Case Report

Extensive solitary lymphatic malformation of the liver in a child: a case report and literature review

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doi: 10.1016/j.radcr.2021.11.022

ABSTRACT

Intrabdominal lymphatic malformations are rare benign congenital vascular anomalies that account for less than 5% of benign masses in childhood, with an extremely variable clinical presentation. For this reason, although their radiological appearance is usually typical, diagnosis can be challenging and not always immediate. This report describes a unique case of extensive solitary hepatic lymphatic malformation in a 10-year-old boy with both extra- and intraparenchymal development with no associated symptoms. A literature review of reported cases of solitary hepatic lymphatic malformation is also included.

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Introduction

Intrabdominal lymphatic malformations (LMs) are rare benign congenital vascular anomalies that account for less than 5% of benign masses in childhood [1,2]. Their clinical presentation is extremely variable, as they can be completely asymptomatic and found incidentally or produce symptoms that lead to medical evaluation [3].

Particularly, hepatic lymphatic malformations are usually associated with other visceral LMs, while solitary hepatic LMs are very rare [4]. We report the first case described in literature thus far of an extensive mixed cystic LM of the liver with both extr- and intraparenchymal development, illustrating its main radiological features and its chosen management.

Acknowledgements: none.
Competing interests: none.
Patient Consent: Written, informed consent for publication of the case was obtained from patient’s parent.
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Case report

A 10-year-old boy presented to the Radiology department for mild abdominal pain focused in the lower quadrants, without fever nor other relevant clinical symptoms. His past medical history was unremarkable and he had never been subjected to prior imaging studies.

In the clinical suspicion of acute appendicitis, the patient underwent blood tests, which resulted normal (Alvarado score system for acute appendicitis was 3). Abdomen ultrasound (US) examination of the lower right quadrant showed a normal sized appendix with minimal increased hyperechogenicity of the adjacent visceral fat. Some small lymphnodes were detected nearby as well as a slight amount of fluid in the pelvis. Given the US indeterminate inflammatory state and the clinical and laboratory data, acute appendicitis was excluded adopting a “wait-and-see” approach.

US examination of the liver revealed intense hyperechogenicity of the hepatic parenchyma along the portal branches, in the absence of focal lesions. Between the gallbladder, the duodenum and the pancreas there was a multiseptated cystic mass, homogeneously hypoechoic with thin septa, where the larger cyst had a diameter of approximately 25 mm. The gallbladder was normally distended, with homogeneous content (Fig. 1).

The patient was hospitalized in order to better characterize the liver findings, and abdominal magnetic resonance imaging (MRI) with contrast medium (Dotarem®, gadoterate meglumine) was obtained the following day for further evaluation.

MRI confirmed the presence of some thin-walled cystic structures clustered together along the mid-lower edge of the liver, adjacent to the gallbladder and towards the hepatic hilum. As reported by the US evaluation, the extrahepatic cystic mass was in continuity with the areas of high signal-intensity in T2-weighted images that formed a tissue cuff around the portal axis and its main intrahepatic branches, also with small contextual septa suggesting that the lesion was made by a cluster of cysts rather than solid tissue (Fig. 2). Post-contrast MRI showed mild contrast enhancement of the cystic septa and minimal enhancement of the intrahepatic periportal tissue (Fig. 3). The findings were considered suggestive of a mixed type of hepatic lymphatic malformation, with both macro- and microcystic components.

There were no alterations of the remaining organs; particularly, there were no signs of acute appendicitis, suggesting a non-surgical self-limiting illness, also supported by normal blood tests and abdominal pain resolution.

The patient subsequently underwent exploratory laparoscopy (Fig. 4) with biopsy of the cystic liver mass; histological examination of the resected specimen confirmed the diagnosis of lymphatic malformation. Considering the benign nature of the lesion and the absence of clinical symptoms, a six-monthly radiological follow-up through US examination was planned, evaluating surgical treatment only in case of lesion growth or onset of symptoms.

Discussion

Etiology & demographics

Lymphatic malformations (LMs) are benign congenital vascular anomalies due to defective embryologic development.
Fig. 2 – Coronal (A) and axial (B-D) T2-weighted fat saturated MRI scans show an extensive area of hyperintense hepatic parenchyma signal consisting of a thin-walled cystic mass forming a tissue cuff around the portal axis and its main intrahepatic branches, with small contextual septa (arrowheads). The cystic mass is in continuity with the extrahepatic component (arrows) along the mid-lower edge of the liver, adjacent to the gallbladder (asterisk) and towards the hepatic hilum.

