INVITED ARTICLE

Lymphatic malformations: Review of current treatment

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ABSTRACT

OBJECTIVE: Summarize current knowledge of lymphatic malformation medical, sclerotherapy, and surgical treatment; and highlight areas of treatment controversy and treatment difficulty that need improvement.

METHODS: Panel presentation of various aspects of lymphatic malformation treatment.

RESULTS: The mainstay of lymphatic malformation treatment has been surgical resection, which has been refined through lesion staging and radiographic characterization. Intralesional sclerotherapy in macrocystic lymphatic malformations is effective. Suprahyoid microcystic lymphatic malformations are more difficult to treat than macrocystic lymphatic malformations in the infrahyoid and posterior cervical regions. Bilateral suprahyoid lymphatic malformations require staged treatment to prevent complications. Lymphatic malformation treatment planning is primarily determined by the presence or possibility of functional compromise. Problematic areas include chronic lymphatic malformation inflammation, dental health maintenance, macroglossia, airway obstruction, and dental malocclusion.

CONCLUSIONS: Lymphatic malformation treatment improvements have been made through radiographic characterization and staging of lymphatic malformations. Direct malformation involvement of the upper aerodigestive tract can cause significant functional compromise that is difficult to treat.

Lymphatic malformations (LMs) are one type of vascular malformation and consist of masses of abnormal lymphatic channels that most commonly involve the head and neck, occurring in one out of 2000 to 4000 live births.[1] Consequently, otolaryngologists/head and neck surgeons play a central role in the team management of these patients. LMs frequently involve the oral cavity/pharynx, skin, and/or mediastinum; occasionally affect vital functions; and frequently cause disfigurement. Standard LM treatment is ablative and variably successful, necessitating multiple treatments and long-term management.[2-4] An estimated 3000 LM-specific procedures are performed in the United States annually.[5] Tongue procedures are necessary in 30 to 50 percent of LM cases.[6,7] All current indications for LM therapy in the upper airway and digestive tract are related to improving function, as complete LM ablation is impossible in this area. Although LM and radiographic characterization are beneficial for planning treatment and predicting lower-stage lesion treatment outcomes, further progress in treatment assessment is still necessary for improving treatment of all LMs.

This document summarizes current knowledge and the panel's opinions regarding LM treatment and highlights problematic treatment areas.

Indications for Lymphatic Malformation Treatment

The principal goal of LM management is restoration or preservation of functional and aesthetic integrity. All treatment is based on a thorough initial assessment to detect the degree of functional impairment and/or disfigurement. It is the panel's opinion that severe life-threatening functional impairment necessitates early treatment. When there is no significant functional deficit, treatment can be delayed well past infancy and may consist of surgery, sclerotherapy, or observation. Treatment timing relative to the age of the patient is somewhat debatable. LMs of small dimensions, without functional impairment or cosmetic disfigurement, do not necessarily require treatment. The possibility of spontaneous regression in low-stage macrocystic LM suggests that observational monitoring may also be appropriate in children with asymptomatic cervical LM, regardless of
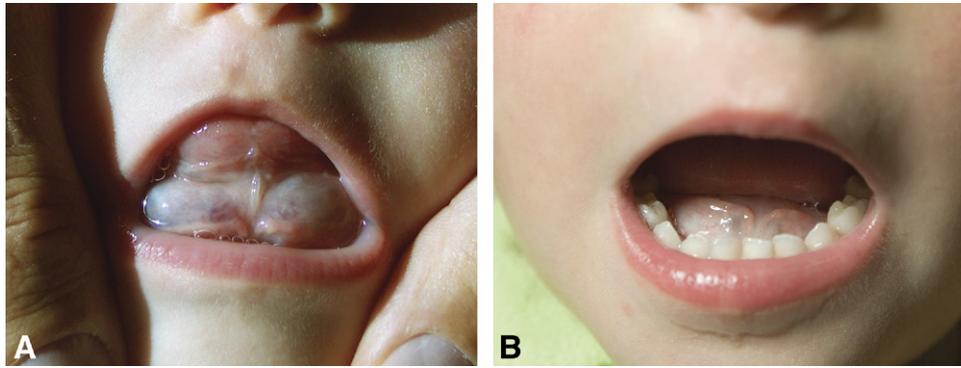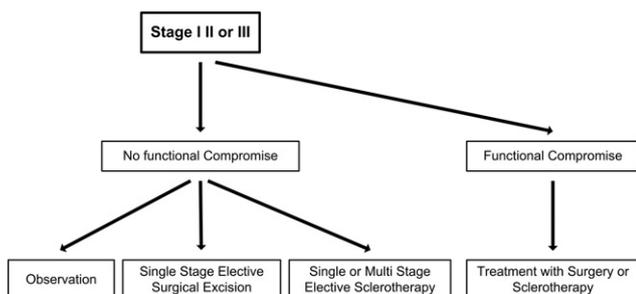
Figure 1   Regression of lymphovenous malformation, floor of mouth. Patient with stage II suprahyoid lesion involving only the floor-of-mouth and submental region (**A**), showing regression over two years without treatment (**B**). No functional compromise or malocclusion present in this patient.

size, particularly when they are located in the posterior neck (Fig 1).[1,6] Even small LMs can, however, suddenly and impressively expand in size in the setting of intra-LM hemorrhage, infection, or trauma. Extensive cervicofacial LMs have the potential for aerodigestive tract compromise, in addition to causing long-term sequelae such as mandibular distortion, dental malocclusion, and speech impairment.[8] The panel's opinion is that these lesions require careful treatment planning with multidisciplinary input. The stigma of cosmetic deformity during childhood cannot be ignored. All these factors contribute to the indications and timing of intervention.

