Diagnosis and surgical treatment of cervical macrocystic lymphatic malformations in infants

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Abstract. The treatment of lymphatic malformations (LMs) represents a great clinical challenge. The present study reported on the treatment of 68 infants with cervical macrocystic LMs using surgical resection. The cases were retrospectively analyzed. All patients underwent pre-operative ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) examinations. The surgery was performed under general anesthesia with endotracheal intubation. Ultrasonograms showed that 24 cases were monolocular, 44 were multilocular, 16 had no echo, 20 had a uniform low-level echo and 32 had a non-uniform low-level echo. CT showed non-enhancing low-attenuating cystic lesions and attenuation values of 10-45 HU. The magnetic resonance images of the LMs showed a low signal intensity on T1-weighted imaging (WI) and a high signal intensity on T2-WI. Complete resection was achieved in 56 patients, subtotal resection in eight and partial resection in four. Two complications were noted, including reversible paresis of the marginal mandibular branch of the facial nerve and a surgical-site infection. One patient in whom partial resection was achieved had recurrence at ~2 months after the surgery. Ultrasonography, CT and MRI clearly demonstrated the size, shape, extent and adjacent structures of LMs, which aided in surgical planning and assessment of potential risks. Surgical excision increased the chances of cure and was relatively safe for infants aged <1 year. Location and extent, rather than age, were determined to be the most important factors for successful surgical treatment.

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Introduction

Lymphatic malformations (LMs), previously termed lymphangioma, are benign congenital malformations that stem from a malformation of the lymphatic vessels in the soft tissues (1). Although LMs have been studied, no consensus has been found regarding their cause or treatment (2). They primarily occur in the head and neck, accounting for 75% of all cases (3), and grow proportional to a patient's body growth (4). In approximately half of the cases, the LMs are obvious at birth and as many as 90% are diagnosed by the end of the second year of life due to clinical symptoms (5). LMs can be solitary or multifocal and have a variety of clinical presentations based on their size and location (6). Bleeding, trauma and/or infection may rapidly increase the cyst's size, leading to respiratory obstruction, swallowing difficulties and speech problems. In a small number of cases, rapid tumor growth may occur as a result of increasing lymphatic flow and the sudden closure of drainage channels due to infection and/or the inflammatory process.

LM can be divided into three morphological types: Microcystic, macrocystic and combined (combination of microcystic and macrocystic components) (7). Various types may coexist in the same lesion. Macrocystic LMs were historically referred to as 'cystic hygroma', while microcystic LMs were referred to as 'capillary and cavernous lymphangioma'. The previous classification of lymphangioma into capillary, cavernous and cystic types, however, has little clinical value and should be abandoned (8). A dominating histological feature of LMs is endothelial-lined lymphatic channels separated by connective tissues (9).

Clinically, the treatment of LMs has remained a challenge. Current major treatments for LMs include surgical excision and sclerotherapy. Due to the tendency of LMs to gradually increase and compress the surrounding tissues, surgical resection has been recommended by numerous clinicians as the first-line treatment. For macrocystic LMs, surgical excision has been the first choice of treatment, but total excision is not easy due to their infiltration of the surrounding nerves and muscles. Complete excision without damage to vital structures is possible in most cases; however, improper surgical treatment may result in disfigurement, scarring or injury to vital structures such as the recurrent laryngeal nerve, cranial nerves and

carotid artery. The present study reported on cervical macrocystic LMs in 68 infants encountered over a 5-year period as well as their treatment.

Materials and methods

Patient data. A total of 68 infants (aged between 3 and 36 months) with macrocystic LMs in the head and neck region were included in the present study and underwent surgical resection between January 2009 and December 2015 at the Department of Otolaryngology and Head and Neck Surgery of Kunming Children's Hospital (Kunming, China). The present study was performed in accordance with the declaration of Helsinki and with approval from the Ethics Committee of Kunming Children's Hospital (Kunming, China). Written informed consent was obtained from the guardians of all participants. For all patients, the diagnosis was confirmed by histological examination after the resection. The LMs had grown slowly, a compressible mass being the only sign. The majority of the lesions were elliptical or irregularly shaped, soft, multiloculated and well-circumscribed masses with sound trans-illuminance. Exclusion criteria for the present study consisted of patients that had not undergone surgery and/or exhibited anesthetic contraindication diseases.

