Liposuction-Like Sclerotherapy Technique for Microcystic Lymphatic Malformation

Huajie Wang Jr., Chong Xie, Weilong Lin, Jinhang Zhou, Weijia Yang, Zhengtuan Guo

1. Department of Pediatric Surgery, Xi’an International Medical Center Hospital, Xi’an, CHN

Corresponding author: Zhengtuan Guo, guozhengtuan@hotmail.com

Abstract

Background
The treatment for microcystic lymphatic malformation (LM) remains challenging. We describe the liposuction-like sclerotherapy technique, a new treatment for extensive microcystic LM.

Methods
LM data was retrospectively reviewed. This study included patients with a microcystic LM component treated by liposuction-like technique with bleomycin sclerotherapy.

Results
Between June 2016 and October 2019, 39 consecutive patients (male/female ratio: 21:18; mean age, 33.6 months; range: 5 months to 15 years) with microcystic LM were treated by liposuction-like sclerotherapy (LS-LS) technique. Fifty-six sessions of LS-LS were performed (mean of 1.44 sessions per patient; range: one to four sessions). Follow-up ranged 6-30 months (mean of 21 months). We observed no major complications. Transient minor complications included: postoperative noninfectious fever, vomiting, temporary skin edema, pigmentation, mild local depressions, and/or irregularities, and a small hyperpigmented scar at the incision. No postoperative infection, skin ulcer, or necrosis occurred. The patients’ symptoms were successfully resolved or stable. A sub-complete response and partial response were observed for 26 (76%) and 13 patients (33%), respectively.

Conclusion
The LS-LS technique for microcystic LMs is safe, feasible, and effective. This technique is an effective intervention with which it is possible to manage and potentially cure microcystic LM clinically.

Introduction
Lymphatic malformations (LMs) are congenital lymphatic anomalies, which may result from abnormal lymphatics development, often with underlying somatic PIK3CA mutation [1]. LMs can be solitary or multifocal and can be classified into macrocystic (≥2 cm), microcystic (≤1 cm), or mixed cystic lesions [2]. Sclerotherapy is the mainstay treatment for macrocystic LMs but has a poor response in microcystic and mixed cystic lesions [3-5]. The microcystic lesion typically consists of multiple small cysts (≤1 cm), in which traditional sclerotherapy and direct injection are less effective due to the small size of the lumen. Recently, encouraging results were obtained in microcystic LMs (mLM) with intralesional bleomycin sclerotherapy [4-7]. In traditional percutaneous sclerotherapy, the cyst was accessed and then sclerosant was injected with or without imaging guidance. However, in cases with extensive microcystic component, it is difficult to obtain successful results despite multiple sclerotherapy sessions with traditional techniques. In the microcystic lesions, there is a relatively large amount of soft-tissue component compared to the small cysts. Therefore, even when the cysts are resolved or reduced there is a residual soft-tissue mass that cannot be treated with sclerosants. We have reported a new treatment, liposuction-like sclerotherapy technique (LS-LS) that successfully managed superficial LM in some cases [8]. Herein, we describe the treatment effect of this technique for mLM involving the trunk and extremities. Perioperative data and imaging were studied to evaluate the efficacy of this technique.

Materials And Methods
This review was carried out in accordance with the requirements of and after approval by the institutional ethics committee and Institution Ethics Review Board of Xi’an International Medical Center with approval number XIMED (2019-PedSurg-05). All parents were fully informed about this new and alternative nature of the techniques, including the potential side effects of bleomycin (fever, vomiting, allergy, changes of
pulmonary function, etc.). Treatment was performed after obtaining written informed consent in all patients. Patients with extensive mixed cystic LM or microcystic LM of the trunk and extremities demonstrated on MRI treated by liposuction-like technique with bleomycin sclerotherapy were included. Patients with predominant macrocystic lesions were excluded from this study.

**Diagnosis**

The diagnosis of mLm component was based on clinical and imaging study of our multidisciplinary team, including pediatric interventional radiologists, sonography expert, and pediatric surgeon. The diagnostic criteria were based on clinical, sonographic, and MRI study, including clinical history, dermal vesicles, a soft-tissue cystic mass containing lymphatic fluid or hemorrhagic fluid, and fluid signal on MRI. Imaging was used to examine the extent and the architecture of the lesions. No preoperative biopsy was performed in this case series. Patients with only macrocystic LM were excluded.

