract that commonly involve the small bowel, particularly the ileum. US can demonstrate the gut signature sign, represented as layered rings of varying echogenicity that are formed by an outer muscularis propria and an inner mucosa-submucosa.

Meconium peritonitis

Meconium peritonitis occurs as a result of intrauterine bowel perforation, causing meconium to escape into the surrounding space, leading to peritonitis. US shows irregular thick-walled cysts over the peritoneal cavity and liver surface. Intraperitoneal calcifications are observed in 85% of the cases and ascites is often seen due to inflammation.

Retroperitoneal cystic teratoma or fetus in fetu

The occurrence of retroperitoneal teratoma or fetus in fetu is rare, and the presence of an axial skeleton suggests the diagnosis of fetus in fetu. US demonstrates a well-defined complex mass with internal calcifications and mixed fluid and solid components. Visualization of vertebral bodies within the mass is diagnostic and helps distinguish the fetus in fetu from teratoma. MRI can be used to better evaluate the origin of the mass, and color Doppler US may be helpful in differentiating a hypovascular fetus in fetu from neoplasms.

Isolated ascites

Isolated ascites refers to an abnormal fluid collection in the fetal peritoneal cavity. The etiology could be associated with immune and non-immune hydrops fetalis, chromosomal abnormality, gastrointestinal perforation, intrauterine infections, genitourinary tract abnormalities or rupture, and cardiac malformations. It is rare and usually carries a much better prognosis with spontaneous resolution.

Treatment and fetal outcome

No definite fetal chromosome or structural abnormality was found in the previously reported cases. In rare cases, pregnancy termination was performed due to the rapid growth of the tumor and expected poor prognosis. Thus, fetal abdominal LM possibly carry a better prognosis depending on their growth rate and infiltrating area. Because of the paucity of available data, we still need more cases to draw a firm conclusion on this point. Management options for fetal LM are limited; the injection of sclerosing agents such as OK-432 (low virulence group-A *Streptococcus pyogenes* cultured with penicillin) has been reported to cause shrinkage or complete resolution of the lesions before delivery in 50–90% of patients [44–46]. Postnatally, needle aspiration of LM is usually ineffective and is associated with rapid re-accumulation of fluid or the development of infection. Treatment using sclerosing agents such as bleomycin or OK-432 or embolization with Ethibloc may cause shrinkage of the lesions [2,11,17,19,21,25]. The optimal treatment for LM is complete surgical excision, with a recurrence rate ranging around 5% or 10%, even in favorable cases [11].

Conclusions

Fetal abdominal LM seem to have a better outcome and exhibit the same US and MRI features. Both US and MRI can detect the exact cystic components, US can monitor the growth profiles conveniently, and MRI can evaluate the extent of the lesions and their relationship with the adjacent structures. Additionally, MRI is a complementary diagnostic tool adjunct to US for further characterization of fetal LM, especially when US findings are inconclusive or inadequate. Thus, a precise prenatal diagnosis is essential for both prenatal counseling of the parents and to guide the perinatal and postnatal management in selected patients.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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