

CASE REPORT

A histopathological diagnosis of mesenteric cystic lymphangioma, clinically misdiagnosed as simple mesenteric cyst – case report

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Abstract

Abdominal cystic lymphangiomas are relatively rare congenital malformations, predominantly found in the pediatric age group. They are usually found in the head and neck of affected children. Lymphangioma of the small-bowel mesentery is rare, having been reported for less than 1% of all lymphangiomas. The gross and histopathological findings may resemble benign multicystic mesothelioma and lymphangiomyoma. The immunohistochemical study for factor VIII-related antigen, D2-40, calretinin and human melanoma black-45 (HMB-45) is essential for diagnosis. Factor VIII-related antigen and D2-40 are positive in lymphangioma but negative in benign multicystic mesothelioma. HMB-45 shows positivity in the smooth-muscle cells around the lymphatic spaces of the lymphangiomyoma. This report describes a case of a large mesenteric lymphatic cyst identified in the neonatal period. Early diagnosis was possible due to the prenatal imaging methods. Fetal ultrasound identified in the 17th week of gestational life an abdominal tumor that increased with fetal growth. The anatomopathological differential diagnosis and modalities of treatment are also discussed.

Keywords: anatomopathological, lymphangioma, mesenteric lymphatic cyst.

Introduction

Mesenteric cystic lymphangioma is a rare benign intra-abdominal anomaly with uncertain etiology, predominantly occurring in children. Almost 60% of mesenteric cystic lymphangiomas are diagnosed before the fifth year of life [1]. There appears to be a male predominance. Mesenteric cystic lymphangioma is distinguished from mesenteric cysts in location, histological feature and recurrence rate [2]. Mesenteric cysts occur later in life (1:100 000 in adults and 1:20 000 in children), also show female predominance, and as a rule are asymptomatic [3].

Aim

We report the case of a large mesenteric lymphangioma diagnosed antenatal and the difficulties encountered in its diagnosis and management.

Case presentation

The patient, a boy, 2-day-old, was transferred to our Hospital from "Cuza Vodă" Obstetrics and Gynecology

Hospital, Neonatology Ward, Iași, Romania, for the identification, on clinical examination, of a mobile mass in the upper abdominal area certified by ultrasound. We specify that the pregnancy was monitored by serial fetal ultrasounds, which made possible the identification in the 17th week of gestational age of an abdominal tumor (hyper-echoic, nonhomogeneous and vascularized) (Figure 1). He was born naturally, at the gestational age of 38 weeks, and his birth weight was 4 kg. He is the second son, and his 4-year-old brother is apparently healthy. The mother is apparently healthy and his father is suffering from arterial hypertension and non-insulin dependent diabetes. The mother had no infections during the pregnancy, did not take any drugs, did not drink or smoke and has not been exposed to ionizing radiation.

On clinical examination, he was found to be a healthy looking boy with no other abnormalities apart from an ill-defined diffuse abdominal swelling. Complete blood count (CBC), inflammatory syndrome, electrolytes, liver and renal functions tests were normal. Abdominal ultrasound highlighted an expansive tumor of mixed solid

and liquid structure with left paravertebral location, with calcifications inside, and Doppler signal present, extending lower, to the left iliac fossa, hovering above the retroperitoneal vessels and incorporating the inferior mesenteric artery. Computed tomography (CT) scan showed an expansive multilocular cystic tumor with fluid densities and calcifications inside, imprecisely delimited, located above the retroperitoneal vessels (aorta and inferior vena cava), which cover a length of about 7 cm (Figures 2 and 3).

We decided to perform an exploratory laparotomy in the 4th day of life. Intraoperatively, a diagnostic of lymphatic vascular malformation developed within the basis of the mesentery is established. A partial excision of cystic formations containing lactescent liquid (Figure 4) is achieved and the chyloperitoneum collected intraoperatively is drained.

