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Video assisted sclerosis of endoabdominal lymphangiomas with OK432: An effective, safe and minimally invasive choice

Sara Silvaroli [a,*], Laura Merli [a], Filomena Valentina Paradiso [a], Lorenzo Nanni [a,b]

[a] Dipartimento Scienze Salute della Donna, del Bambino e di Sanità Pubblica-UOC Chirurgia Pediatrica, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[b] Istituto di Patologia Speciale Chirurgica, Università Cattolica del Sacro Cuore, Rome, Italy

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ABSTRACT

Lymphatic malformations (LM) or lymphangiomas are congenital errors in vascular embryogenesis. Percutaneous sclerosis is considered the best treatment for LM with external localization and yields excellent results. Surgical resection for deep LM is currently the mainstay of therapy, but high recurrence and morbidity rates are reported. Uniform therapeutic protocols are still unavailable.

We describe two cases of abdominal LM treated by video-assisted sclerosis with OK432.

The first case was a 5-month-old girl with pre-natal diagnosis of a left retroperitoneal LM with vascular encasement. A laparoscopic approach was used to expose the mass and a video-assisted injection of OK-432 in major cysts was performed. A remarkable reduction of the lesion size was observed after 18 months.

The second case was a 15-year-old boy who presented at the ER acute abdominal pain. A mesenteric LM was diagnosed and a video-assisted sclerosis of the lesion with OK432 was performed. The LM completely disappeared. Follow-up was of 12 months.

In our experience, video-assisted sclerosis of abdominal LM with OK-432 is a valid alternative to surgical resection. The procedure is feasible, safe, effective and minimally invasive; complete resolution may be observed in some cases. Long-term follow-up is required to rule out recurrences.

1. Introduction

Lymphatic malformations (LM) are rare benign anomalies caused by defective embryological development of primordial lymphatic structures. They consist in dilated lymphatic channels forming multiple cysts.

LM can be classified into macrocystic, microcystic, or mixed cystic lesions [1]. Spontaneous regression of LM has been described in 15% of cases, though they can enlarge over time [2,3].

Cystic lymphangiomas can occur in any body part in which lymphatics are normally found but the cervicofacial region is most frequently affected (48%). LM of the trunk, axilla, and extremities account for 42% of cases. Mediastinal and abdominal locations are rare (10%) [4]. Some cases involve the small or the large bowel mesentery, omentum or retroperitoneum, sometimes invading the bladder, spleen, pancreas or liver.

Abdominal lesions can cause acute abdominal pain often leading to emergency surgery [5]. They can also present with vomiting, peritonitis, intestinal obstruction, volvulus and intestinal necrosis has also been described [6]. Additional complications of intrabdominal LM include anaemia due to intracystic bleeding and sepsis due to bacterial translocation [3].

In 21.7% of cases, cysts are detected prenatally [7].

Therapeutic options may include injection of sclerosing agents into the cyst or surgical removal [8]. In asymptomatic cases, a conservative approach may be an option, considering a possible spontaneous regression [1]. Some oral drugs, e.g., sirolimus are considered effective in LM. However, few studies to analyse the efficacy and long-term adverse events to clarify the potential role of sirolimus to manage lymphatic malformations [9].

Recurrence after treatment may be observed in 27% of cases [10].

Ultrasound guided percutaneous sclerotherapy is the best treatment choice in accessible lesions, with low recurrence rates, good aesthetic results and few complications [11]. Sclerotherapy involves aspiration of the cyst fluid and subsequent injection of an equal volume of a sclerosing agent causing scarring of cyst walls [12,13].

Laparotomy and complete cyst excision are still considered the

* Corresponding order. UOC Chirurgia Pediatrica, Fondazione Policlinico Universitario A. Gemelli IRCCS, Largo A. Gemelli, 8, 00168, Rome, Italy.
E-mail address: sara.silvaroli@policlinicogemelli.it (S. Silvaroli).