Pretreatment Imaging and Staging of Lymphatic Malformations

Preoperative staging is a necessity for both treatment planning and prognostic discussion[2] (Figs 2 and 3). Computed tomography (CT), magnetic resonance imaging (MRI), or a combination thereof provides diagnostic confirmation, delineates LM anatomical extension and relationship to surrounding cervicofacial structures, differentiates macrocystic versus microcystic characteristics, and documents potential complicating factors such as an associated venous malformation component or prominent draining blood vessels.[9,10] Imaging also identifies LMs that are more likely to regress without treatment.[6] A clinicoradiologic staging system has

been devised based on cervical LM laterality (unilateral or bilateral) and relationship to the hyoid bone (infrahyoid or suprahyoid).[2] This classification yields five possible stages that have demonstrated clinical relevance in terms of predicting operative risk and surgical outcome (Fig A1, available online at www.otojournal.org).[2,11] The presence of mediastinal disease extension further increases the risk of infrahyoid LM.[11] In general, bilateral microcystic suprahyoid LMs are more difficult to treat than infrahyoid (macrocystic or microcystic) LMs, especially when there are microcystic LMs involving the oral cavity, tongue, and/or pharynx.[12,13]

Surgical Lymphatic Malformation Treatment

The principal goal of surgical LM management is lesion excision with restoration of functional and aesthetic integrity. The operative approach must take into account that this is a benign disease process that warrants preservation of vital structures. Although complete LM excision is desired, subtotal or partial LM removal, which often is adequate treatment, may be dictated by specific organ involvement or

Figure 2   Treatment decision making algorithm for stage I, II, and III lymphatic malformations.
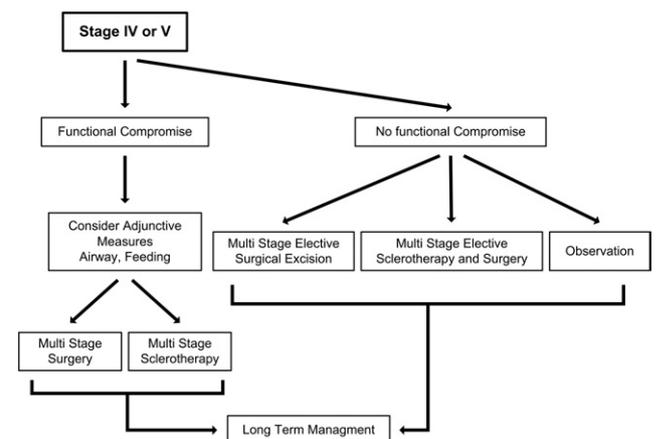
Figure 3   Treatment decision making algorithm for stage IV and V lymphatic malformations.

Figure 4   (A) Preoperative axial MRI and (B) clinical appearance. Patient with stage IV lymphovenous malformation after two staged surgical procedures separated by greater than one year. (C) Clinical appearance after right neck surgery. (D) Clinical appearance after left neck surgery. Tracheotomy was avoided and normal masticatory and respiratory function was maintained.

proximity to neurovascular structures.[14] Although residual LM is left in such circumstances, incomplete excision does not absolutely imply recurrence requiring additional therapeutic intervention.[4]

Total or subtotal resection of macrocystic infrahyoid and suprahyoid LM is often possible, even in cases of bilateral disease with extrinsic compression of the aerodigestive tract.[14] Such surgery may require unilateral or bilateral functional neck dissection(s), sometimes in staged fashion (Fig 4). LM macrocyst size or relationship to the hyoid bone does not seem to affect the possibility of surgical or sclerotherapy treatment. Infiltrative microcystic LM in any location is much less amenable to surgical resection, due to infiltrative fibrotic changes in this tissue that obscure normal anatomy.[3] This is particularly true of bilateral suprahyoid LM with intrinsic aerodigestive tract compromise, where posttreatment swelling can cause oropharyngeal obstruction. Tracheotomy and gastrostomy tube placement may be necessary in such cases, and partial LM removal may be all that is possible to ensure postoperative functional integrity. Adjuvant treatments, such as laser phototherapy or coblation, may help control symptomatic aerodigestive tract mucosal disease.[15-17]

The presence of extensive tongue and floor-of-mouth involvement in stage IV or stage V LM is common. The oral cavity LM, if amenable to surgical treatment, will need to be addressed along with cervical LM resection due to postoperative floor-of-mouth and tongue edema. A divergence of opinion exists regarding the timing of the treatment of the neck and oral cavity.[18] Some advocate early tongue and floor-of-mouth treatment to enlarge the upper aerodigestive tract and then remove bulky neck LM. Others prefer removing neck and floor-of-mouth LM and reducing tongue size if macroglossia develops. The panel's opinion is that if surgery is done for LM in this region, a unilateral neck and floor-of-mouth dissection should be performed, followed by at least a one-year recovery period for regrowth of lymphatic drainage before operating on the opposite side. There is no publication that specifically analyzes posttreatment outcomes for floor-of-mouth and/or tongue LM or this staged approach.[19] In all bilateral neck LMs with tongue and floor-of-mouth involvement, airway stabilization needs to be anticipated, particularly if the child has not required a

bypass tracheotomy to date, and the panelists recommend perioperative use of high-dose dexamethasone therapy to reduce postoperative swelling.