The pathological examination of the resected specimens revealed a cystic mass containing lactescent fluid, which was cultured and yielded no bacterial growth.

Tissue sections from resected specimens were processed by standard histological methods.

The collected samples were specifically fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned (4 μ m) and stained with Hematoxylin–Eosin (HE) and Szekely, using a standard protocol. The microscopic exam

was performed using a Nikon Eclipse E600 optical microscope.

Microscopically, the cyst wall showed attenuated endothelial lining and a small number of smooth muscle fibers (Figure 5), lymphoid aggregates (Figure 6), fibrovascular and adipose tissue (Figure 7).

Immunohistochemical (IHC) staining (Department of Pathology, “St. Mary” Emergency Children’s Hospital, Iași) was performed by manual protocol using the EnVision™ FLEX/HRP (Horseradish peroxidase) (Dako), stained with CD34 (endothelial cell marker) mouse monoclonal antibody (Novocastra), CD45 mouse anti-human monoclonal antibody (Dako) and desmin mouse anti-human monoclonal antibody (Dako). The antigen retrieval for CD45 was citrate buffer and for desmin – ethylenediamine-tetraacetic acid (EDTA) (Figures 8 and 9).

CD34 or the human hematopoietic progenitor cell antigen is a potential indicator of vascular differentiation. It is highly sensitive for endothelial differentiation. CD45, also known as leukocyte common antigen (LCA), is a family of transmembrane protein tyrosine phosphatase. It is expressed on the surface of all hematopoietic cells except erythroid and megakaryocytic cells. Desmin is a cytoplasmic intermediate filament protein that is characteristically found in muscle cell and in neoplasms with myogenic differentiation [4].



Figure 1 – Antenatal diagnosis: fetal ultrasound (17th week of gestational life).



Figure 2 – CT scan: expansive cystic tumor, multilocular with fluid densities and calcifications inside.

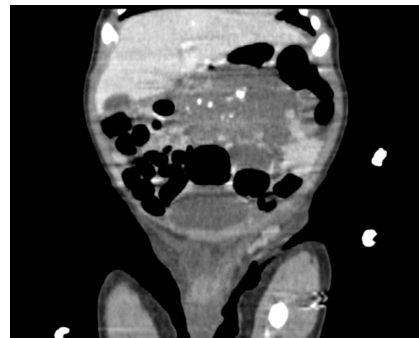


Figure 3 – CT scan: expansive cystic tumor, multilocular with fluid densities and calcifications inside.

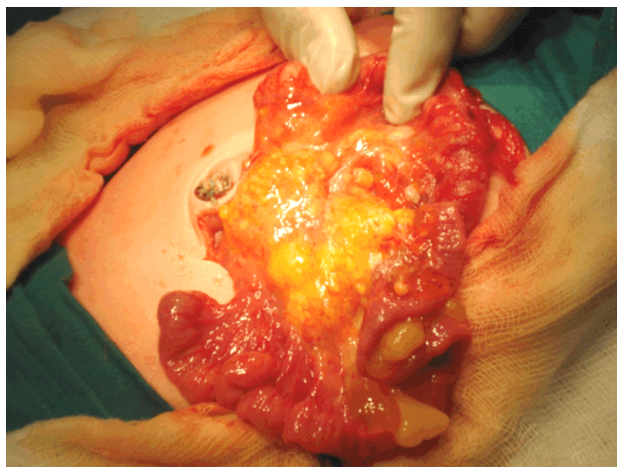


Figure 4 – Cystic formations containing lactescent liquid.