Fig. 3 – Coronal (A) and axial (B) T2-weighted fat saturated MRI scans with maximum intensity projection (MIP) 3D reconstructions show the extensive liver lymphatic malformation. Axial (C) and coronal (D) T1-weighted post contrast fat saturated MRI scans demonstrate mild contrast enhancement of the cystic septa and of the intrahepatic periportal tissue (arrows).
and consist of multicystic dilated lymphatic channels separated by fibrous septa, without cellular atypia [1,5]. LMs derive from failure of communication between lymphatic tissue and main lymphatic vessels; they usually contain serous or chylous fluid, which occasionally can be proteinaceous or hemorrhagic [6].

They are subclassified into macrocystic, microcystic and mixed types, a combination of both [7]. Even if two centimeters is usually used as cut-off to discriminate between micro- versus macrocystic, there are no strict size criteria, as the cystic size is assessed in relation to the type of treatment that can be applied: specifically, whether the cyst can be successfully aspirated to achieve evident decompression [8].

Macrocystic malformations are large, smooth, multicellular structures that can be compressible or non-compressible, while microcystic lesions consist of tiny individual or interconnected cysts presenting as clear vesicles that contribute to a firm spongy appearance [9].

LMs account for about 6% of benign masses in childhood and they can occur in every part of the body, with prevalence in the cervicofacial region (95%), while intraabdominal LMs are rare (less than 5%) and fewer than 1% of reported LMs arise from a visceral organ [1].

The most typical onset site of abdominal LMs is the mesentery, followed by omentum, mesocolon, and retroperitoneum[10]. Particularly, hepatic LMs are very rare, and they can be both isolated or more commonly an expression of diffuse lymphangiomatosis involving various organs [6,11,12]. Literature describes also a case of coexisting multiple cutaneous and visceral cavernous haemangiomas and two intraabdominal lymphatic malformations [13].

Nevertheless, some vascular malformation syndromes are characterized by multiple vascular anomalies, including lymphatic malformations, as Klippel–Trenaunay syndrome and CLOVES (Congenital Lipomatous Overgrowth, Vascular malformations, and Epidermal nevi syndrome) associated to the mutation of gene PIK3CA, and Proteus’ syndrome, which is due to AKT1 gene mutation [14].

Clinical & imaging findings

Abdominal LMs typically appear as soft painless masses that grow proportionally with the child, so that they are often diagnosed incidentally in early childhood [5]. Diagnosis usually depends on the location of the lesion: superficial lesions are visible and therefore diagnosed earlier since may come to attention as abdominal palpable lump. Deeper LMs might present later, either incidentally, or due to associated symptoms as abdominal pain or complications such as intestinal obstruction, hemorrhage and peritonitis caused by cysts infection [3,4,10,15].

The diagnosis of abdominal lymphatic malformations is based both on clinical history and imaging, typically US and MRI, necessary for a reliable evaluation of the extent of the LM and its features.

On ultrasound, macrocystic LMs appear as anechoic cystic lesions with thin septa or with inhomogeneously hyperechoic content in case of debris due to hemorrhage or infection [2]. Microcystic lymphatic malformations are multiseptated and might look as hypoechoic or more often echogenic lesions due to small cysts diameters and the multiple septa [8,16].

On magnetic resonance imaging macrocystic LMs are clearly defined cysts with thin septa and low signal-intensity in T1-weighted images and high signal-intensity in T2-weighted images; nonetheless, signal intensity can be variable due to proteinaceous or hemorrhagic components, with possibly fluid-fluid levels [2,5].

In contrast, in case of microcystic LMs, the cysts are usually too small to be identifiable as discrete structures in MRI, as they normally appear as diffuse areas of low signal-intensity in T1-weighted images and high signal-intensity in T2-weighted images [16].

Gadolinium-enhanced MRI may show minimal enhancement of septations and peripheral wall in macrocystic LMs, and allows superior tissue contrast resolution [1,5].

Computed tomography (CT) imaging is usually not required for the assessment of LMs, and the finding of LMs on
CT is typically occasional. LMs appear as low-attenuation non-enhancing cystic masses with thin or imperceptible walls; if the cystic fluid is chylous it shows negative attenuation, while hemorrhagic-proteinaceous fluid has high attenuation and may mimic a solid mass [16].

Even if CT scan allows an excellent spatial definition, MRI is considered the gold standard diagnostic method especially in pediatric population, with the unquestionable advantage to be radiation free and to provide high tissue contrast resolution even without contrast medium administration [10].