LM involvement of the parotid gland also deserves special mention. Macrocystic LM of the parotid is resectable by total parotidectomy with facial nerve dissection.[20] Parotid LMs, however, are usually a mixture of both macrocystic and microcystic components, making complete resection difficult and complicating management from a facial nerve protection standpoint. Intraoperative facial nerve monitoring is essential. LM is usually present lateral and medial to the facial nerve. The surgeon operating in this region must be prepared to perform a total facial nerve dissection to remove LM medial to the facial nerve. It is the panel's opinion that if surgically treated LMs involve the neck and parotid region, surgery must address both regions simultaneously. There is no consensus regarding the efficacy of a total or partial parotidectomy, but frequently a total facial nerve dissection is necessary for LM resection.

The higher the clinicoradiologic stage, the greater the potential risk of intraoperative and postoperative complications.[2,11] Depending upon LM location, there is potential operative risk to cranial nerves VII, IX, X, and XII as well as to the sympathetic nerve. Postoperative seroma or lymphocele formation is very common, with subsequent secondary risk of wound infection. Postoperative suction drainage is required, and prolonged lymphorrhea may require medical management akin to that used for iatrogenic thoracic duct injury.[21]

Issues in Sclerotherapy

Recent advances in sclerotherapy have expanded contemporary LM management options. Complete surgical resection may be difficult due to the presence of multiple loculations and extensive disease.[22-28] Sclerotherapy provides a treatment option in such patients, offering a viable alternative to surgery in patients with macrocystic LMs.[22-29] Although the popularity of sclerotherapy in the treatment of LM is growing, there is no consensus regarding the type of sclerosant. This is largely due, in part, to a lack of understanding on sclerosant mechanism of action (Table 1).

Table 1
Sclerosants used in lymphatic malformation treatment

| Sclerosant |
| --- |
| Picinabil (OK-432) |
| Bleomycin |
| Doxycycline |
| Acetic acid |
| Alcohol |
| Hypertonic saline |

Following Ogita et al's initial description in 1987,[29] the sclerosant OK-432 has prompted research in order to obtain Food and Drug Administration (FDA) approval for use in the United States.[30] OK-432 is a lyophilized mixture of group A *Streptococcus pyogenes* and benzylpenicillin. After injection, OK-432 remains confined within the malformation, resulting in obliteration of lymphatic channels, reportedly with minimal local fibrosis.[31] It is thought that LM endothelial damage occurs secondary to activation of the host immune system. There is evidence that OK-432 activates neutrophils, macrophages, natural killer cells, and cytotoxic T cells and elevates levels of many soluble immune mediators such as interleukin 1 and 2 and natural killer–activating factor.[31-33] There have been numerous case series reporting that macrocystic lymphatic malformations were completely or satisfactorily treated with OK-432, while mixed or microcystic lymphatic malformations responded less favorably.[26,29,31-34] The main disadvantage of OK-432 therapy is a theoretical risk of shock-like symptoms, particularly in those with penicillin allergy. Additional drawbacks include local edema and the need for multiple applications.[30,31,33,34] Published series have reported means of 2.0 to 4.3 OK-432 treatment sessions, with a total length of treatment ranging from one to 10 months.[26,31,33,34]

Bleomycin was initially developed as an anti-tumor agent in 1966.[35] In addition to its activity as an inhibitor of DNA synthesis, bleomycin incites a mild inflammatory effect on endothelial cells. Bleomycin may be administered in one of two forms, as bleomycin oil or bleomycin hydrochloride (aqueous). Reports of macrocystic LM treatment have shown good or excellent results in as many as 88 percent of cases. Common immediate side effects of bleomycin sclerotherapy are slight local swelling and inflammation. However, the major concern with bleomycin use is the potential risk of interstitial pneumonia and pulmonary fibrosis, which has been associated with intravenous bleomycin administration exceeding the total cumulative dose of 400 mg.[27,35] Bleomycin doses used in sclerotherapy are small in comparison, typically one to five percent of the lowest dose associated with possible pulmonary fibrosis. Renal insufficiency with creatinine clearance of less than 25 to 35 mL per minute can variably increase bleomycin dose and therefore increase risk of complications.[36]

Doxycycline, a broad-spectrum antibiotic, is also a metalloproteinase inhibitor. Based on this finding, it has been used as a vascular malformation sclerosant alone or in combination with ethanol. It is a safe and effective sclerosant for macrocystic LM. Doxycycline is used by some as a first-line treatment for macrocystic LM[37] and has been combined with surgery for microcystic LM.[38] This agent creates an inflammatory effect and produces fibrosis similar to other agents. Administered at a concentration of 5 to 20 mg/mL, the typical infusion technique is based on lesion size. If LM cysts are smaller than 3 cc in diameter, doxycycline is administered with fluoroscopy and left within the lesion for variable periods of time. LM cysts greater than 3 cc are typically sclerosed through a temporary pigtail catheter, with or without a drain. Six hours after doxycycline injection, all sclerosant is removed. This process is typically repeated once daily for three days with variable periods of percutaneous drainage.[37] Shiels has used doxycycline for microcystic LM placed through direct needle injection.[37] Doxycycline is favored among some pediatric interventional radiologists as an effective lymphatic sclerosant and is effective in sclerosing chylous pleural effusions.[39] Potential complications include tooth discoloration when administered to patients less than eight years of age, electrolyte abnormalities (acidosis and hypoglycemia), local infection, and significant local inflammation and pain.