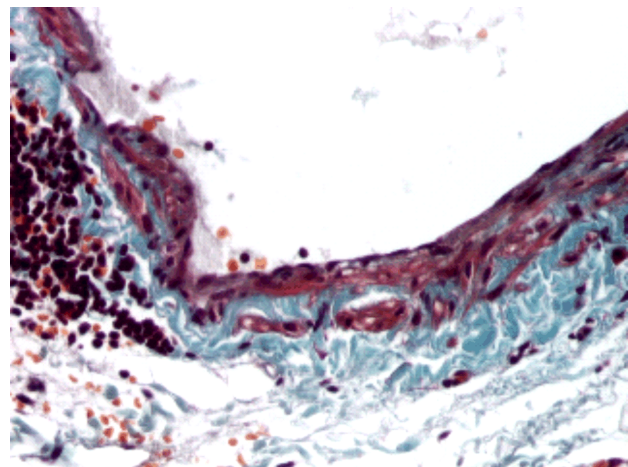


Figure 5 – Cyst wall with smooth muscle fibers (Szekely staining, ×200).

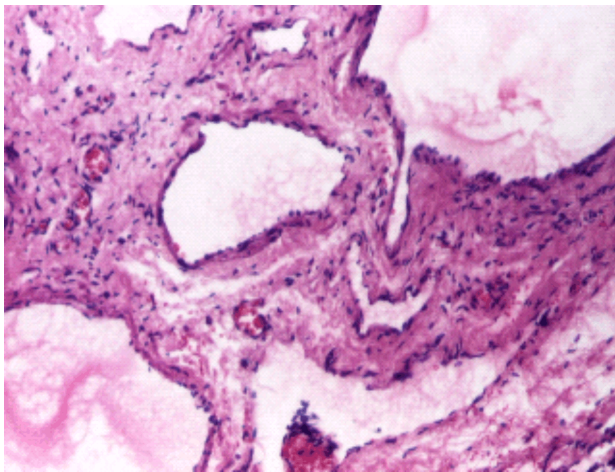


Figure 6 – Cystic spaces in a fibrovascular stroma (HE staining, $\times 100$).

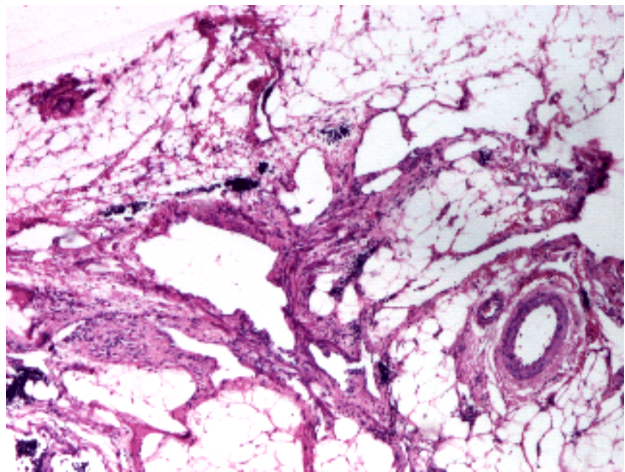


Figure 7 – Cystic spaces and adipose tissue (HE staining, $\times 40$).

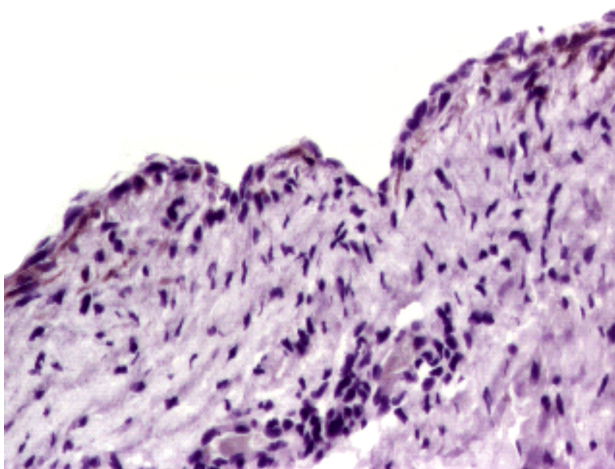


Figure 8 – Smooth muscle fibers were positive for desmin (Anti-desmin antibody immunomarking, $\times 200$).