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standard treatment for abdominal LM in children [14]. The wider use of laparoscopy in children enabled treatment of some lesions [5,15]. Regardless of the location, some lesions tend to infiltrate vital structures and are poorly demarcated; in these cases, complete excision is difficult and can require staged procedures [16].

Intracystic injection of a sclerosing agent is considered appropriate to treat surgically unresectable lesions [16,17] and, according to Ogita et al., OK-432 is one of the preferred sclerosing agents [12]. The minimal invasive percutaneous approach is limited by position and accessibility of the lesions [18].

To the best of our knowledge, no descriptions of video-assisted sclerotherapy for abdominal LM in children can be found in literature. We describe two cases of abdominal LM successfully treated by video-assisted sclerosis with OK-432.

2. Cases description

2.1. Case 1

A 5-month-old female was referred to our unit with a prenatal diagnosis of abdominal cystic mass compatible with LM. At birth, abdominal ultrasound confirmed the prenatal findings showing an irregular mass measuring 6 × 4 × 3 cm surrounded by the left kidney, spleen and pancreas, composed by several cysts within a minimal stromal component (Fig. 1). An abdominal MRI showed that the multilocular mass grew in the root of the mesentery, displacing the stomach, colon, pancreas and spleen encasing the celiac axis, portal vein, superior mesenteric artery and vein; radiological features suggested LM as possible diagnosis (Fig. 2). The baby was asymptomatic, her weight gain was regular and no mass was palpable at physical examination. Tumour markers performed (aFP; bHCG) were negative (Table 1).

Due to the location and the involvement of several major vessels, surgical removal of the lesion was deemed too risky. Thus, our team decided for a sclerosing treatment with laparoscopic access. Through an open access at the umbilicus, a 5mm trocar was placed for the telescope. Another 3 mm operative port in the right flank was placed.

Abdominal exploration was unremarkable. The gastrocolic ligament was opened and the stomach was lifted; a yellowish swelling was evidenced extending along the superior border of the pancreas to the medial aspect of the spleen. A needle was introduced percutaneously in the left flank and, after aspiration of a few millilitres of fluid from the mass, an equivalent volume of OK-432 was injected (0.1 mg diluted in 10 ml of saline).

The procedure lasted 60 minutes. Oral feeding was allowed on the first post-operative day and was well tolerated. Post-operatively the patient presented fever and diarrhoea, which spontaneously subsided within 24 hours. The baby was discharged on post-operative day 4. Follow-up ultrasound examinations were performed at 1, 3, 6 and 12 months: a progressive decrease of the mass diameter was documented, with a residual size of one cm. No symptoms occurred in an 18-month

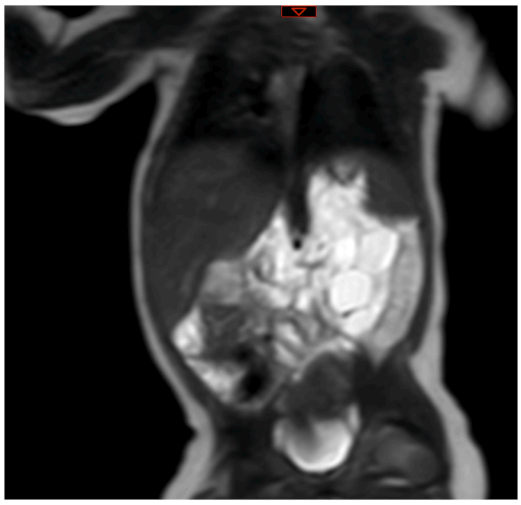

Fig. 2. MRI aspect of 5-month-old girl's lymphangioma.

Table 1
Patients characteristics.