LM sclerosis with 40 to 50 percent acetic acid usually requires only one treatment session and its effects are reported to be rapid. It is thought that the desiccating action of acetic acid produces a powerful protein-induced coagulation necrosis within lymphatic channels.[40] Although effective, serious side effects such as significant local tissue loss, scarring, and potentially acute renal failure may occur.[40,41] Ethanol, although used for other vascular malformations, is infrequently utilized today for LM due to its substantial side effects.[38] Ethanol is used in combination with Sotradecol (Bioniche Pharma USA, Lake Forest, IL), by some, for macrocystic LM. In this method, the macrocystic lesions are drained with one or two percutaneous drains, after opacifying them with contrast to rule out a venous component (Figs 5 and 6). The contrast is drained, and then half the volume of the contrast is replaced with three percent Sotradecol and left in the LM cyst for three minutes. After draining the Sotradecol, the same volume of absolute ethanol is placed in the LM cyst for 15 minutes, and then the cyst is percutaneously drained for three to five days.[37] Current indications for absolute ethanol sclerotherapy are limited to very select cases.[42] Complications such as respiratory depression, cardiac arrhythmia, seizure, rhabdomyolysis, and hypoglycemia are well documented. Hypertonic saline is also occasionally used for LM. It is thought to sclerose by localized dehydration and hyperosmotic endothelial cell damage.[43] Side effects of hypertonic saline use include risks of hypernatremia, hyperchoridia, and significant fluid shifts.

Special consideration is required when planning sclerotherapy for LMs in sensitive areas such as the orbit or any
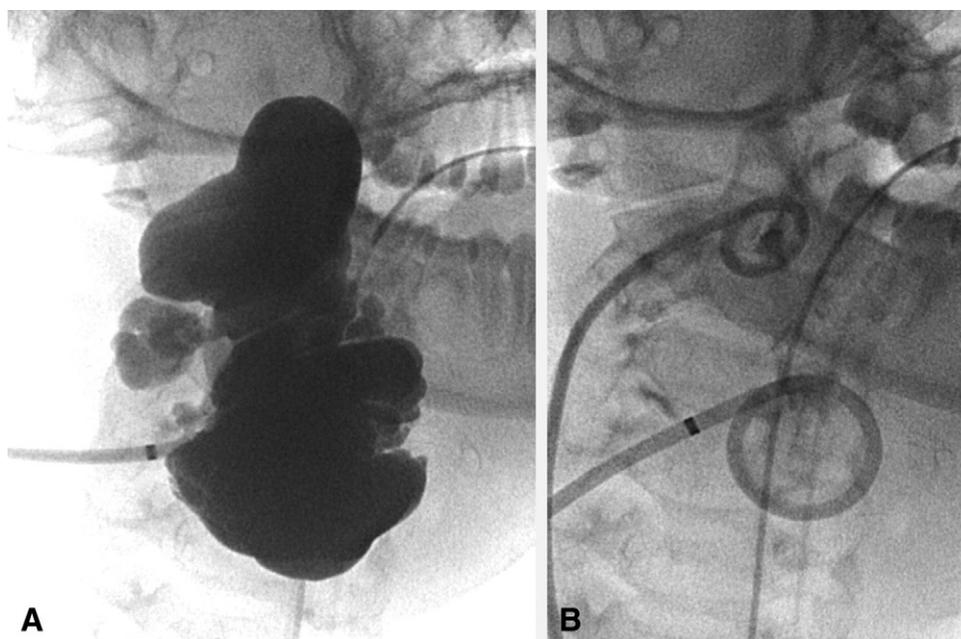
Figure 5 (A) Percutaneous drainage through one catheter filled two large spaces but only drained the lower portion. (B) A second catheter placement effectively drained 45 mL from the whole malformation. A total of 24 mL of Sotradecol was placed for three minutes in the catheters and redrained; subsequently, 25 mL of absolute ethanol was placed for 15 minutes and then redrained. The catheters were left in for five days and then removed.

area where the airway might be compromised. Most sclerosants are associated with significant posttreatment edema.[27,31] In locations in which swelling may compromise the airway, bleomycin may be preferable as it causes less inflammation. This is an especially beneficial application of sclerotherapy because LM treatment in these sensitive areas can be difficult or associated with complications. The orbit is another area where sclerotherapy is typically avoided for fear of swelling. Surgical planning for intraorbital lesions is difficult and the results can be discouraging, as the risk of vision loss is high.

Although sclerotherapy has been most effective in the management of macrocystic LM, it is important to consider that microcystic disease may also improve with sclerotherapy. A 14 percent complete response rate following sclerosant treatment of microcystic lesions has been reported,[38,42] while others have found intermediate improvements in clinical appearance approximating 50 percent.[44] These positive results, although inferior to the results with macrocystic disease, are important to consider when thinking about a long-term strategy for large microcystic LM.