**Liposuction-like sclerotherapy technique**

Preoperative topographic markings were made on the patient with permanent markers to delineate the position and extent of lesions by an ultrasonologist. The operation was performed under general endotracheal anesthesia in a hybrid or interventional operation room. Patient positioning was planned to provide optimal exposure of treatment areas and the ability to assess lesions during operation. Like liposuction in body contouring and fat grafting, tumescent local anesthesia was used in this procedure. Tumescent infiltration was performed in the lesion area according to the liposuction procedure. The tumescent solution used for operations consists of lidocaine, epinephrine, and saline (2% lidocaine 20 mL + 1:1000 epinephrine 1 mL + saline 1000 mL). Waiting at least 10 minutes after injection could ensure the optimal vasoconstrictive effect. The maximum dose for lidocaine in tumescent solution was limited to 35 mg/kg. A small incision was made at the border of the treatment area rather than within the area. We used 2 mm in diameter, 15-30 cm in length, blunt/sharp, and triple hole (Mercedes) cannulas in single or double row configurations. Using the vacuum-assisted liposuction technique, part of the subcutaneous fat and lymph fluid of LM was removed. During aspiration, we feathered the periphery of a treated area also to cover the potential, nonvisible lymphatic lesions. In order to destroy all small cysts within the lesion, we used pinch test and sonographic exam to judge the endpoint when the treatment area became smooth and flattened. After completion of aspiration, the bleomycin dilution was injected through 22-gauge needles directly inserted into the treatment area subcutaneously. Bleomycin was diluted with 5-10 mL of contrast medium (iopamidol injection) to obtain the mixture. The maximum dose for bleomycin was 1 mg/kg per session, injected in children (maximum 15 mg). At the end of the injection, a fluoroscopic image was obtained to check spontaneous diffusion of the mixture in the treatment area. Thereafter, the probe was used to dispense bleomycin. The liposuction process was redone without vacuum to obtain more even distribution and better infusion of the bleomycin dilution in the operated area. Finally, the diffusion of the mixture was rechecked by fluoroscopic imaging (Figures 1-3). Local compressive dressing over the small incision was applied for preventing bleomycin dilution overflow from the incision after completion of the operation.
FIGURE 1: Operative technique of the liposuction-like sclerotherapy.
Panel a: A microcystic lymphatic malformation of the lower extremity. Panel b: After topographic marking and tumescent infiltration, the vacuum-assisted liposuction-like operation was performed. Panel c: The wall of lymphatic malformation was destroyed after suction. Panel d: Showing the diffusion of the mixture of contrast medium and bleomycin in the treatment area.

FIGURE 2: Microcystic lymphatic malformation. Photograph of the liposuction-like sclerotherapy process.
Panel a: A microcystic lymphatic malformation of the right thigh. Topographic marking has been made before operation. Panel b: Immediate appearance after the liposuction-like operation was performed. Part of subcutaneous fat and lymph fluid was removed through the sharp, triple hole (Mercedes) cannula. Panel c: Showing the diffusion of the mixture of contrast medium and bleomycin in the treatment area.
FIGURE 3: Mixed cystic lymphatic malformation. Details of the liposuction-like sclerotherapy on photographic and imaging view.

Panel a, e, i, and j: An extensive mixed cystic lymphatic malformation of the right thoracic and abdominal wall. The position and extent of the lesion were topographically marked. Panel b: Showing the tumescent infiltrated lesion area. Panel c: During the vacuum-assisted liposuction-like operation, a pinch test was used to judge the endpoint. Panel d: At the endpoint of operation, the treatment area became smooth and flattened. Panel f and g: Showing the diffusion of the mixture of contrast medium and bleomycin in the treatment area, confirmed on lateral and frontal fluoroscopic imaging. A 2-mm in diameter, sharp, triple hole (Mercedes) cannulas in double row configurations were noticed on Panel g. Panel h: Showing the cosmetic appearance eight months after the operation. Panel k and l: Showing the MRI eight months after the operation. The result of treatment in this patient was graded as sub-complete response.

Treatment details
The tumescent technique used in the LS-LS technique was the same as that in liposuction for body contouring and fat grafting. The volume of tumescent solution for this technique varied as the size of the lesion. We inject the tumescent solution regardless of whether the infiltration needles were intra- or pericystic placed. The endpoint of infiltration was the skin becoming pale. The dose of bleomycin used was 0.5-1 mg/kg per session (maximum 15 mg). The mean operation time was 50 minutes (range: 30-90 minutes).