**Differential diagnosis**

The differential diagnosis of solitary hepatic LMs includes other hepatic cysts as polycystic liver disease, hydatid cysts, and cystic tumors like mesenchymal hamartoma, neoplasms of the biliary system, or cystic metastasis [2]. Polycystic liver disease classically appears as multiple homogeneous cystic lesions with a regular border and no internal septa, hypoattenuating on nonenhanced CT scans, hypchoic on US evaluation and with typical homogeneous high signal intensity on T2-weighted images on MRI, with no wall or content enhancement on contrast-enhanced images [17].

Bile duct hamartomas, also called Von Meyenburg complexes, are cystic lesions that do not communicate with the biliary tree, usually less than 1.5 cm in diameter. They present more irregular borders in comparison to simple cysts and appear hypoattenuating on nonenhanced CT, hyperintense on T2-weighted MR images, with no contrast enhancement [18].

Biliary cystadenoma and cystadenocarcinoma are rare neoplasms of the biliary system and at CT and MR imaging appear as large, solitary, multilocular cystic masses with well-defined thick fibrous capsule and internal septa, often presenting mural nodules, and more rarely capsular calcification [17,18]. Walls, internal septa and solid nodular components commonly demonstrates contrast enhancement both on CT and MR imaging [19].

Cystic hepatic metastasis can be attributed to the necrosis of hypervascular metastases secondary to rapid growth or to the production of mucin by acinar structures and glandular tissues from mucinous adenocarcinoma [19]. Contrast-enhanced CT and MR imaging usually shows multiple hypoattenuating/hypointense nodular lesions with irregular borders and peripheral rim-enhancement.

Hepatic echinococcal cyst may appear as purely cystic lesion with no internal septa or as complicated heterogeneous mass, that typically contains multiple daughter cysts arranged in a distinctive wheel-spoke pattern. At CT evaluation, mother cyst shows higher attenuation in comparison to daughter cysts due to proteinaceous material consisting in hydatid sand and fragmented detached cyst walls. At MR imaging, the hydatid matrix appears hypointense on T1-weighted images, depending on the entity of proteinaceous debris, and markedly hyperintense on T2-weighted images, with daughter cysts more hypointense than the matrix [18,20]. Cyst walls and internal septa demonstrate enhancement after contrast medium administration [19].

The hepatic perportal lymphatic system, together with the perihepatic vein lymphatic system, constitutes the deep lymphatic system of the liver [21]. In specific conditions that lead to liver congestion, as cirrhosis or liver transplantation, the perportal lymphatic system may appear thickened in relation to periportal lymphedema, which manifests with a typical “halo sign” around the vascular branches at US or MRI [21,22]. Nonetheless, malignancies like liver lymphoma or metastasis may appear in the form of perportal tubular infiltration, with vessels compression and stenosis [6,22]. This particular imaging appearance goes into differential diagnosis with microcystic LM, as it can be difficult to discriminate individual small cysts which rather appear as a diffuse perportal area of low signal-intensity on T1-weighted images and high signal-intensity in T2-weighted images.

**Management and treatment options**

In case of LMs with radiological typical aspects, percutaneous biopsy is not recommended, as their low cellularity often results in negative yield; however, some authors consider it may be necessary when the lesion does not have regular features or shows atypical site and growth pattern [1,2].

The decision on the appropriate LMs management is complex and based on a multidisciplinary approach which evaluates several factors as clinical presentation, anatomic location, lesion size and type (microcystic or macrocystic). The most common therapeutic strategies used in the treatment of LMs include pharmacotherapy, sclerotherapy and surgery [9,16,23,24].

Since LM is a benign condition, in case of asymptomatic LMs discovered incidentally conservative management is the first-line preferable option [25–27]. Currently, treatment algorithm is based on the type of LM, in particular sclerotherapy is considered the first line treatment option for macrocystic/combined LMs, as the large cystic spaces allow the aspiration of the fluid followed by percutaneous administration of sclerosing agents that induce endothelial destruction and subsequent lesion shrinking [9,16]. However, due to their small size, it is usually not possible to perform sclerotherapy in microcystic LMs, so that their optimal management is still under debate, even though bleomycin administration has shown promising results [9,16,23].

Complete surgical excision is often difficult due to anatomical complexity since LMs do not usually respect fascial planes, so that surgery frequently leads to incomplete removal, which is burdened with high recurrence rate [27]. Therefore, resection is mostly reserved for small, well-localized LMs that can be resected in full, as well as symptomatic microcystic LMs or symptomatic macrocystic/combined LMs already treated with sclerotherapy [28].