Several technical aspects of sclerosant application are important to consider. Prior to any sclerosant injection, the aspirated fluid should be examined to confirm the diagnosis. The fluid should be thin and tan in color. If mixed with blood, the fluid should easily separate from the blood when examined. In order to enhance the sclerosant effect, it is helpful to maximize the interaction between the sclerosant and the endothelial cell. Removing all fluid from within the malformation prior to introducing the sclerosant is the most
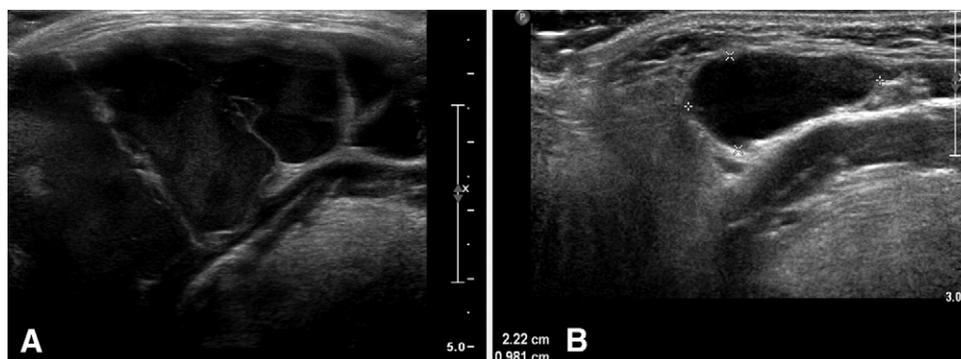
Figure 6 (A) Ultrasound demonstrated a lymphatic malformation right parotid region in a 12-year-old girl admitted for antibiotic therapy that contained approximately 107 mL of bloody fluid. (B) Follow-up ultrasound showed only 3 mL of fluid remained three months after sclerotherapy.

Figure 7 Infection in six-month-old with stage IV lymphovenous malformation. The patient required parenteral antibiotics and skin care for infection resolution.

important technical aspect. Using an appropriate volume of sclerosant may also be important. In a small lesion, a large volume of sclerosant may distend the lesion, preventing the resulting inflammation from obliterating the cavity. Even though recent decades have seen a rapid evolution in this exciting therapy, further improvements in technique and materials may enhance the ability to treat lymphatic vascular malformations.

Problem Areas in Lymphatic Malformation Treatment

Infection and Immunodeficiency

Infection is a common problem with LM, especially in the suprahyoid microcystic or mixed variety with mucosal involvement. Infection can trigger marked swelling and thereby aggravate airway and feeding issues. Recurrent infection often provides motivation for considering surgical excision. Infection is treated acutely with appropriate broad-spectrum antibiotics, and the addition of systemic corticosteroids seems to offer a significant treatment benefit[1] (Fig 7).

Recent studies have shown that patients with large bilateral or microcystic LM have significant lymphocytopenia involving T, B, and NK cell subsets. The lymphocytopenia does not appear to be related to lymphocyte sequestration within the malformations, as histologic examination of surgical specimens does not demonstrate unusual lymphocyte density.[45] Lymphocytopenia may be part of the fundamental developmental process of lymphatic malformations. In a follow-up study, patients with large bilateral or microcystic lesions with lymphocytopenia were found to have more hospitalizations, more central line placements for antibiotics, and more treatment complications versus LM patients without lymphocytopenia.[46]

### Dental Health and Lymphatic Malformation Management

Basic oral care and dental health maintenance for patients with oral and tongue involvement are important. Even rudimentary oral hygiene efforts are troublesome and uncomfortable, and may cause bleeding and irritation of the affected soft tissues. Unfortunately, the consequences of poor oral hygiene, such as dental caries and periodontal inflammations, can contribute significantly to tongue and floor-of-mouth LM swelling, leading to airway compromise. When orthodontic appliances are used to treat malocclusion, tongue LM inflammation is common. Frequent hygiene visits, basic dental restorative care, and occasionally the removal of troublesome teeth are required to best control these issues.

Skeletal and Soft Tissue Malformation and Hypertrophy

Primary bony involvement of the mandible is common with larger beard-distribution suprahyoid lesions, and a large percentage of these high-stage patients will have significant mandibular deformities[47] (Fig 8). Skeletal overgrowth may be, in part, due to local effects of the LM, but primary histologic LM involvement of the bone is also common.
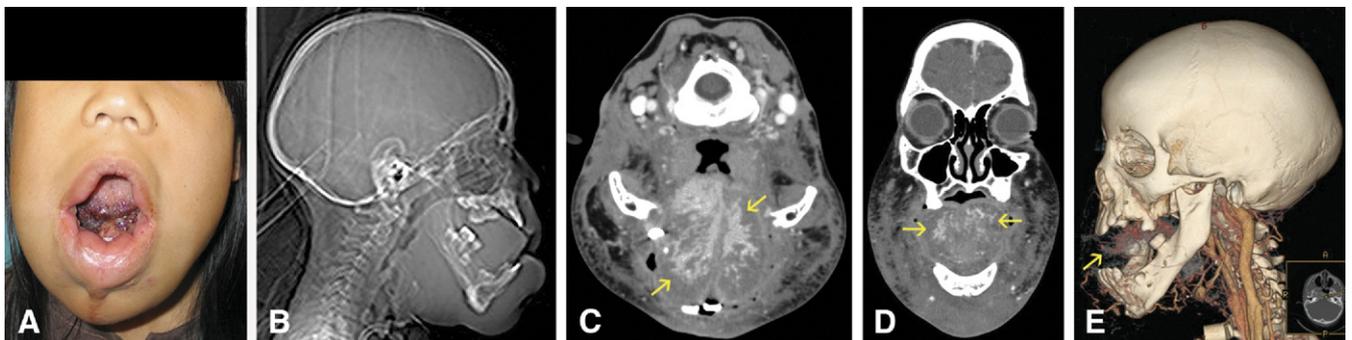
Figure 8 Stage IV lymphovenous malformation (**A**) in an adolescent patient born with an enlarged mandible (**B**). Note the increased vascularity of the tongue as seen on CT angiography (*yellow arrows*, **C, D, E**) years after initial tongue surgery. Dental extraction of primary dentition was performed to reduce tongue trauma.
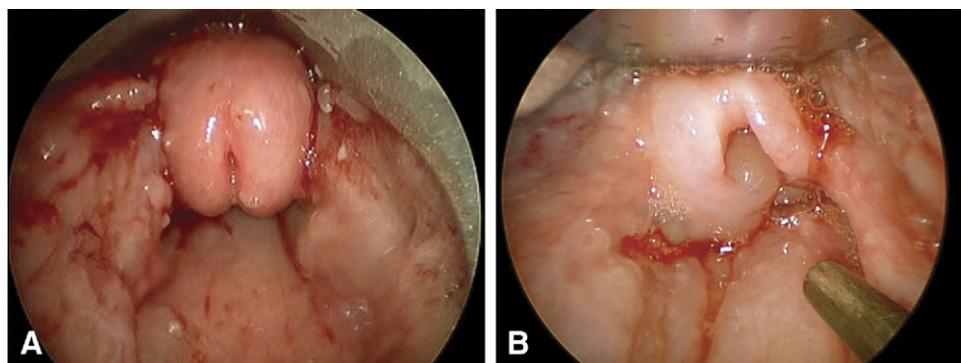
Figure 9   (A) Laryngeal involvement with lymphovenous malformation in patient with stage IV malformation. Note the symmetric enlargement of the epiglottis. The glottic and subglottic airways are normal. (B) Lymphovenous malformation causing swelling of the left pharyngoepiglottic fold, arytenoids, and epiglottis.