	Case 1	Case 2
Prenatal diagnosis	Yes	No
Sex	F	M
Age	5 months	15 years
Clinical findings	No signs	Fever, abdominal pain
Radiological findings	US and MRI with contrast: multicystic lymphangioma	US, CT and MRI with contrast: multicystic lymphangioma
Localization	Retroperitoneal	Mesenteric
Organs involved	Celiac axis, portal and superior mesenteric vessels	Ileocolic vessels
Maximum diameter of cysts	6 × 4 cm	18 × 13 cm
Complications	None	Intracystic bleeding and inflammations
Tumour markers	Not relevant	Not relevant
Blood routine analysis	Not relevant	Not relevant
Time of intervention	5 months	15 years
Number of ports	2	3
Number of major cysts treated	1	4
Cytology	Fibrin, lymphocytes	Fibrin, lymphocytes
Results	Partial reduction of mass	Complete resolution
Complications	Fever, diarrhoea	None
Time of follow-up	18 months	12 months

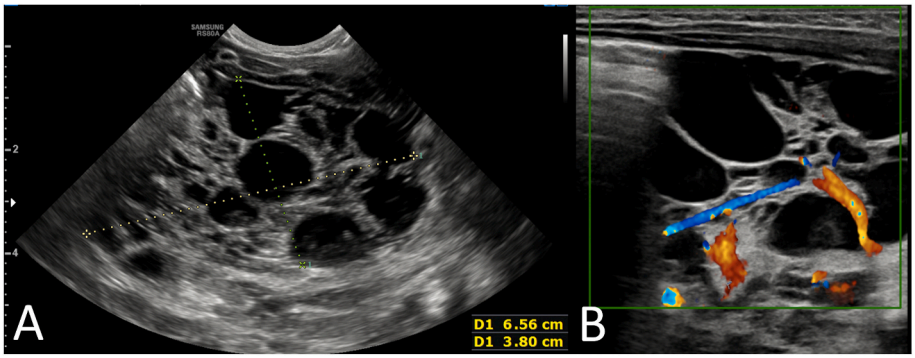

Fig. 1. A) Sonographic aspect of 5-month-old girl's lymphangioma B) Colordoppler exam showing major vessels encased in the lesion.

follow-up period.

2.2. Case 2

A 15-year-old boy came to the ER for abdominal pain, fever, elevated white blood cell count and CRP. Two similar episodes had occurred during the last month. A CT scan performed during one of the previous episodes showed an irregular mass, formed by multiple cysts caudal to the liver, compatible with LM.

The patient was admitted and intravenous antibiotic and anti-inflammatory therapy was started. After resolution of the inflammatory episode, an abdominal MRI was performed, which confirmed a polilobulated mass 18 × 13 × 7 cm in diameter originating in the root of the mesentery, which extended longitudinally from the right colic flexure to the pelvis. Ileocolic vessels were incorporated into the mass. Density of the fluid content of the cysts was not homogeneous probably due to a previous bleeding within the cysts (Fig. 3). Tumour markers were performed (aFP, bHCG, CA19-9 and CEA) and were negative . Colonoscopy was performed to verify the absence of infiltration of the large intestine (Table 1)

A surgical excision of the mass would have carried a high risk of intestinal resection due to the vascular encasement and the huge extension of the mass; therefore, laparoscopy in combination with sclerotherapy was performed. The peritoneal cavity was entered via an open access at the umbilicus for the laparoscope. Two operative ports were placed in the right and left iliac fossae.

Abdominal exploration confirmed a large multicystic swelling caudal to the liver, extending within the mesentery. A flexible needle was inserted through the right flank and multiple injections of OK-432 (0.1 mg diluted in 10 ml of saline) were performed in the major cysts. Sclerosing agent volume injected into the cysts was equal to the volume of the fluid aspirated from each macrocyst (Fig. 4).

The procedure lasted 90 minutes. No adverse events were registered in the post-operative period. The patient was discharged on post-operative day 2 in good clinical conditions.

Follow-up ultrasound examinations, performed after 3 and 6 months, showed that the lesion had completely disappeared; the patient has been asymptomatic during the 12-month follow-up.