Postoperative care and follow up
No antibiotics were applied perioperatively. During the first six hours, a cold compress was routinely applied to reduce excessive local edema and to delay the absorption of bleomycin by blood vessels. We instructed the patient or parents to observe operative complications such as skin pigmentation, ecchymosis, edema, or re-enlarging after discharge. One month later, patients came back to the outpatient room for complication evaluation. If no complication was observed, a monthly follow-up was performed between two treatment sessions. At the sixth-month follow-up, patients underwent an MRI study.

Two independent radiologists assessed the imaging to evaluate treatment response. The response of sclerotherapy was initially assessed by a six-month follow-up on MRI. On the archived MRIs of the picture archiving and communication system (PACS), we used self-contained tools to assess the treated lesion. Postoperative MRI responses were divided into sub-complete (≥80% of the lesion decreased), partial (25-80%), and no response (≤25%). Sclerotherapy was repeated if required. The final result of therapy was evaluated by our multidisciplinary consensus at the vascular anomalies center during follow-up.
Results

Between June 2016 and October 2019, 39 consecutive patients with microcystic LM were treated by the LS-LS technique. The patient characteristics are summarized in Table 1.

| Patient characteristics                      |          |
|----------------------------------------------|----------|
| Age                                          | 5 months-15 years, mean 33.6 months |
| Sex (male: female)                           | 21:18    |
| The anatomic sites of microcystic lymphatic malformation |          |
| Right thoracic and abdominal wall            | n=8      |
| Left thoracic and abdominal wall             | n=7      |
| Bilateral thoracic and abdominal wall        | n=1      |
| Left upper arm and thoracic wall             | n=5      |
| Left lower extremity                         | n=4      |
| Right buttock                                | n=2      |
| Left buttock                                 | n=3      |
| Right forearm                                | n=3      |
| Right leg                                    | n=3      |
| Right thigh                                  | n=2      |
| Right upper arm                              | n=1      |
| Transient minor complications                |          |
| Fever (>39.0°C) during the first 24 hours    | n=8      |
| Vomiting                                     | n=3      |
| Response                                     |          |
| Sub-complete response                        | n=26     |
| Partial response                             | n=13     |

TABLE 1: Summary of patients with microcystic lymphatic malformation treated with liposuction-like sclerotherapy technique.

Three patients in this study presented with extensive mixed cystic LM with predominantly microcystic component involving the entire left lower extremity and buttock. Nine patients had a history of LM treatment before the LS-LS technique, five patients had a previous resection, and four patients had previous bleomycin and/or absolute ethanol sclerotherapy. The interval between previous treatments and the LS-LS technique was at least 6 months.

Fifty-six sessions of LS-LS were performed (mean of 1.44 sessions per patient; range: one to four sessions). The three patients, with extensive mixed cystic LM with predominantly microcystic component involving the entire left lower extremity and buttock, received three sessions of LS-LS. Some patients with an mL of thoracic and abdominal wall underwent multiple sessions of LS-LS (two-four sessions) because the lesion was too thick or extensive to be fully tumescent infiltrated. There was a risk of excessive intra- and postoperative bleeding in unfully tumescent infiltrated areas. Therefore, the staged operation was performed in these patients. The mean follow-up was 21 months (range: 6-30 months).

Complications

No major complication was observed. Transient minor complications included: eight patients developed severe postoperative noninfectious fever (>39.0°C) during the first 24 hours, three patients experienced postoperative vomiting that resolved with nonspecific intravenous fluid administration within 24 hours (Table 1). Temporary skin edema, pigmentation, mild local depressions and/or irregularities, and a
small hyperpigmented scar at the incision were noticed in all patients. Pigmentation over the treatment area gradually faded but persisted for at least months or more than a year without intervention. Excessive skin was observed in seven patients with too extensive lesions during follow-up. No postoperative infection, skin ulcer, or necrosis occurred.

**MRI evaluation**

Response (25% of the lesion decreased by imaging criteria) was observed on MRI for all patients (Figures 3–4). A sub-complete response was observed in 26 patients (67%), and partial response in 13 patients (33%) (Table 1). A minor or no change in the size of the lesion was not observed.

![MRI of an extensive lymphatic malformation before and after treatment.](image)

Panel a, b, d, and f: An extensive mixed cystic lymphatic malformation with predominantly microcystic component involved entire left lower extremity and buttock. Panel c, e, and g: After 6 months following treatment, the lesion had largely decreased by imaging criteria. It was noticed that the obviously enlarged left buttock had a great improvement on MRI. Furthermore, a dramatic improvement in the intramuscular component was observed simultaneously, which implies interconnection with subcutaneous component. The result of treatment in this patient was graded as partial response.