Anecdotally, early surgical excision of the soft tissue LM does not appear to change the rate or incidence of bony involvement. In some series of beard-distribution LM, a large percentage of patients undergo mandibular osteotomies at some point. The timing of orthodontic care and mandibular osteotomies is dependent on multiple factors, including tongue size, airway status, and oral hygiene, so these interventions are usually planned in adolescence. Maxillary and/or mandibular osteotomies for patients with LM are considered for multiple reasons. These reasons include improvements in both function and aesthetics. Distortions of jaw shape can have significant impact on oral and masticatory functions. Open-bite deformities and oral incompetence, with associated problems of excessive drooling, difficulty with speech articulation, and occasionally airway maintenance, are seen in severe cases, especially where tongue and floor-of-mouth involvement is prominent. Consideration of jaw surgery to minimize these deformities and improve quality of life is appropriate. When jaw surgery is contemplated, the surgical plan for jaw movement needs to account for the increased soft tissue bulk seen with intraoral LM. Most often, jaw surgery is offered when skeletal growth is complete, but occasionally patients with severe facial skeletal distortion may benefit from earlier surgery. Osteotomies used are commonly used for orthognathic procedures, but also may include facial contouring procedures and ostectomies to improve facial symmetry and jaw form.[6] Ideally, it is best to coordinate jaw surgery and orthodontic alignment of the dental arches. In reality, the use of orthodontic appliances with significant oral mucosal LM involvement may be problematic due to local tissue trauma, causing inflammation, bleeding, and swelling of the affected tissue.

Tongue and floor-of-mouth involvement with hypertrophy and bleeding is also common with large suprahyoid LM and can result in severe problems with airway patency, feeding, and speech (Fig 8). Results in the few published case reports of surgical excision of LM in the floor of mouth suggest that complication rates can be surprisingly high, including rates of infection (81%), nerve damage (27%), and speech compromise (23%).[48] Further investigation is

necessary to improve treatment of LM involvement of deep and superficial structures in the floor of mouth and oral cavity.

LM-induced macroglossia management is controversial and, as previously discussed, there is no consensus regarding treatment. Acute exacerbations of tongue edema are treated initially with antibiotics and steroids, and bleeding from mucosal blebs can be managed with cautery, coblation, or laser.[18] With time, flare-ups of infection tend to diminish, perhaps due to maturation of systemic immunity, and often mandibular growth starts to catch up to tongue size. If the macroglossia and flare-ups persist, then immune dysfunction could be present.[46] Tongue reduction surgery is used for refractory macroglossia to reduce dental trauma to the tongue, create room for jaw movement in mandibular surgery, and allow tracheotomy decannulation if necessary.

Airway Compromise

LM can cause airway compromise or extrinsic compression or intrinsic involvement of key structures such as the tongue or larynx (Fig 9). Airway compression is usually most evident in infancy or after acute hemorrhage into an LM macrocyst, and can necessitate early treatment or a tracheotomy for airway stabilization. Prenatal detection of LM can prompt the need for ex utero intrapartum treatment (EXIT). This is a technique for delivery of fetuses at risk for postnatal upper airway obstruction from neck masses and other lesions. EXIT involves partial delivery by cesarean section and establishing airway control while maintaining placental circulation and oxygenation, allowing orderly stabilization of the neonatal airway. Direct laryngeal or tongue involvement is most evident in infants or in association with LM swelling from inflammation. In these situations, hospitalization is necessary, along with aggressive medical therapy consisting primarily of antibiotics and steroids. If this is ineffective, then a tracheotomy is necessary. Tracheotomy may make LM treatment more difficult when the LM involves the airway, due to the chronic inflammation associated with this device, causing LM edema.