Patient treatment. Imaging examinations, including ultrasonography (Philips IU22; Royal Philips Electronics, Holland), computed tomography (CT; GE Optima CT660; General Electric Company, Boston, MA, USA) and magnetic resonance imaging (MRI; GE HDi 1.5T; General Electric Company) were performed. Uncooperative patients were given 10% chloral hydrate (0.5 ml/kg) orally prior to the examination. Ultrasonography was routinely performed in the axial and coronal views. The transducer frequency was 5 MHz. Lesion size, internal echo, morphology and correlation with the surrounding structures were noted. Blood supply to the lesions was observed using color Doppler imaging. The CT scan was performed from the skull to the root of the neck. When necessary, it was extended to the superior mediastinum, with a layer thickness of 5-mm, interval of 5-mm, pitch of 1.0, tube voltage of 120 kV and tube current of 240 mA. Contrast enhancement was performed via iohexol administration. The MRI scanning sequence was spin-echo (SE) T1-weighted imaging (T1WI), SE T2WI and T2WI with fat suppression.

Therapeutic decisions were individualized based on clinical features, imaging appearance and parental preference. Meticulous planning was required for surgical excision of the lesions. In all patients, the surgery was performed under general anesthesia with endotracheal intubation. Soft tissue masses were excised as completely as possible with particular attention paid to the identification and preservation of vital structures such as the carotid sheath, hypoglossal nerve, glossopharyngeal nerve, vagus nerve, accessory nerve, branch of the facial nerve, and sublingual and submandibular glands. A negative pressure drainage tube was placed after the operation. All lesions were pathologically confirmed. After the operation, side effects and complications, including fever, infection, pain, hematoma, injury to the facial nerve and respiratory difficulties were monitored and recorded.

Results

Clinical features. The patients included 35 males and 33 females with a gender ratio of approximately 1:1, and no significant difference in the incidence of complications was observed with regard to gender. Forty of the subjects were newborns (0-1 years), while the other 28 were infants (1-3 years). The mean age of the patients was 15 months (range, 3 months to 3 years) at their first treatment. The mean follow-up period was 27.8±10.5 months (range, 3-60 months), including two patients who were lost to follow-up (Table I).

Distribution and location. The anatomical locations of LMs included the left cervical region (28/68 cases), right cervical region (36/68 cases) and median cervical region (4/68 cases). A total of 24 were located in the suprahyoid region, while 44 were located in the subhyoid region (Table I). Six patients previously underwent resection in other hospitals but experienced local recurrence within 5 months. In four cases, the LMs had extended into the parotid region and infiltrated the facial nerve. Lesion size ranged from 2.8x3.2 to 6x7.8 cm (mean, 4.5x6.2 cm). The disease course was 3-12 months.

Imaging features and diagnosis. By ultrasonography, 24 LMs appeared monolocular and 44 were multilocular; 16 LMs had no echo, 20 had a uniform low-level echo and 32 had a non-uniform level echo. Their boundary with the surrounding tissues was usually clear and the lesion tension was low. Ultrasonograms of monolocular LMs showed elliptical and circular dark space. The lesion wall was thin, smooth or slightly coarse and accompanied by posterior wall acoustic enhancement. The ultrasonic manifestation of multilocular LMs was a lobulated lesion with irregular fine septation (Table I). Loose alveolar tissue was characteristic of multilocular LMs. Color Doppler imaging demonstrated no blood flow signal within the mass. Solid components were not seen in any case.

A total of 36 patients underwent CT examinations. The CT features of cervical LMs were non-enhancing, well-circumscribed lesions showing no calcifications and varying attenuation values. CT attenuation values were 10-45 HU (mean, 26 HU). Most of the LMs (32/36) had low densities, while the densities of the remaining four were identical. Eight patients underwent MRI examinations. On MRI, the lymphanigomas appeared as irregular, well-defined lesions with signs of vessel encasement. Compared with the adjacent muscles, the LMs had low signal intensity on T1WI and a high signal intensity on T2WI. Six cases had been misdiagnosed as branchial cysts, four as hemangioma and two as cervical abscesses by their local hospitals.

