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Surgical excision is the treatment of choice for cervical lymphatic malformations with mediastinal expansion

Nader Ghaffarpour *, Carmen Mesas Burgos, Tomas Wester

Unit of Pediatric Surgery, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden

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ABSTRACT

Background: Lymphatic malformations (LMs) in the mediastinum are uncommon. However, cervical LMs may expand into the mediastinum. The aim of this study was to review our experience with the management of patients with LMs involving the mediastinum and to propose a treatment algorithm to guide the management of these rare malformations.

Material and Methods: This was a descriptive retrospective chart review of all patients with LMs involving the mediastinum treated at our Institution between 2009 and 2015. We collected demographic data, data on investigations, management, and complications of the treatment, as well as outcomes at follow-up. Complications were defined and described according to the Clavien-Dindo classification. The clinical outcome was assessed using a clinical assessment scale.

Results: The cohort consisted of seven patients. Airway compromise at the time of diagnosis was seen in 4 patients. Three patients had anatomical compression of the trachea and two patients had sub-total compression of the right lung. All three patients with tracheoscopy-verified compression of the trachea had compromise of the distal trachea, and a tracheostomy would not have been protective. All patients received sclerotherapy. The median time with mechanical ventilation at the neonatal intensive care unit after each sclerotherapy was eleven days (range 8–31). Each patient received sclerotherapy in median three times (range 1–9). Five of the patients (71%) were operated with excision of the LM in the mediastinum. Two of the patients were operated primarily and three patients were operated after major complications to sclerotherapy. The patients treated with sclerotherapy and the operated patients had comparable amount of mild complications, Clavien-Dindo grade I-II complications. Severe complications, Clavien-Dindo grade III-IV, were seen five times more commonly after sclerotherapy than after surgery. The clinical outcome was excellent for the operated patients and fair to good for the patients receiving only sclerotherapy.

Conclusion: Patients with cervical LM involving the mediastinum represent a high-risk group with respect to the severity of complications following sclerotherapy. The swelling is unpredictable and requires extended observation at an intensive care unit with ventilation support. Tracheostomy does not prevent tracheal compression in mediastinal LM, as the malformation may compress trachea distal to the stoma. Surgical resection of the LM in the mediastinum is recommended, with the possibility of intra-operative sclerotherapy as an adjunctive.

Level of Evidence: IV.

Lymphatic malformations (LMs) are rare congenital vascular malformations classified according to the International Society for study of Vascular Anomalies as macro-, micro-, or mixed cystic lesions [1]. The incidence of LMs at birth is 1 in 5000 [2]. Most LMs occur in the head–neck region and on anatomic sites with high accumulation of lymphatic glands such as the armpits and the groins. The pathogenesis of LMs is an abnormal budding of lymphatic tissue from the cardinal vein or failures to connect with or separate from the venous system during the embryogenesis [3]. LMs in the mediastinum are uncommon, however cervical LMs may expand into the mediastinum. Superficial, palpable LMs expand into deeper cavities in 6% of the cases [4]. LMs may develop in all organs and all parts of the body just as the normal distribution of the lymphatic system. The usual clinical presentation of LMs is a slowly expanding mass of lymphatic tissue, however occasionally rapid expansion of the malformation occurs due to local infections, inflammation or bleeding into the malformation. Depending on size and localization the malformation can be asymptomatic and left with only watchful observation, or cause complications by compressing vital structures and thus requiring advanced medical attention. A sudden swelling in LMs involving the mediastinum may result in a life-

* Corresponding author at: Karolinska University Hospital, Pediatric Surgery, Solna, S3:02, 171 76 Stockholm, Sweden. Tel.: +46 8 51777550.
E-mail address: nader.ghaffarpour@ki.se (N. Ghaffarpour).

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threatening complication due to compression of the airways, the large vessels and the heart [5,6]. There is insufficient evidence to develop treatment algorithms for the management of LMs. Surgical excision has traditionally been regarded as the treatment of choice for LMs [7]. Although LMs are benign lesions, they frequently, especially micro-cystic LMs, infiltrate adjacent structures, such as, vessels and nerves [7], making total resection difficult and potentially hazardous. Large LMs often require staged excisions [8]. Percutaneous sclerotherapy has replaced surgery in most cases of macro-cystic malformations [9,10]. Patients who undergo sclerotherapy with OK-432 or bleomycin as first-line therapy for head and neck LMs achieve a good to excellent clinical response [4,10].

However, sclerotherapy has limitations, and is effective in treatment of LMs in 40–80% of the cases, depending on size of the cysts in the malformation [11]. Sclerotherapy may also cause complications. There is a lack of a systematic classification system in grading complications with sclerotherapy on LM. The Clavien-Dindo classification is widely used in evaluating surgical complications [12], and objectively grades complications after surgery in relation to the extent of treatment required to cope with the complications. The Clavien-Dindo classification has been successfully used for a systematic evaluation of complications after sclerotherapy on venous malformations [13]. Although sclerotherapy for lymphatic malformations is minimally invasive and often safe, complications may occur ranging from mild systematic symptoms such as fever and fatigue to local swelling causing compression to vital functions requiring prolonged intensive care.