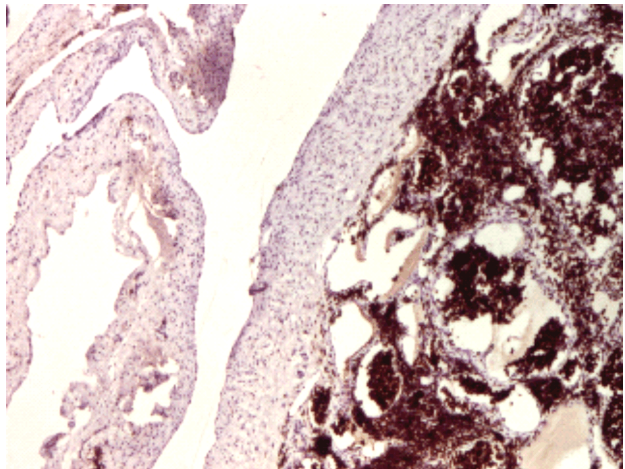


Figure 9 – Lymphoid aggregates were positive for CD45 (Anti-CD45 antibody immunomarking, $\times 40$).

Paraffin-embedded tissue sections (4 μ m) were also immunostained in the Department of Pathology of the Regional Institute of Oncology, Iași, with anti-D2-40 mouse monoclonal antibody (Ventana), using Ventana Bench Mark XT (Ventana, Arizona, USA) automated system. Similar sections were immunostained with anti-CD31 mouse monoclonal antibody (Novocastra), following the

manual protocol: the sections were subjected to antigen retrieval (using 0.01 M citrate buffer, pH 6), followed by incubation with the recommended dilution of the mentioned antibody and treatment with Novocastra Novolink™ Polymer System Kit (Leica Biosystems). Flattened endothelial cells were positive for CD31 and D2-40 immunomarkers (Figures 10 and 11).

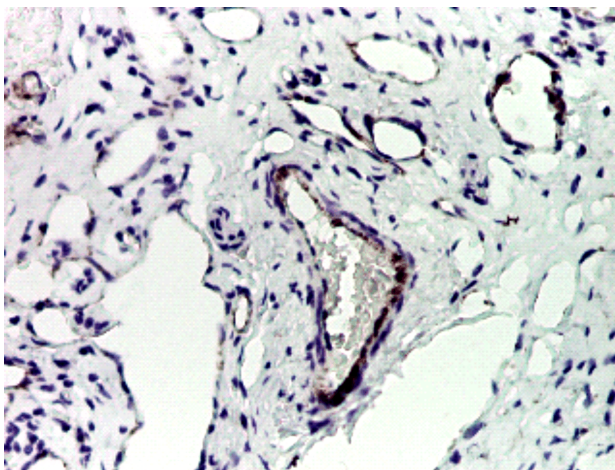


Figure 10 – Endothelial cells were positive for CD31 (Anti-CD31 antibody immunomarking, $\times 200$).

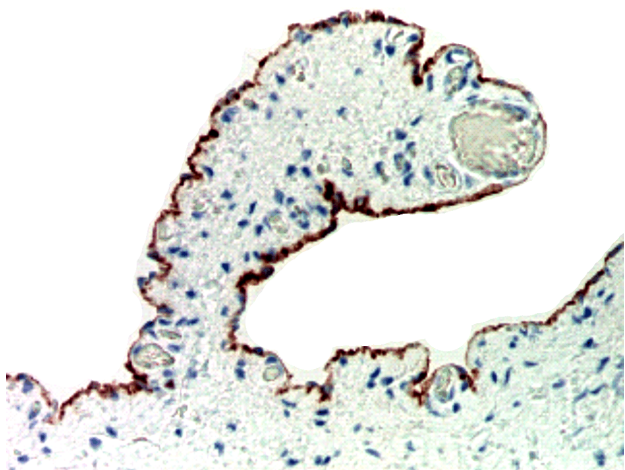


Figure 11 – Immunoreaction for D2-40 showing positivity of the flattened endothelial cells lining the lymphatic spaces (Anti-D2-40 antibody immunomarking, $\times 200$).