An extensive review of the literature identified 23 cases of solitary hepatic lymphatic malformations from 1994 to 2020 (13 males and 10 females), with an age range from 22 days to 75 years [15,29–49]. According to our review, the management of symptomatic LMs of the liver is still predominantly based on surgical resection [15,29–36,38,40,43–49]. This can be explained by the fact that the cases described concerned LMs
with well-defined profiles and sufficiently distant from vascular or nerve structures, for which surgical approach could guarantee a complete resection and important neurovascular structures sparing. Only in one case first line treatment was aspiration of the cystic mass, which however was followed by lesion recurrence after two months, requiring laparotomy and formal resection [37]. Four cases of solitary hepatic LM were asymptomatic, and a conservative approach was adopted in 3 cases after a diagnostic biopsy [39,41,42]; in one case surgical resection was performed even if the patient had no clinical symptoms, since the lesion didn’t show radiological typical features and the hypothesis of malignancy could not be excluded [47].

In our report, given a multi-specialty evaluation, a conservative approach was preferred due to the absence of clinical symptoms and the complexity of the LM. In fact, it presented a combination of macrocystic and microcystic components and an extensive intra- ed extrhepatic growth pattern, in close proximity to liver important neurovascular structures, so that radiological follow-up with observation only was considered the most suitable option.

**References**

[1] Francavilla MI, White CL, Oliveri B, Lee EY, Restrepo R. Intra-abdominal lymphatic malformations: Pearls and pitfalls of diagnosis and differential diagnoses in pediatric patients. Am J Roentgenol 2017;208:637–49.

[2] Lal A, Gupta P, Singhal M, Sinha SK, Lal S, Rana S, et al. Abdominal lymphatic malformation: Spectrum of imaging findings. Ind J Radiol Imag 2016;26:423–8.

[3] Muramori K, Zaizen Y, Noguchi S. Abdominal lymphangioma in children: Report of three cases. Surg. Today 2009;39:414–17.

[4] Long X, Zhang L, Cheng Q, Chen Q, Chen X. Solitary hepatic lymphangioma mimicking liver malignancy: A case report and literature review. World J. Clin. Cases 2020;8:4633–43.

[5] Ballah D, Cahill AM, Fontalvo L, Yan A, Treat J, et al. Vascular Anomalies: What They Are, How to Diagnose Them, and How to Treat Them. Curr Probl Diagn Radiol 2011;40:233–47.

[6] Pupulin LF, Vilgrain V, Ronot M, Becker CD, Breguet R, Terraz S. Hepatic lymphatics: anatomy and related diseases. Abdom Imaging 2015;104:1997–2011.

[7] Johnson CM, Navarro OM. Clinical and sonographic features of pediatric soft-tissue vascular anomalies part 2: vascular malformations. Pediatr Radiol 2017;47:1196–208.

[8] Kulungowski AM, Patel M. Lymphatic malformations. Semin. Pediatr. Surg. 2020;29.

[9] Elluru RG, Balakrishnan K, Padua HM. Lymphatic malformations: Diagnosis and management. Semin. Pediatr. Surg. 2014;23:178–85.

[10] Levy AD, Cantisani V, Miettinen M. Abdominal lymphangiomas: Imaging features with pathologic correlation. Am. J. Roentgenol. 2004;182:1485–91.

[11] Schmid C, Beham A, Uranus S, Melzer C, Auböck L, et al. Non-systemic diffuse lymphangiomatosis of spleen and liver. Histopathology 1991;18:478–80.

[12] Cutillo DP, Swayne LC, Cucco J, Dougan H. CT and MR imaging in cystic abdominal lymphangiomatosis. J. Comput. Assist. Tomogr. 1989;13:534–6.

[13] Canataroglu A, Gumurdul Y, Gumurdulu D, Balal M, Tuncer I, et al. Coexistence of cystic intra-abdominal lymphangiomas and diffuse venous haemangiomas in adult life. J. Med. 2003;61:95–7. https://pubmed.ncbi.nlm.nih.gov/12765232/.

[14] Steiner JE, Drolet BA. Classification of Vascular Anomalies: An Update. Semin. Intervent. Radiol. 2017;34:225–32.

[15] Budusan A, Cocian A, Gocan H. Isolated hepatic lymphangiomas in children: two case reports. J. Pediatr. Surg. Case Reports 2020;56:101430.

[16] Barque IM, Sousa J, Mansilha A. Vascular malformations: classification, diagnosis and treatment. Int. Angiol. 2018;37:127–42.

[17] Lantinga MA, Gevers TJG, Drent JPH. Evaluation of hepatic cystic lesions. World J. Gastroenterol. 2019;25:3543–54.

[18] Gomotel KJ, Ros PR. Cystic focal liver lesions in the adult: Differential CT and MR imaging features. Radiographics 2001;21:895–910.