Furthermore, the use of sclerosing agents sometimes causes scarring due to the penetration of adjacent tissues, to the extent that subsequent surgery might be difficult or impossible. Disadvantages of sclerotherapy are the need for repeated injections, skin and soft tissue necrosis, blistering, and to some extent unpredictable swelling with the risk of causing obstruction of vital structures after discharge from the hospital. Lesions in the mediastinum represent a special challenge in this sense due to the narrow compartment with vital structures it represents. A multidisciplinary team should always tailor the treatment for LM for each patient individually and the potential risks for each treatment modality must be considered.

The aim with this study was to review our experience in the management of patients with LMs involving the mediastinum and to propose a treatment algorithm to guide the management of these rare malformations. We used the Clavien-Dindo classification to assess the complications to treatment both for the patients who had received sclerotherapy as the treatment for the LM or surgery.

1. Patients and methods

This was a descriptive retrospective chart review of all patients with LMs involving the mediastinum treated at our institution between 2009 and 2015. We collected demographic data, data on investigations, management, and complications of treatment, as well outcomes at follow up. We used the Clavien-Dindo classification system [12] to stratify the complications (Table 1). The need of antibiotics, pain relief, parenteral nutrition and blood transfusion was considered to be grade I-II complications. Grade III-IV complications were complications requiring surgery or radiological intervention and need of intensive care in general anesthesia. The need of mechanical ventilation more than eight days in the PICU after sclerotherapy was considered grad III complication. The use of repeated sclerotherapies without symptomatic relief in an intensive care patient was considered as grad III complications and comparable with other radiological interventions. Each complication was counted in order to quantify complications per treatment.

The patients were assessed with a clinical assessment scale (CAS) based on the clinical findings at last follow up (Table 2) [4]. Last MRI was analyzed for post operative or post sclerotherapy evidence of remaining LM in the mediastinum.

Table 1
Clavien-Dindo classification of surgical complications.

Grade	Description
1	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs such as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside.
2	Requiring pharmacological treatment with drugs other than allowed for grade 1 complications. Blood transfusions and total parenteral nutrition are also included.
3a	Surgical, endoscopic, or radiological intervention without general anesthesia.
3b	Surgical, endoscopic, or radiological intervention with general anesthesia.
4a	Life-threatening complication requiring intermediate care or intensive care unit management, single organ dysfunction.
4b	Life-threatening complication requiring intermediate care or intensive care unit management, multi-organ dysfunction.
5	Death of a patient.

Data are presented as frequencies, median and range. The study was approved by the Regional Ethics Review Board in Stockholm (2011/1784–32).

2. Results

Between 2009 and 2015 we treated seven patients, five girls and two boys, with LMs expanding into the mediastinum. Patient characteristics are summarized in Table 3.

Diagnosis was prenatal in three patients, neonatal in three patients and delayed to two years of age in one patient. One patient was delivered preterm (28 weeks of gestation) by emergent cesarean section due to intrauterine stress. Six patients were full-term. One of the full-term babies was delivered with an EXIT-procedure (Ex-utero Intrapartem Treatment-procedure). The vast majority of the patients (71%) had respiratory distress when the diagnosis was confirmed at postnatal MRI. All patients had predominately macro-cystic LMs with part of the malformations containing micro-cystic components, being classified as mixed LMs. Airway compromise at the time of diagnosis was common, and was encountered in 57% of the patients. Three patients had anatomical compression of the trachea and two patients had sub-total compression of the right lung. All three patients with tracheoscopy-verified compression to the trachea had compromise of the distal trachea, and a tracheostomy would not have been protective. Only one patient was given a pre-treatment protective tracheostomy and one patient required a post-operative tracheostomy due to prolonged need of mechanical ventilation.

All patients received sclerotherapy. Five patients were treated with sclerosing agents as first line of treatment and two had sclerotherapy as an adjunctive intra- and postoperatively. The sclerosing agents and doses used were OK-432 0.1 mg in four patients and bleomycin 6000 IE, doxycycline 50 mg, and sotradecol 3% 6.5 mL in one patient respectively. Two of the patients that were treated with sclerotherapy, were observed at the pediatric intensive care unit, PICU, and on

Table 2
Clinical Assessment Scale (CAS) for clinical evaluation of LM.

Clinical evaluation	Result	Score
No remaining signs and symptoms	Excellent	5
Small palpable lumps or regress of mass > 50%, rarely symptomatic	Good	4
Larger palpable lumps or regress of mass < 50%, occasionally symptomatic	Fair	3
No regress of signs and symptoms	Poor	2
Worsening of signs and symptoms	Worse	1

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