**Clinical outcome of symptoms**

The patients’ symptoms comprised dermal grouped hemorrhagic vesicles (n=2), obvious mass (n=7), pain (n=8), hypertrichiasis (n=1), and limb asymmetry in girth (subcutaneous LM and fat thickened, n=16). During follow-up, local mass became flattened. Dermal grouped hemorrhagic vesicles also decreased. Pain (n=8) was successfully resolved. Hypertrichiasis was stable. Limb asymmetry in girth was successfully controlled responding to graded responses on MRI.
Conclusions

The treatment of mLMs remains challenging, and a new therapeutic technique is required. We report a new
treatment technique for these lesions. The LS-LS technique for mLMs is safe and effective, especially for extensive lesions. Prospective studies comparing traditional percutaneous sclerotherapy with this new technique are warranted.

**Additional Information**

**Disclosures**

**Human subjects:** Consent was obtained or waived by all participants in this study. Institution Ethics Review Board of Xi’an International Medical Center issued approval XIMED (2019-PedSurg-05). This review was carried out in accordance with the requirements of and after approval by the institutional ethics review board of Xi’an international medical center. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

**References**

1. Luks VL, Kamitaki N, Vivero MP, et al.: Lymphatic and other vascular malformative/overgrowth disorders are caused by somatic mutations in PIK3CA. J Pediatr. 2015, 166:1048-54.e5. 10.1016/j.jpeds.2014.12.069
2. ISSVA Classification of Vascular Anomalies. (2018). Accessed: January 1, 2019: http://www.issva.org/UserFiles/file/ISSVA-Classification-2018.pdf.
3. Acord M, Srinivasan AS, Cahill AM: Percutaneous treatment of lymphatic malformations. Tech Vasc Interv Radiol. 2016, 19:305-11. 10.1053/j.tvir.2016.10.001
4. Burrows PE, Mitri RK, Alomari A, et al.: Percutaneous sclerotherapy of lymphatic malformations with doxycycline. Lymphat Res Biol. 2008, 6:209-16. 10.1089/lrb.2008.1004
5. Chaudry G, Guevara CJ, Rialon KL, et al.: Safety and efficacy of bleomycin sclerotherapy for microcystic lymphatic malformation. Cardiovasc Interv Radiol. 2014, 37:1476-81. 10.1007/s00270-014-0952-z
6. Da Ros V, Iacobucci M, Puccinelli F, Spelle L, Saliou G: Lymphographic-like technique for the treatment of microcystic lymphatic malformation components of <3 mm. AJNR Am J Neuroradiol. 2018, 39:530-4. 10.3174/ajnr.A5449
7. Lee J, Lee S-I, Chung HY, Huh S, Kim H-K: Infusion sclerotherapy of microcystic lymphatic malformation: clinicoradiological mid-term results. J Korean Soc Radiol. 2016, 74:26-36. 10.3348/jksr.2016.74.1.26
8. Wang H, Guo X, Liu Q, et al.: Liposuction-like sclerotherapy technique: a deep approach to superficial lymphatic malformations. J Am Acad Dermatol. 2019, 81:255-7. 10.1016/j.jaad.2019.01.082
9. Venkataрамن J: Tumescent liposuction: a review. J Cutan Aesthet Surg. 2008, 1:49-57. 10.4103/0974-4159
10. Klein JA, Jeske DR: Estimated maximal safe dosages of tumescent lidocaine. Anesth Analg. 2016, 122:1550-9. 10.1213/ANE.0000000000001119
11. Perkins JA: New frontiers in our understanding of lymphatic malformations of the head and neck: natural history and basic research. Otalaryngol Clin North Am. 2018, 51:147-58. 10.1016/j.otc.2017.09.002
12. Balakrishnan K, Menezes MD, Chen BS, Magit AE, Perkins JA: Primary surgery vs primary sclerotherapy for head and neck lymphatic malformations. JAMA Otolaryngol Head Neck Surg. 2014, 140:41-5. 10.1001/jamaoto.2013.5849
13. Jin Y, Zhou Y, Hua C, et al.: Treatment of early-stage extracranial arteriovenous malformations with intraleisonal interstitial bleomycin injection: a pilot study. Radiology. 2018, 287:194-204. 10.1148/radiol.2017162076