Treatment. Complete resection was possible in 56 patients (82.4%), while subtotal resection was performed in eight and partial resection was performed in four. For the subtotal resection cases, the lesions had extended toward the mouth floor and beneath the mandible and their complete removal was not possible. In the four partial resection cases, the LMs had wrapped around the parotid gland, including the posterior lobe. To avoid injury to the facial nerve trunk, partial resection was performed. Two complications were observed: A

Table I. Clinical features of cervical macrocystic lymphatic malformations in infants (n=68).

Characteristic	Number	Percentage of patients (%)
Age at diagnosis, months		
Mean	15	-
Range	3-36	-
Gender		
Male	35	51.5
Female	33	48.5
Age, months		
3-12	40	58.8
12-36	28	41.2
Follow-up period, months		
Mean	27.8	97[a]
Range	3-60	
Distribution		
Left region	28	41.2
Right region	36	52.9
Cervical midline	4	5.9
Location		
Suprahyoid region	24	35.3
Subhyoid region	44	64.7
Shape		
Elliptical	24	35.3
Lobulated	44	64.7

[a]In total, 2 (3%) of 68 patients lost to follow-up.

Table II. Type of treatment and outcome of cervical macrocystic lymphatic malformations in infants (n=68).

Treatment	Number	Percentage of patients (%)
Surgical procedure		
Complete resection	56	82.4
Subtotal resection	8	11.8
Partial resection	4	5.8
Outcome		
Cured	66	97.1
Recurrence	2	2.9

reversible paresis of the marginal mandibular branch of the facial nerve and a local infection.

After the resection, a histopathological examination showed that in all cases, the lesions had formed from the fibromuscular walls and lymphatic vessels with endothelial cells. No signs of malignancy were noted. Only two patients who underwent partial resection had recurrences at ~2 months after the operation (Table II). For those patients, a sclerotherapy injection with pingyangmycin (PYM; a widely used sclerosing agent for the treatment of venous malformations) was performed under general anesthesia with ultrasonographic guidance to accurately localize the cysts. The solution was prepared by dissolving 8 mg PYM in 8 ml isotonic sodium chloride. Under ultrasonographic guidance, a 22-gauge needle was inserted into the cystic space under sterile conditions. The cystic fluid was aspirated and the PYM solution was instilled into the cyst at a dose of 0.2-0.3 mg/kg. In all patients, the treatment with PYM injection achieved satisfactory results.

Case presentations

Case 1. An 8-month-old male patient presented with a giant macrocystic LM in the right lateral cervical region (Fig. 1A) which was subsequently removed (Fig. 1B). The mass was noted at birth as a small lesion and he had no obvious clinical symptoms. Over time, the mass gradually enlarged but remained painless. Ten days before the patient presented at the clinic, the size of the lesion had rapidly increased. Fine-needle aspiration obtained a slightly bloody fluid (Fig. 1C). The lesion was diagnosed as an LM with hemorrhage and was 5.9x4.8 cm in size (Fig. 1D-G). The patient underwent radical surgery under general anesthesia. The course of anesthesia and surgery was smooth. The wound healed satisfactorily within reasonable time (Fig. 1H). No complications occurred. Histopathological examination after the resection demonstrated a macrocystic LM (Fig. 1I). The patient was followed up with ultrasonography for 1 year and no sign of recurrence was noted.

Case 2. A 2-year-old boy presented with a mass that was found in the left sternocleidomastoid 1 year previously. Upon admission, ultrasonography showed a cystic mass of 3.8x2.5 cm on the deep surface of the left sternocleidomastoid with an ill-defined border. The CT attenuation value was 10-20 HU (Fig. 2A). Ultrasound-guided centesis obtained a pale-yellow liquid suggestive of left submandibular LM. The patient underwent LM resection under general anesthesia. During the operation, the mass was observed to be attached to the surrounding muscular tissues and to have infiltrated the deep surface of the internal jugular vein, and complete removal was therefore not possible. For this reason, subtotal resection was performed (Fig. 2B). The surgery proceeded smoothly and no notable post-operative complications occurred. After the resection, the wound was rinsed with bleomycin. Histopathological examination after the resection demonstrated a macrocystic LM (Fig. 2C). The patient was followed up for 1 year with no significant recurrence.