3. Discussion

Diagnosis of LM is based mainly on imaging, especially ultrasound [6]; CT and MRI can accurately localize the cysts in relation with the surrounding structures and most importantly with major blood vessels. In the Nam et al. case series, only 13% of patients had a radiological diagnosis. Imaging of large LM are sometimes not indicative and lead to a false diagnosis such as ascites or intestinal duplications, because of possible bleeding within the cysts [7]. In such cases, laparoscopy may be indicated as both a diagnostic and treatment method [15].

The goals of LM management are to maintain functionality, to preserve aesthetic integrity and to control associated symptoms. Surgical excision is the most common treatment for abdominal LM to avoid rapid growth, superinfection, rupture, bleeding or intestinal obstruction that may require an emergency laparotomy [5]. However, surgery presents a high complication rate of up to 33% [19]. Common complications include bleeding, infection, and damage to neurovascular structures. Surgically resected abdominal LM can result in chylous ascites due to transected lymphatics resulting in patient morbidity and mortality. Post-operative scars and deformities after removal of the LM should be weighted.

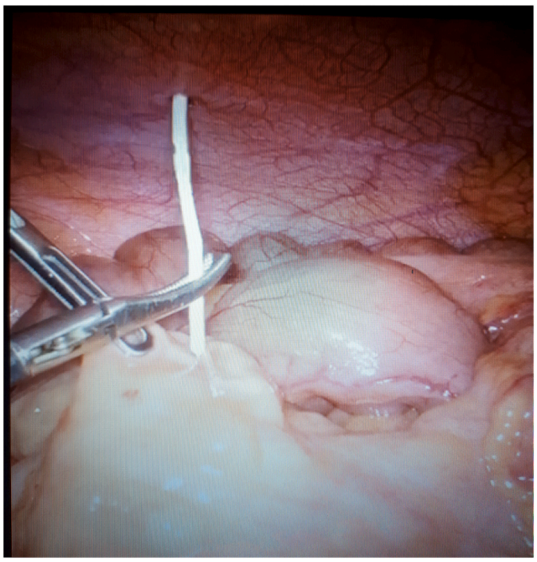

Fig. 4. Intra-operative injection image of a 15-year-old boy.

Abdominal or mesenteric LM can require segmental bowel resection. Total excision may not be possible if lesions surround great vessels and vital nerves, or in case of high risk of adjacent structure damage, or diffuse retroperitoneal involvement. Marsupialization may be an option [20] but it is usually complicated by free peritoneal fistulisation [16]. Incomplete resection may result in recurrence in about 35–64% of cases; recurrence rates decreases to 17–22% in case of total excision [21].

Amodeo et al. proposes a conservative approach ("watchful waiting") by carefully monitoring smaller asymptomatic lesions, which are known to spontaneously regress in up to 45% of cases [1]. However, malignant degeneration to low-grade sarcoma has been reported in very rare cases [14,22].

Laparoscopic resection has been proposed [5,15]. Laparoscopy is associated with minimal parietal scars, reduced post-operative ileus, and decreased risk of intestinal adhesion with subsequent obstruction [5]. LM invading the colonic or intestinal mesentery are a contraindication to laparoscopic resection because of extended bowel resection risk and