Summary of Lymphatic Malformation Management

The mainstay of LM treatment has been surgical resection of the LM. With lesion staging and radiographic characterization, surgical treatment has been refined. Advancement in intralesional sclerotherapy in macrocystic LM has shown significant efficacy and reduced the need for other forms of therapy in some instances. It is recognized that suprahyoid microcystic or macrocystic LMs and infrahyoid microcystic LMs are more difficult to treat than macrocystic LMs in the infrahyoid and posterior cervical regions. The reasons for this difference are unclear. Bilateral LMs in the suprahyoid region need to be treated in a staged fashion to prevent treatment complications. With this knowledge and the understanding of LM natural history, LM treatment planning is primarily determined by the presence of or possibility of functional compromise. LM characterization and staging, as well as functional compromise, can be assessed on the initial patient evaluation. Once the LM is staged and the extent of the lesion is determined, the following treatment algorithms can be applied to LM management. For stage I and II lesions, treatment that is usually curative can be initiated (Fig 2). For larger lesions, careful planning and long-term management must be discussed (Figs 2 and 3) As our understanding of LM evolves, these management algorithms are sure to change.

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Author Contributions

Jonathan A. Perkins, composition of manuscript, compilation of and critical review of all manuscript components; **Scott C. Manning,** composition of one or more sections of manuscript, critical review of manuscript; **Richard M. Tempero,** composition of one or more sections of manuscript, critical review of manuscript; **Michael J. Cunningham,** composition of one or more sections of manuscript, critical review of manuscript; **Joseph L. Edmonds, Jr.,** composition of one or more sections of manuscript, critical review of manuscript; **Fredric A. Hoffer,** composition of one or more sections of manuscript, critical review of manuscript; **Mark A. Egbert,** composition of one or more sections of manuscript, critical review of manuscript.

Disclosures

References

1. Kennedy TL, Whitaker M, Pellitteri P, et al. Cystic hygroma/lymphangioma: a rational approach to management. Laryngoscope 2001; 111:1929–37.
2. de Serres LM, Sie KC, Richardson MA. Lymphatic malformations of the head and neck. A proposal for staging. Arch Otolaryngol Head Neck Surg 1995;121:577–82.
3. Fliegelman LJ, Friedland D, Brandwein M, et al. Lymphatic malformation: predictive factors for recurrence. Otolaryngol Head Neck Surg 2000;123:706–10.
4. Raveh E, de Jong AL, Taylor GP, et al. Prognostic factors in the treatment of lymphatic malformations. Arch Otolaryngol Head Neck Surg 1997;123:1061–5.
5. Harsha WJ, Perkins JA, Lewis CW, et al. Pediatric admissions and procedures for lymphatic malformations in the United States: 1997 and 2000. Lymphat Res Biol 2005;3:58–65.
6. Perkins JA, Maniglia C, Magit A, et al. Clinical and radiographic findings in children with spontaneous lymphatic malformation regression. Otolaryngol Head Neck Surg 2008;138:772–7.
7. Perkins JA, Garrison M. Variation in lymphatic malformation treatment in pediatric hospitals (unpublished data). 2007.
8. Bloom DC, Perkins JA, Manning SC. Management of lymphatic malformations. Curr Opin Otolaryngol Head Neck Surg 2004;12: 500–4.
9. Borecky N, Gudinchet F, Laurini R, et al. Imaging of cervico-thoracic lymphangiomas in children. Pediatr Radiol 1995;25:127–30.
10. Legiehn GM, Heran MK. Classification, diagnosis, and interventional radiologic management of vascular malformations. Orthop Clin North Am 2006;37:435,74, vii–viii.
11. Hamoir M, Plouin-Gaudon I, Rombaux P, et al. Lymphatic malformations of the head and neck: a retrospective review and a support for staging. Head Neck 2001;23:326–37.
12. Ricciardelli EJ, Richardson MA. Cervicofacial cystic hygroma. Patterns of recurrence and management of the difficult case. Arch Otolaryngol Head Neck Surg 1991;117:546–53.
13. Charabi B, Bretlau P, Bille M, et al. Cystic hygroma of the head and neck—a long-term follow-up of 44 cases. Acta Otolaryngol Suppl 2000;543:248–50.
14. Riechelmann H, Muehlfay G, Keck T, et al. Total, subtotal, and partial surgical removal of cervicofacial lymphangiomas. Arch Otolaryngol Head Neck Surg 1999 Jun;125:643–8.
15. Hartl DM, Roger G, Denoyelle F, et al. Extensive lymphangioma presenting with upper airway obstruction. Arch Otolaryngol Head Neck Surg 2000;126:1378–82.
16. Grimmer JF, Mulliken JB, Burrows PE, et al. Radiofrequency ablation of microcystic lymphatic malformation in the oral cavity. Arch Otolaryngol Head Neck Surg 2006;132:1251–6.
17. Roy S, Reyes S, Smith LP. Bipolar radiofrequency plasma ablation (coblation) of lymphatic malformations of the tongue. Int J Pediatr Otorhinolaryngol 2009;73:289–93.
18. Bloom DC, Perkins JA, Manning SC. Management of lymphatic malformations and macroglossia: results of a national treatment survey. Int J Pediatr Otorhinolaryngol 2009;73:1114–8.

19. Bloom DC, Perkins JA, Manning SC. Management of lymphatic malformations and macroglossia: results of a national treatment survey. Int J Pediatr Otorhinolaryngol 2009;73:1114–8.