Discussion

LMs are rare congenital malformations of the lymphatic system that are generally thought to be malformations of segregated lymphatic tissues that have failed to develop into lymphatic tissues with normal communications with the regional lymphatic drainage, resulting in the dilatation of abnormal channels. The incidence of LMs is 4/10,000 to 1/16,000 at birth, accounting for 5-6% of all benign types of soft-tissue tumor in children. No significant sex or racial differences have been noted in the incidence of LMs (10). An estimated 50%

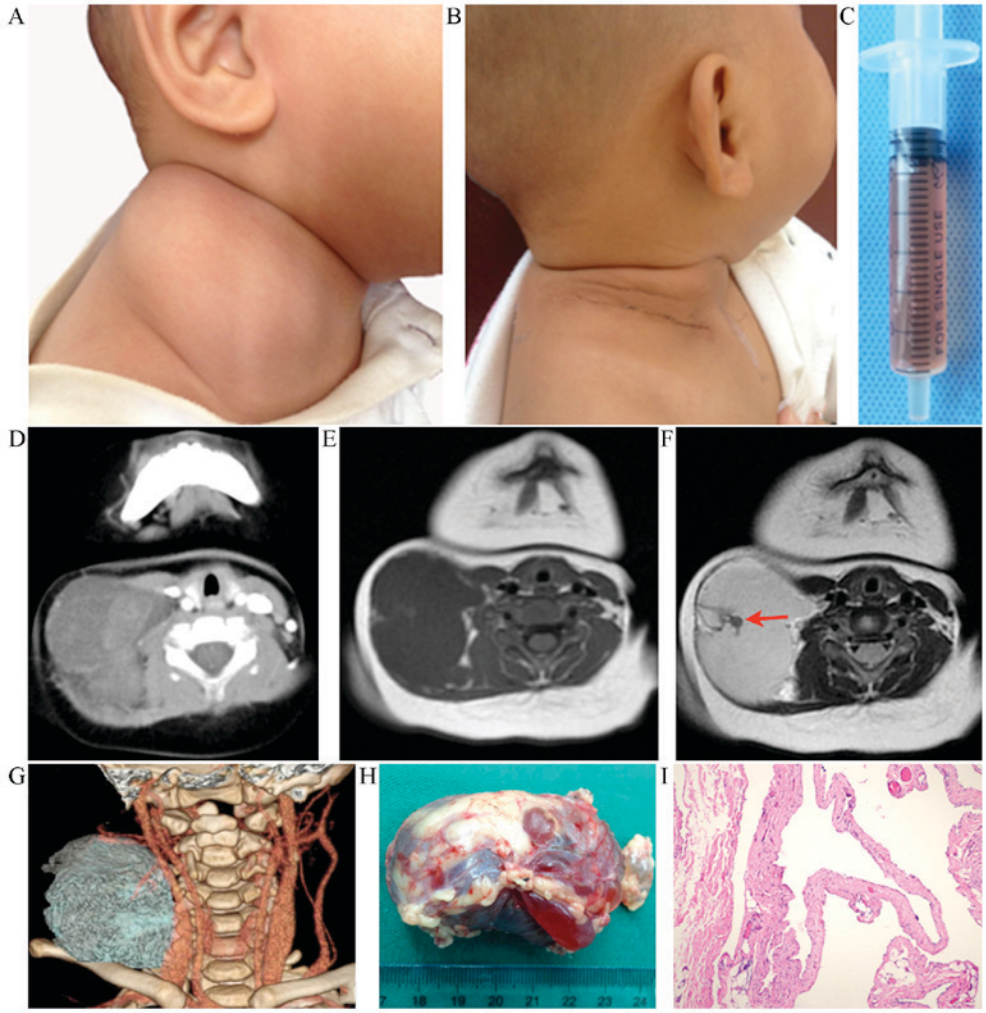

Figure 1. Case no. 1. (A) An 8-month-old male patient presented with a macrocystic lymphatic malformation in the right neck. (B) Appearance at 10 days after the operation. (C) Aspired fluid appeared to be slightly bloody. (D) CT scan revealed a huge cystic lesion (5.9x4.8 cm) in the right lateral cervical region. (E) Axial T1-weighted MRI showed low signal intensity. (F) Axial T2-weighted MRI showed high signal intensity accompanied with local hemorrhage (red arrow). (G) Three-dimensional reconstruction of CT showed new vessels on the surface of the mass. (H) A mass with hemorrhage was removed by the operation. (I) Hematoxylin and eosin staining revealed spaces lined by flat endothelial cells (magnification, 40x). CT, computed tomography; MRI, magnetic resonance imaging.

of LMs are correctly diagnosed prior to the patients reaching an age of 2 years. In the cohort of the present study, 32 cases (88.23%) were identified at birth, eight were diagnosed by 1 year, and 20 were diagnosed by reaching 2 years of age.

The clinical manifestations of faciocervical LMs vary in size and location. At birth, the lesions were usually small and patients had no obvious symptoms. Over time, clinical manifestations may gradually present, with a painless mass being the only sign. Due to the elasticity of the faciocervical skin and subcutaneous