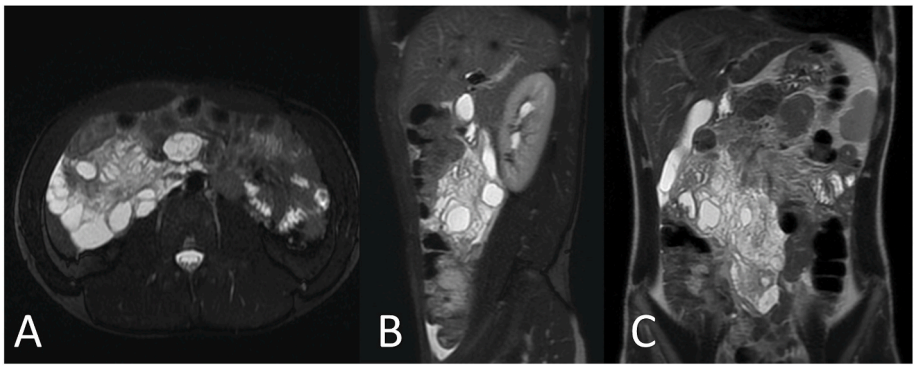

Fig. 3. MRI aspect of 15-year-old boy's lymphangioma in trasverse view (A); sagittal view (B); coronal view (C).

post-operative chylous ascites; cases of complex or large LM with intimate relation to major blood vessels suggest a high probability of conversion and the choice of laparoscopy for their management should be carefully considered [5,15].

In both of our reported cases , the LM had a large extension and involved vital structures such as major vessels, therefore, surgical resection was considered challenging and may have resulted in unnecessary tissue damage.

In recent years sclerotherapy has become the mainstay of treatment for macrocystic lesions owing to its effectiveness and low morbidity rates [13,14]. Results of sclerotherapy for LM, reported in literature, are largely based on studies conducted on craniofacial and cervical tumours, necessitating extrapolation of the approach for abdominal LM. Sclerotherapy preserves vital structures such as intestines, nerves, arteries and veins. Intra-cystic administration of a sclerosing agent is regarded as an adjuvant therapy in unresectable tumours [12,16]. Abdominal LM treatment using intracystic injection of sclerosing agents have been reported; in all cases sclerotherapy has been applied only in percutaneously accessible LM or during laparotomy after limited resection [16,17,23,24].

OK-432 is one of the favourite sclerosing agents inducing neutrophil and macrophage infiltration, which increases tumour necrosis factor production. The use of OK-432 has proved to be safe and effective to treat lymphangiomas in children yielding a complete resolution in 92% of cystic lymphangiomas [4,12]. Its application is confined to superficial lesions. It may cause systemic reactions such as fever, malaise, and anorexia.

In our cases, the LM were positioned in the mesenteric or retroperitoneal site not amenable to a percutaneous access. Therefore, laparoscopy was used to confirm the diagnosis and to precisely localize the sclerosing agent injection site. Sclerotherapy is safe and preserve adjacent structures.

Laparoscopy provides a less invasive approach and aids localizing the lesion through its inherent magnification; the use of laparoscopic instruments helps targeting the injections even in deep or unresectable lesions without damaging nearby structures. The procedure lasts on average an hour and shows low intraoperative risks. The post-operative course is uneventful and typical for minimally invasive procedures with a short hospital length of stay. The episode of diarrhoea, observed in the first case, may be explained with possible spillage of the sclerosing agent in the peritoneal cavity with consequent irritation of the intestinal serosa.

In our opinion sclerotherapy should be the preferred method to treat abdominal LM and due to vast experience reported in the literature, OK-432 should be considered the first choice among sclerosing agents. In both reported cases, the sclerosing agent led to a remarkable lesions size reduction without causing damage to the surrounding structures or overlying skin.

4. Conclusions

Based on our experience, sclerotherapy with OK-432 should be considered a valid and complete treatment option also for deep LM and not only for superficial lesions. In our cases, sclerotherapy in the abdomen showed satisfactory results reducing lesion size and obtained durable symptom resolution. In our experience, sclerotherapy in combination with laparoscopy permits to reach inaccessible LM and preserves vital structures. Therefore, we consider video-assisted sclerosis with OK-432 of abdominal LM a valid alternative to surgical resection for its feasibility, safety, as well as effectiveness and should be considered the first treatment option in lesions difficult to reach. The minimally invasive procedure is related to less complications and satisfactory aesthetic results and, if necessary, could be performed several times if one proves not decisive. We recommend long-term follow-up to rule out late recurrences.

Patient Consent

Consent to publish the case report was obtained by the parents of patients.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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