The platelet endothelial cell adhesion molecule-1 (PECAM-1) is also known as CD31. It is a 130-kD transmembrane glycoprotein that is shared by vascular lining cells, megakaryocytes, platelets and selected other hematopoietic elements. This marker is highly restricted to endothelial neoplasms, and its sensitivity is also excellent. D2-40 monoclonal antibody is a highly sensitive and specific marker of lymphatic endothelium in normal tissue and a subset of vascular lesions, including lymphangioma [4].

Based on the findings, the final diagnosis of mesenteric cystic lymphangioma was established. Differential diagnosis was established with lymphatic cyst that is lined by cuboidal and columnar cells and lacks smooth muscle.

The patient was followed at the ages of two, three, and six months postoperatively by serial abdominal ultrasounds (Figure 12).

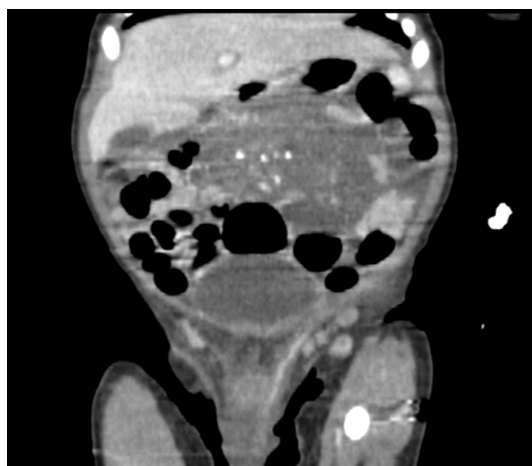


Figure 12 – CT scan at 11 months.

At the age of 11 months, the patient was admitted again in our Hospital, because of diffuse abdominal swelling. CT scan revealed an expansive cystic tumor measuring 6.52×13.48×11.1 cm, with adipose components inside. The iterative laparotomy revealed the tumor, which was biopsied. Pathological examination confirms the diagnosis of mesenteric cyst lymphangioma. The cyst wall showed attenuated endothelial lining, lymphoid aggregates and

a greater number of smooth muscle fibers than the first biopsy (Figures 13–15).

Clinical and ultrasound evaluation at the age of one year and three months old is stationary. One year and nine months postoperatively, left hydrocele occurs and peritesticular liquid turns out to be lymph. At the age of two years old, the patient was admitted again in our Hospital because of sub-occlusive syndrome by compression and we decided a new intervention through an iterative laparotomy. The lymphatic content was partially evacuated and 8 mg of 0.5% Bleomycin was injected intralesionally.

Further, every month, after the last intervention, Bleomycin was injected intralesionally five times, under ultrasound guidance. At present, patient evaluation is favorable and he is followed by abdominal appearance and ultrasound (reduced abdominal perimeter and cystic lesions minimized at abdominal ultrasound) (Figure 16).

Written informed consent was obtained from the parents and the Ethical Committee of the Hospital approved the publication of this article.

Discussion

Lymphangiomas are uncommon congenital malformation of the lymphatic system. They can occur at any site in the body, but most commonly in the neck area [1]. Only a small proportion of cystic lymphangiomas are multilocular and most contain a single cavity [5].

The tumors are usually located in the neck (75% also called cystic hygroma), in the axilla (20%), and rarely (4% to 5%) in the mediastinum [6], lungs [7], esophagus [8], diaphragm [9], duodenum [10], stomach [11], small [12] and large intestine [13], spleen [14] and liver [15]. Less than 1% affects the mesentery, greater omentum and retroperitoneum [16]. Among all intra-abdominal lymphangiomas, 10% involve the mesocolon and 5% the retroperitoneum. The small bowel mesentery is affected more frequently [17].