tissue, large LMs do not always cause serious symptoms. Rapid growth of the LMs may occur and cause a faciocervical deformity to interfere with breathing and/or swallowing. This may be attributed to lymphatic vessel obstruction and intracystic hemorrhage due to upper respiratory infection and/or trauma.

In the cohort of the present study, the only clinical manifestation observed in the majority of patients (56/68) was a painless mass accompanied by a cosmetic deformity of varying degrees. One infant had faciocervical motor dysfunction, another had airway obstruction and another had dysphagia. The LMs (macrocystic LMs in particular) were usually diagnosed in the clinic and had a certain degree of light transmittance. The aspirated cystic fluid had a straw-yellow color, and was transparent and apt to solidification.

Ultrasonography, CT and MRI have been widely used to assess the size and extent of LMs. In the present case series, a pre-operative ultrasound examination was routinely performed. Ultrasonography typically showed a multiloculated cystic lesion with cystic cavities divided by septa of variable thickness, but certain cases also showed an irregular or calcified appearance. Doppler imaging demonstrated no blood flow within the lesions. CT features of macrocystic LMs have included a well-circumscribed lesion showing no calcifications and varied attenuation values therein (11). Macrocystic LMs may present as low-intensity signals on T1WI and high-intensity signals on T2WI but signal intensity may be variable due to varying amounts of protein and/or hemorrhage (12). Each of the two techniques was helpful for determining the extent and nature of the cysts and their correlation with the surrounding structures. Such imaging techniques were also essential for the identification of LMs and differentiating them from other vascular malformations, branchial and thyroglossal cysts, lipomas, abscesses or thyroid masses (13).