[19] Qian LJ, Zhu J, Zhuang ZG, Xia Q, Liu Q, et al. Spectrum of multicystic hepatic cystic lesions: CT and MR imaging findings with pathologic correlation. Radiographics 2013;33:1419–33.

[20] Mehta P, Prakash M, Khandelwal N. Radiological manifestations of hydatid disease and its complications. Trop. Parasitol. 2016;6:103–12.

[21] Arrive L, Monnier-Cholley L, Cazzagon N, Wendum D, Chambenois E, et al. Non-contrast MR lymphography of the lymphatic system of the liver. Eur. Radiol. 2013;29:5879–88.

[22] Ly JN, Miller FH. Periportal contrast enhancement and abnormal signal intensity on state-of-the-art MR images. Am. J. Roentgenol. 2001;176:891–7.

[23] Greene AK, Perlyn CA, Alomari AI. Management of lymphatic malformations. Clin. Plast. Surg. 2011;38:75–82.

[24] Sun RW, Tuchin VV, Zharov VP, Galazhina EJ, Richter GT. Current status, pitfalls and future directions in the diagnosis and therapy of lymphatic malformation. J. Biophotonics 2018;11.

[25] Elbaaly H, Piché N, Rypens F, Kleiber N, Lapière C, et al. Intra-abdominal lymphatic malformation management in light of the updated International Society for the Study of Vascular Anomalies classification. Pediatr. Radiol. 2021;51:760–72.

[26] Makni A, Chebbi F, Fetirich F. Surgical management of intra-abdominal cystic lymphangioma. Report of 20 cases. World J. Surg. 2013;36:1057–43.

[27] Alqahtani A, Nguyen LT, Flageole H, Shaw K, Laberge JM. 25 Years’ experience with lymphangiomas in children. J Pediatr Surg 1999;34:1164–8.

[28] Bertozzi M, Ruffoli M, Vatta F. The effectiveness of abdominal lymphangioma laparoscopic removal in children: a single center experience. J. Laparoendosc. Adv. Surg. Tech. 2021. doi: 10.1089/laq.2021.0323.

[29] Chan SC, Huang SF, Lee WC, Wan YL. Solitary hepatic lymphangioma - A case report. Int. J. Clin. Pract. 2005;59:100–2.

[30] Zhang Y-Z. Rare case of a solitary huge hepatic cystic lymphangioma. World J. Clin. Cases 2013;152 1.

[31] Nzewu MA, Ekenze SO, Okafor OC, Anyanwu PA, Odetunde OA, et al. Solitary hepatic lymphangioma in an infant [2]. J. Perinat. Med. 2007;35:164–5.

[32] Soares AWL, Tajar CEF, Soares VVR, Soares JL, Costa JJA. Hepatocectomy por linfangioma em situs inversus totalis - relato de caso. Rev. Col. Bras. Cir. 2011;38:490–1.

[33] Matsumoto T, Ojima H, Akishima-Fukasawa Y, Hiraoka N, Onaya H, et al. Solitary hepatic lymphangioma: Report of a case. Surg. Today 2010;40:883–9.

[34] Stavropoulos M, Vagianos C, Dragotis C, Androulakis J, Scopa CD. Solitary hepatic lymphangioma: a rare benign tumour: a case report. HPB Surg 1994;8:33–6.

[35] Zeidan S, Delarue A. Uncommon etiology of a cystic hepatic tumor. Dig. Surg. 2008;25:10–11.
Linfangioma quístico hepático: Una causa excepcional de dolor abdominal en el adulto. Cir. Esp. 2013;91.

Stunell H, Ridgway PF, Torreggiani WC, Crotty P, Conlon KC. Hepatic lymphangioma: A rare cause of abdominal pain in a 30-year-old female. Ir. J. Med. Sci. 2009;178:93–6.

Huang L, Li J, Zhou F, Jan J, Liu C, et al. Giant cystic lymphangioma of the liver. Hepatol. Int. 2010;4:784–7.

Choi WJ, Jeong WK, Kim Y, Kim J, Pyo J, et al. MR imaging of hepatic lymphangioma. Korean J. Hepatol. 2012;18:101–4.

Nakano T, Hara Y, Shirokawa M, Shioiri S, Goto H, et al. Hemorrhagic giant cystic lymphangioma of the liver in an adult female. J. Surg. Case Reports 2015 rjv033–rjv033 (2015).

Bartelheimer MW, Schlegel HM, Picolin K. Das solitäre adulte lymphhämagangiom der leber als äußerst selten variante einer benignen raumforderung der leber. [Solitary adult lymphangioma of the liver as a very rare variant of benign space-occupying lesion of the liver] RoFo. Verfahren 2001;173:771–2.