Mesenteric cystic lymphangioma occurs at all ages, though most (65%) are present at birth, and 90% became symptomatic before the second year of life. Nearly 60% are diagnosed before the fifth year of life [18].

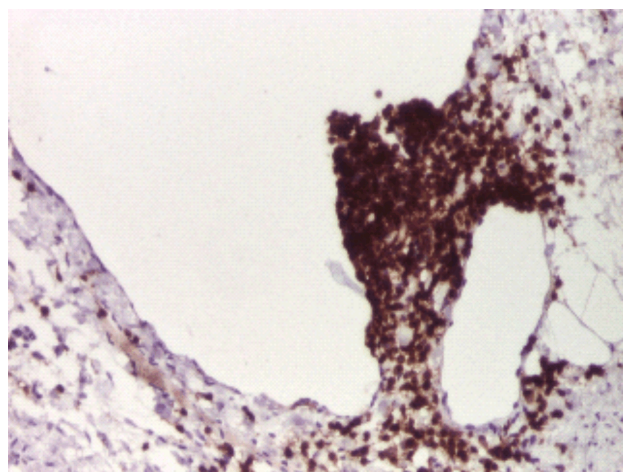


Figure 13 – Immunoreaction for CD45 showing positivity staining of the lymphoid aggregates disposed into cyst wall (Anti-CD45 antibody immunomarking, ×100).

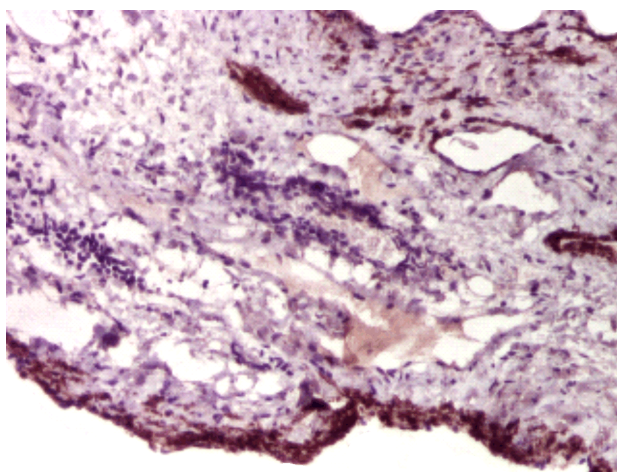


Figure 14 – Immunoreaction for desmin showing positivity staining of the smooth muscle fibers (Anti-desmin antibody immunomarking, ×100).

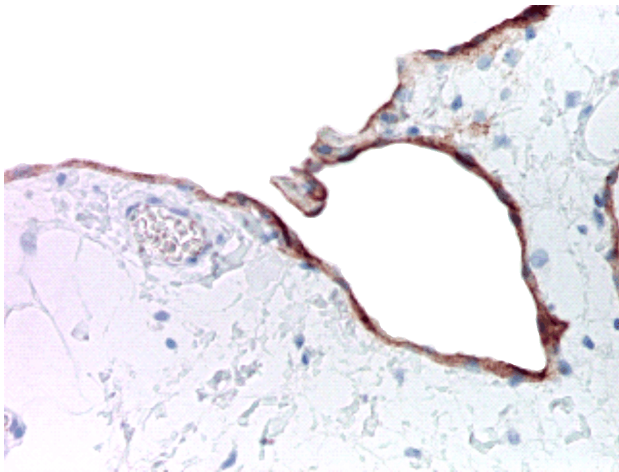


Figure 15 – Immunoreaction for D2-40 showing positivity of the flattened endothelial cells lining the lymphatic spaces (Anti-D2-40 antibody immunomarking, $\times 200$).