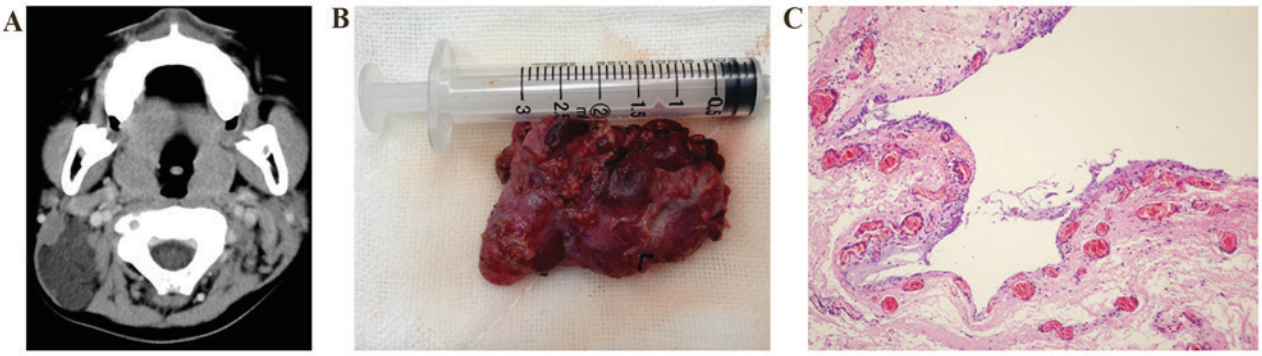

Figure 2. Case no. 2. (A) A cystic mass was found underneath the left sternocleidomastoid, with an ill-defined border and a size of 3.8x2.5 cm and a computed tomography attenuation value of 10-20 HU. (B) During the operation, the tumor was found to be attached to the surrounding muscular tissues to have deeply infiltrated the internal jugular vein. It could therefore not be completely removed. (C) Hematoxylin and eosin staining revealed that the wall of the lymphatic malformation was composed of fibrous tissue, partially lined with endothelial cells, and infiltrated by a small number of lymphocytes (magnification, x200).

In the present case series, six patients had been misdiagnosed with branchial cysts, which included four hemangiomas and two cervical abscesses, at external hospitals. Although lymphangiomas are benign, their treatment is difficult due to their propensity to infiltrate and extend to important adjacent structures. The mainstays of treatment have included the injection of sclerosing agents and surgical excision. Balakrishnan *et al* (14) found that sclerotherapy and initial surgery for head and neck LMs were similar in effectiveness in a multisite comparison, including total hospital days, total intensive care unit days and higher likelihood of subsequent tracheostomy. Sclerotherapy appears accurate, minimally invasive, safe, low-cost and reliable without complications, particularly for cervicofacial LMs in infants and children (7). However, most cases may require repeated injections with intervals varying from weeks to months. Certain patients may have poor reactions and/or serious allergic reactions to the sclerosing agents. Therefore, this strategy must be abandoned in certain cases. Moreover, this does not necessarily exclude later surgical treatment.

In 2007, Okazaki *et al* (15) reported their experience of treating 128 cases with lymphangioma with OK-432 and surgery. They found that sclerotherapy may cause fever, infection, upper respiratory tract obstruction or anaphylactic shock and suggested that sclerotherapy with OK-432 was not as effective as previously reported, although it may be efficient for a relatively long time. In the past 20 years, intralesional laser therapy (carbon dioxide or neodym-yttrium-aluminium garnet laser) has also been introduced for the treatment of LMs (16). Laser ablation is suitable for superficial mucosal lesions. However, in most LMs, the cysts are often connected with the expansion of a deep cyst connected to the muscular tissue. Due to their pathological features and the limitations of laser penetration, deep lesions are difficult to eradicate and prone to relapse.

In 2012, Swetman *et al* (17) reported a marked regression of severe LMs in three children after the treatment with orally administered sildenafil. The authors suggested that the drug may act by relaxing smooth muscles, resulting in decompression of the cyst. This relaxation may also allow the secondary lymphatic space to reopen. Sildenafil may also normalize endothelial dysfunction of the lymphatic system.

Surgery has retained an important role in the treatment of head and neck LMs in children (18). Surgical excision achieves higher cure rates and may be an appropriate first-line therapy for giant macrocystic LMs involving the cervicofacial region. The surgical results depend on the location and extent of the lesion. Lesions located in low-risk regions, such as the posterior cervical triangle, should be subjected to surgery as soon as possible, the outcomes of which are usually satisfactory. Secure surgery may be achieved for lesions located in the submaxillary and parotid regions. Should complete excision jeopardize vital structures and/or functions, partial resection should be performed.

In general, isolated neck lesions have the highest rate of complete resection. In the present case series, total resection was achieved in 56 of 68 patients, while eight patients underwent subtotal resection and four underwent partial resection. In two cases, post-operative complications were observed, namely reversible paresis of the marginal mandibular branch of the facial nerve and local wound infection. Each of the two cases was treated conservatively.

Chen *et al* (19) reported their experience of surgical excision of cervicofacial giant macrocystic LMs in infants and children. In 89.4% of the cases, complete resection was achieved, with minor complications occurring in 19.1%. Surgical excision was considered safe and yielded satisfactory esthetic and functional results.