20. Lee GS, Perkins JA, Oliaei S, et al. Facial nerve anatomy, dissection and preservation in lymphatic malformation management. Int J Pediatr Otorhinolaryngol 2008;72:759–66.

21. Suver DW, Perkins JA, Manning SC. Somatostatin treatment of massive lymphorrhea following excision of a lymphatic malformation. Int J Pediatr Otorhinolaryngol 2004;68:845–50.

22. Fronkalsrud EW. Disorders of the lymphatic system. In: Welch KJ, Randolph JG, Ravitch MM, editors. Pediatric surgery. 4th ed. Chicago: Year Book Medical; 1986. p. 1506–7.

23. Levine C. Primary disorders of the lymphatic vessels—a unified concept. J Pediatr Surg 1989;24:233–40.

24. Emery PJ, Bailey CM, Evans JN. Cystic hygroma of the head and neck. A review of 37 cases. J Laryngol Otol 1984;98:613–9.

25. Broomhead IW. Cystic hygroma of the neck. Br J Plast Surg 1964;17:225–44.

26. Smith RJ, Burke DK, Sato Y, et al. OK-432 therapy for lymphangiomas. Arch Otolaryngol Head Neck Surg 1996;122:1195–9.

27. Orford J, Barker A, Thonell S, et al. Bleomycin therapy for cystic hygroma. J Pediatr Surg 1995;30:1282–7.

28. Okazaki T, Iwatani S, Yanai T, et al. Treatment of lymphangioma in children: our experience of 128 cases. J Pediatr Surg 2007;42:386–9.

29. Ogita S, Tsuto T, Tokiwa K, et al. Intracystic injection of OK-432: a new sclerosing therapy for cystic hygroma in children. Br J Surg 1987;74:690–1.

30. Smith MC, Zimmerman MB, Burke DK, et al. Efficacy and safety of OK-432 immunotherapy of lymphatic malformations. Laryngoscope 2009;119:107–15.

31. Rautio R, Keski-Nisula L, Laranne J, et al. Treatment of lymphangiomas with OK-432 (picibanil). Cardiovasc Intervent Radiol 2003;26:31–6.

32. Saito M, Ebina T, Koi M, et al. Induction of interferon-gamma in mouse spleen cells by OK-432, a preparation of Streptococcus pyogenes. Cell Immunol 1982;15;68:187-92.

33. Ishida N, Hoshino T. A streptococcal preparation as a potent biological response modifier, OK-432. In: Excerpta Medica. 2nd ed. Amsterdam: 1985. p. 1,2–5,26–47,60–2.

34. Hall N, Ade-Ajayi N, Brewis C, et al. Is intralesional injection of OK-432 effective in the treatment of lymphangioma in children? Surgery 2003;133:238–42.

35. Muir T, Kirsten M, Fourie P, et al. Intralesional bleomycin injection (IBI) treatment for haemangiomas and congenital vascular malformations. Pediatr Surg Int 2004;19:766–73.

36. Sanlialp I, Karnak I, Tanyel FC, et al. Sclerotherapy for lymphangioma in children. Int J Pediatr Otorhinolaryngol 2003;67:795–800.

37. Shiels WE 2nd, Kenney BD, Caniano DA, et al. Definitive percutaneous treatment of lymphatic malformations of the trunk and extremities. J Pediatr Surg 2008;43:136–9; discussion 140.

38. Alomari AI, Karian VE, Lord DJ, et al. Percutaneous sclerotherapy for lymphatic malformations: a retrospective analysis of patient-evaluated improvement. J Vasc Interv Radiol 2006;17:1639–48.

39. Hoffer FA, Hancock ML, Hinds PS, et al. Pleurodesis for effusions in pediatric oncology patients at end of life. Pediatr Radiol 2007;37:269–73.

40. Kim YC, Oh JH, Yoon Y. An experimental study for efficacy of acetic acid as a sclerosing agent. J Korean Radiol 1997;37:233,234-6.

41. Van Hoof M, Joris JP, Horsmans Y, et al. Acute renal failure requiring haemodialysis after high doses percutaneous acetic acid injection for hepatocellular carcinoma. Acta Gastroenterol Belg 1999;62:49–51.

42. Lee BB, Kim YW, Seo JM, et al. Current concepts in lymphatic malformation. Vasc Endovascular Surg 2005;39:67–81.

43. Dubois J, Garel L, Abela A, et al. Lymphangiomas in children: percutaneous sclerotherapy with an alcoholic solution of zein. Radiology 1997;204:651–4.

44. Edmonds J. Unreleased data from ongoing study at Baylor College of Medicine. 2007. Data accessed September 13, 2007.

45. Sires BS, Goins CR, Anderson RL, et al. Systemic corticosteroid use in orbital lymphangioma. Ophthal Plast Reconstr Surg 2001;17:85–90.

46. Tempero RM, Hannibal M, Finn LS, et al. Lymphocytopenia in children with lymphatic malformation. Arch Otolaryngol Head Neck Surg 2006;132:93–7.

47. Padwa BL, Hayward PG, Ferraro NF, et al. Cervicofacial lymphatic malformation: clinical course, surgical intervention, and pathogenesis of skeletal hypertrophy. Plast Reconstr Surg 1995;95:951–60.

48. Edwards PD, Rahbar R, Ferraro NF, et al. Lymphatic malformation of the lingual base and oral floor. Plast Reconstr Surg 2005;115:1906–15.

Figure A1   Staging of cervicofacial lymphatic malformations.