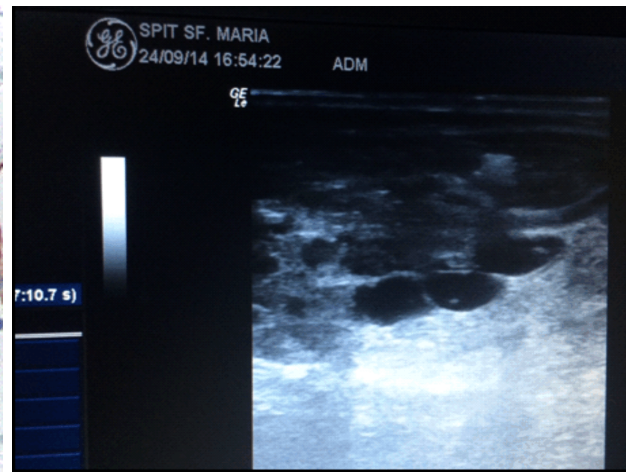


Figure 16 – Cystic lesions minimized at abdominal ultrasound.

Our patient was diagnosed prenatally in the 17th week of gestational life with abdominal tumor. In the 4th day of life, he was diagnosed intraoperatively with lymphatic vascular malformation developed based on mesentery. The final diagnosis based on pathological examination was mesenteric cystic lymphangioma. Microscopically, the cyst wall showed attenuated endothelial lining and smooth muscle fibers, fibrovascular and adipose tissue.

Pathologically, lymphangiomas are subdivided into three main types: capillary, cavernous, and cystic. The first two are predominantly cutaneous lesions; cystic lymphangiomas are generally found in the abdomen and retroperitoneum. Solid lymphangiomas are occasionally found in the abdominal cavity. Cystic lymphangiomas typically occur in spaces surrounded by loose connective tissue, such as the mesentery and retroperitoneum. Based on their specific histology, cystic lymphangiomas are classified as hamartomas. The cystic spaces are lined by a single layer of endothelium; there are small lymphoid aggregates in the cyst wall that help distinguish between lymphangiomas and simple cysts of the mesentery. If there is secondary bleeding into the cavity, lymphangiomas might be difficult to distinguish from hemangiomas; the diagnosis can be established immunohistochemically. Cystic mesothelioma, lymphangiosarcoma and myxoid degeneration of lymphangioma must be further included in the differential diagnosis [1]. The differential diagnosis was mesenteric cyst that is lined by cuboidal and columnar cells and lacks smooth muscle, positive stainings: Alcian blue, keratin, vimentin, Hectol Battifora mesothelial-1 (HBME-1), Wilms tumor 1 (WT1), thrombomodulin and calretinin. The second biopsy showed a greater number of smooth muscle fibers, which highlight the proliferative character of mesenteric cyst lymphangioma compared with simple cyst of mesentery that one excised, does not recur.

The treatment of mesenteric cyst lymphangioma is surgical. Minimally invasive surgery is a surgical treatment option. These cysts can be excised either laparoscopically or in a laparoscopy-assisted manner. Although the lesions have a generally benign course, they tend to recur and

invade neighboring structures. In our case, the complete resection of the tumor was impossible due to the invasive and multilocular character [18, 19].

Sclerotherapy with Bleomycin was initiated at the last intervention and five injections were performed every month, under ultrasound guidance. Patient evaluation is favorable and he is monitored by abdominal appearance and ultrasound. Abdominal perimeter was reduced and cystic lesions appeared minimized at abdominal ultrasound examination.

Compared to mesenteric cystic, mesenteric cystic lymphangioma is, on average, larger, has a more invasive biological behavior and is more often symptomatic because of its proliferative character [1].

Conclusions

Our case illustrates an unusual presentation of mesenteric cyst lymphangioma and options for treatment. The clinicians should consider mesenteric lymphangioma in the differential diagnosis of patients found to have intra-abdominal cystic masses on abdominal CT scans.

Conflict of interests

The authors declare that they have no conflict of interests.

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