Intubation and nursing of the airway may also be a clinical challenge. The infantile throat has a fragile mucosa and narrow airway, particularly at the glottis and cricoid; therefore, it is prone to laryngeal edema. The prophylactic use of corticosteroids prior to intubation is necessary. Laryngoscopy and intubation should be performed gently. Intubation under light anesthesia may induce swallowing and choking, causing friction of the catheter with cricoid mucosa and resulting in post-operative laryngeal edema. Children with huge cervical LMs may also experience tracheal cartilage softening as a result of long-term compression. As the tracheal stent formed by the surrounding tissue may disappear after the resection, tracheal collapse may occur, resulting in airway obstruction. Therefore, tube withdrawal should occur in steps after the surgery once the patients have become fully awake. Extubation should be performed in 1-cm steps. If no sign of airway

obstruction is present, the tube is withdrawn for another 1 cm each time until it is completely removed.

During the first year of life, observation is necessary, since the lesions may cause severe deformity and/or complications. A previous study has suggested that spontaneous regression may occur (20). Kennedy *et al* (21) suggested that the surgery should be performed when the patient is >2 years of age when the cervical mass is the only sign. For such patients, the minimum age at surgery should be 3 months. The results of the present study suggest that patient age is not a crucial factor regarding treatment. The operation may be delayed until the patient is at least 12 months of age, when the cervicofacial tissue has fully developed and the patients can better tolerate general anesthesia. The possibility of complete excision, risk of post-operative complications, injury to adjacent structures as well as scarring should be carefully evaluated.

Surgeons who operate on large macrocystic LMs must be familiar with the complex anatomy of the blood vessels, nerves and muscles (19). Important structures such as nerves, muscles and vessels surrounding the adjacent masses should not be injured. The general goal of surgical treatment is to remove the tissue involved without sacrificing any vital structures. The complications of surgical excision depend on the location of the LM and the affected structures. The most common complications include damage to neurovascular structures such as the cranial nerves, chylous fistula, chylothorax, hemorrhage and recurrence (22).

In conclusion, cervical LMs may manifest with a range of clinical features. Ultrasonography, CT and MRI are effective methods for their pre-operative diagnosis and safety evaluation. Therapeutic decisions should be individualized and based on clinical features, imaging and a multidisciplinary consultation. To achieve optimal treatment, a problem-based approach should be adopted. LM location, size and clinical manifestations may significantly influence the treatment plan. Surgical excision remains the mainstay of treatment. Complete resection is the standard approach and can be achieved in most cases. Should the lesions be too large and their neighboring structures prone to injury, complete resection should not be attempted. Surgeons should be aware of the limitations and potential complications. Leaving a small amount of residual lesion to avoid complications is acceptable.

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References

1. Mulliken JB, Burrows PE and Fishman SJ: Mulliken and Young's vascular anomalies: Hemangiomas and malformations. Oxford, Oxford University Press, 2013.
2. Cho BC, Kim JB, Lee JW, Choi KY, Yang JD, Lee SJ, Kim YS, Lee JM, Huh S and Chung HY: Cervicofacial lymphatic malformations: A retrospective review of 40 cases. Arch Plast Surg 43: 10-18, 2016.
3. Vlahovic A, Gazikalovic A and Adjic O: Bleomycin sclerotherapy for lymphatic malformation after unsuccessful surgical excision: Case report. Acta Otorhinolaryngol Ital 35: 365-367, 2015.
4. Wiegand S and Werner JA: Lymphatic malformations in the head and neck area. HNO 64: 133-142, 2016 (In German).
5. Werner JA, Dünne AA, Folz BJ, Rochels R, Bien S, Ramaswamy A and Lippert BM: Current concepts in the classification, diagnosis and treatment of hemangiomas and vascular malformations of the head and neck. Eur Arch Otorhinolaryngol 258: 141-149, 2001.
6. Farnoosh S, Don D, Koempel J, Panossian A, Anselmo D and Stanley P: Efficacy of doxycycline and sodium tetradecyl sulfate sclerotherapy in pediatric head and neck lymphatic malformations. Int J Pediatr Otorhinolaryngol 79: 883-887, 2015.
7. Yang Y, Sun M, Ma Q, Cheng X, Ao J, Tian L, Wang L and Lei D: Bleomycin A5 sclerotherapy for cervicofacial lymphatic malformations. J Vasc Surg 53: 150-155, 2011.
8. Ameh EA, Caouette-Laberge L and Laberge JM: Lymphangiomas. In: Ameh EA, Bickler SW, Lakhoo K, Nwomeh BC, Poenaru D (eds): Paediatric surgery: A comprehensive text for Africa. GLOBAL HELP Organization Seattle, pp649-654, 2011.
9. Ates LE, Kapran Y, Erbil Y, Barbaros U and Dizdaroglu F: Cystic lymphangioma of the right adrenal gland. Pathol Oncol Res 11: 242-244, 2005.
10. Zadvinskis DP, Benson MT, Kerr HH, Mancuso AA, Cacciarelli AA, Madrazo BL, Mafee MF and Dalen K: Congenital malformations of the cervicothoracic lymphatic system: Embryology and pathogenesis. Radiographics 12: 1175-1189, 1992.
11. Zakaria RH, Barsoum NR, El-Basmy AA and El-Kaffas SH: Imaging of pericardial lymphangioma. Ann Pediatr Cardiol 4: 65-67, 2011.
12. Chaabouni A, Rebai N, Fourati M, Rekik S, Chabchoub K, Slimen MH, Bahloul A and Mhiri MN: Cystic lymphangioma of the kidney: Diagnosis and management. Int J Surg Case Rep 3: 587-589, 2012.
13. Fung K, Poenaru D, Soboleski DA and Kamal IM: Impact of magnetic resonance imaging on the surgical management of cystic hygromas. J Pediatr Surg 33: 839-841, 1998.
14. Balakrishnan K, Menezes MD, Chen BS, Magit AE and Perkins JA: Primary surgery vs primary sclerotherapy for head and neck lymphaticmal formations. JAMA Otolaryngol Head Neck Surg 140: 41-45, 2014.
15. Okazaki T, Iwatani S, Yanai T, Kobayashi H, Kato Y, Marusasa T, Lane GJ and Yamataka A: Treatment of lymphangioma in children: Our experience of 128 cases. J Pediatr Surg 42: 386-389, 2007.
16. Balakrishnan A and Bailey CM: Lymphangioma of the tongue: A review of pathogenesis, treatment and the use of surface laser photocoagulation. J Laryngol Otol 105: 924-930, 1991.
17. Swetman GL, Berk DR, Vasanawala SS, Feinstein JA, Lane AT and Bruckner AL: Sildenafil for severe lymphatic malformations. N Engl J Med 366: 384-386, 2012.
18. Boardman SJ, Cochrane LA, Roebuck D, Elliott MJ and Hartley BE: Multimodality treatment of pediatric lymphatic malformations of the head and neck using surgery and sclerotherapy. Arch Otolaryngol Head Neck Surg 136: 270-276, 2010.
19. Chen WL, Zhang B, Wang JG, Ye HS, Zhang DM and Huang ZQ: Surgical excision of cervicofacial giant macrocystic lymphatic malformations in infants and children. Int J Pediatr Otorhinolaryngol 73: 833-837, 2009.
20. Perkins JA, Maniglia C, Magit A, Sidhu M, Manning SC and Chen EY: Clinical and radiographic findings in children with spontaneous lymphatic malformation regression. Otolaryngol Head Neck Surg 138: 772-777, 2008.
21. Kennedy TL, Whitaker M, Pellitteri P and Wood WE: Cystic hygroma/lymphangioma: A rational approach to management. Laryngoscope 111: 1929-1937, 2001.
22. Kumar V, Kumar P, Pandey A, Gupta DK, Shukla RC, Sharma SP and Gangopadhyay AN: Intralesional bleomycin in lymphangioma: An effective and safe non-operative modality of treatment. J Cutan Aesthet Surg 5: 133-136, 2012.