

Contemporary Management of Vascular Anomalies of the Head and Neck—Part 1: Vascular Malformations

A Review

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IMPORTANCE Vascular anomalies of the head and neck are relatively rare lesions. Management is challenging because of the high likelihood of involvement of functionally critical structures. Multiple modalities of treatment exist for vascular anomalies of the head and neck, including medical therapies, sclerotherapy and embolization procedures, and surgery. This review focuses on the accurate diagnosis and the relative roles of the various therapeutic options.

OBSERVATIONS Vascular anomalies are classified by the International Society for the Study of Vascular Anomalies into 2 major groups: vascular tumors and vascular malformations. Vascular tumors encompass proliferative lesions ranging from infantile and congenital hemangiomas to kaposiform hemangioendothelioma. Alternatively, vascular malformations are embryologic errors in vasculogenesis. This article focuses on the management of vascular malformations. The 3 primary vascular malformation subclassifications are lymphatic, venous, and arteriovenous. The burden of disease, diagnosis, and current management options are discussed in detail for each subtype.

CONCLUSIONS AND RELEVANCE Most vascular malformations of the head and neck require a multidisciplinary approach. Available medical, interventional radiologic, and surgical interventions are constantly evolving. Optimization of function and cosmesis must be balanced with minimization of treatment-associated morbidity. Otolaryngologists–head and neck surgeons must remain up to date regarding options for diagnosis and management of these lesions.

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Vascular anomalies are a heterogeneous group of lesions in terms of clinical presentation, anatomic involvement, and response to therapy. Management has historically been hampered by inconsistent nomenclature; this changed in 1982 when vascular anomalies were divided, based on histologic and clinical presentation, into vascular tumors and vascular malformations.¹ Vascular tumors encompass proliferative lesions ranging from infantile and congenital hemangiomas to kaposiform hemangioendothelioma. Alternatively, vascular malformations are embryologic errors in vasculogenesis. Although vascular anomalies are relatively rare, they often involve the head and neck region. It is thus important that otolaryngologists–head and neck surgeons be well versed in their management. A recent survey of senior otolaryngology residents and pediatric otolaryngology fellows, however, found that only 22% of residents and 50% of fellows felt comfortable treating vascular anomalies.²

The International Society for the Study of Vascular Anomalies has developed classification schemes that expand on vascular tumors and vascular malformations.³ The vascular malformation category is further subdivided into simple lesions consisting of only 1 type of vascular malformation, combined lesions with 2 or more types

of vascular malformations, and malformations associated with other systemic anomalies, the latter often in syndromic format (Table).³ An emerging consideration in classification involves genetic testing. Although most vascular malformations are not inherited, involved tissues carry somatic variants that cause disordered vasculogenesis and other complications. Most variants described to date fall into 2 signaling pathways—PI3K, Akt, and mTOR and Ras, Raf, and MEK. These evolving discoveries have had 3 major impacts on the field: improved understanding of the biology of vascular malformations, grouping of some disorders by genotype (eg, *PIK3CA* [OMIM 171834]-related overgrowth spectrum), and exploration of the role of targeted medical therapy for vascular malformations. Genetic testing of vascular malformations is evolving from an academic endeavor to a key component guiding clinical care. Figure 1 illustrates in simplified fashion which genes have available targeted therapies associated with the more common vascular malformations.

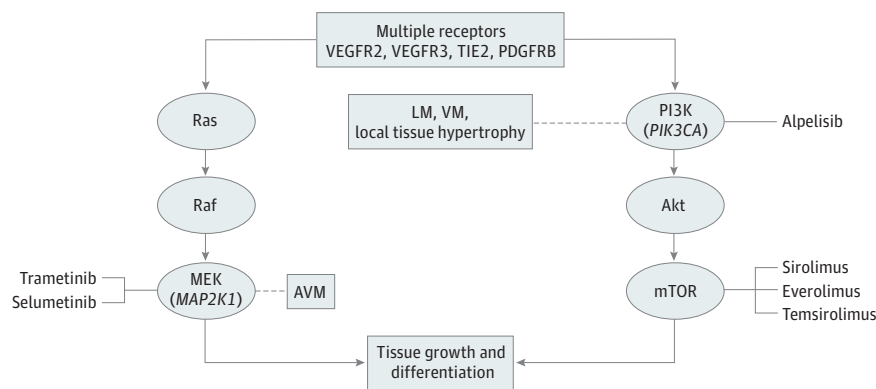
With respect to vascular anomalies of the head and neck, anatomic considerations are critical to both presentation and management. Clinical manifestations may include airway compromise, feeding difficulties, interference with speech, hearing loss caused by

Table. International Society for the Study of Vascular Anomalies Classification^a

Vascular malformations				
Vascular tumors	Simple	Combined	Involving major named vessels	Syndromic
Benign	Capillary malformations	Capillary-venous malformation	Also known as "channel type" or "truncal" vascular malformations	Klippel-Trenaunay syndrome
Locally aggressive or borderline	Lymphatic malformations	Capillary-lymphatic malformation		Parkes-Weber syndrome
Malignant	Venous malformations	Lymphatic-venous malformation	Anomalies of expected origin, course, number, length, diameter, valves	Servelle-Martorell syndrome
	Arteriovenous malformations	Capillary-lymphatic-venous malformation	Abnormal communication between vessels, or fistulae	Sturge-Weber syndrome
	Arteriovenous fistulae	Capillary-lymphatic-arteriovenous malformation	Persistence of embryonal vessels	Maffucci syndrome
		Capillary-arteriovenous malformation		CLOVES
		Capillary-lymphatic-arteriovenous malformation		Proteus syndrome
		Others		CLAPO
				Bannayan-Riley-Ruvalcaba syndrome
				Others

Abbreviations: CLOVES, congenital lipomatous overgrowth, vascular malformations, epidermal nevis, spinal/skeletal anomalies/scoliosis; CLAPO, capillary malformation of the lower lip, lymphatic malformation predominant on the face and neck, asymmetry, and partial or generalized overgrowth.
^a Adapted from International Society for the Study of Vascular Anomalies.³

Figure 1. Vascular Malformation Signaling Pathways and Medical Therapy Targets



A simplified representation of the signaling pathways associated with arteriovenous malformations (AVMs), lymphatic malformations (LMs), venous malformations (VMs), and the tissue overgrowth manifestations thereof, demarcating targets of existing medical therapeutics. Trametinib and selumetinib inhibit MEK activity. Alpelisib inhibits PI3K activity. Sirolimus, everolimus, and temsirolimus inhibit mTOR activity. Although approved for other indications, these medical therapies are not currently approved for the treatment of vascular malformations. Akt indicates protein kinase B (serine and

threonine protein kinase); MEK (MAP2K1), mitogen-activated protein kinase; mTOR, mammalian target of rapamycin (serine and threonine protein kinase); PDGFRB, platelet-derived growth factor; PI3K (PIK3CA), phosphoinositide 3-kinase, catalytic subunit; Raf, protein kinase; Ras, small guanosine triphosphatase protein involved in cellular signal transduction resulting in cell growth and division; TIE2, transmembrane receptor tyrosine kinase functioning as receptor for angiopoetin family proteins; and VEGFR, vascular endothelial growth factor receptor.

ear or temporal bone involvement, visual compromise from orbital involvement, discomfort, pain, and cosmetic disfigurement. Complete surgical excision is often limited by the involvement or proximity of vital structures. Treatment goals are to optimize function and cosmesis while minimizing surgical morbidity.

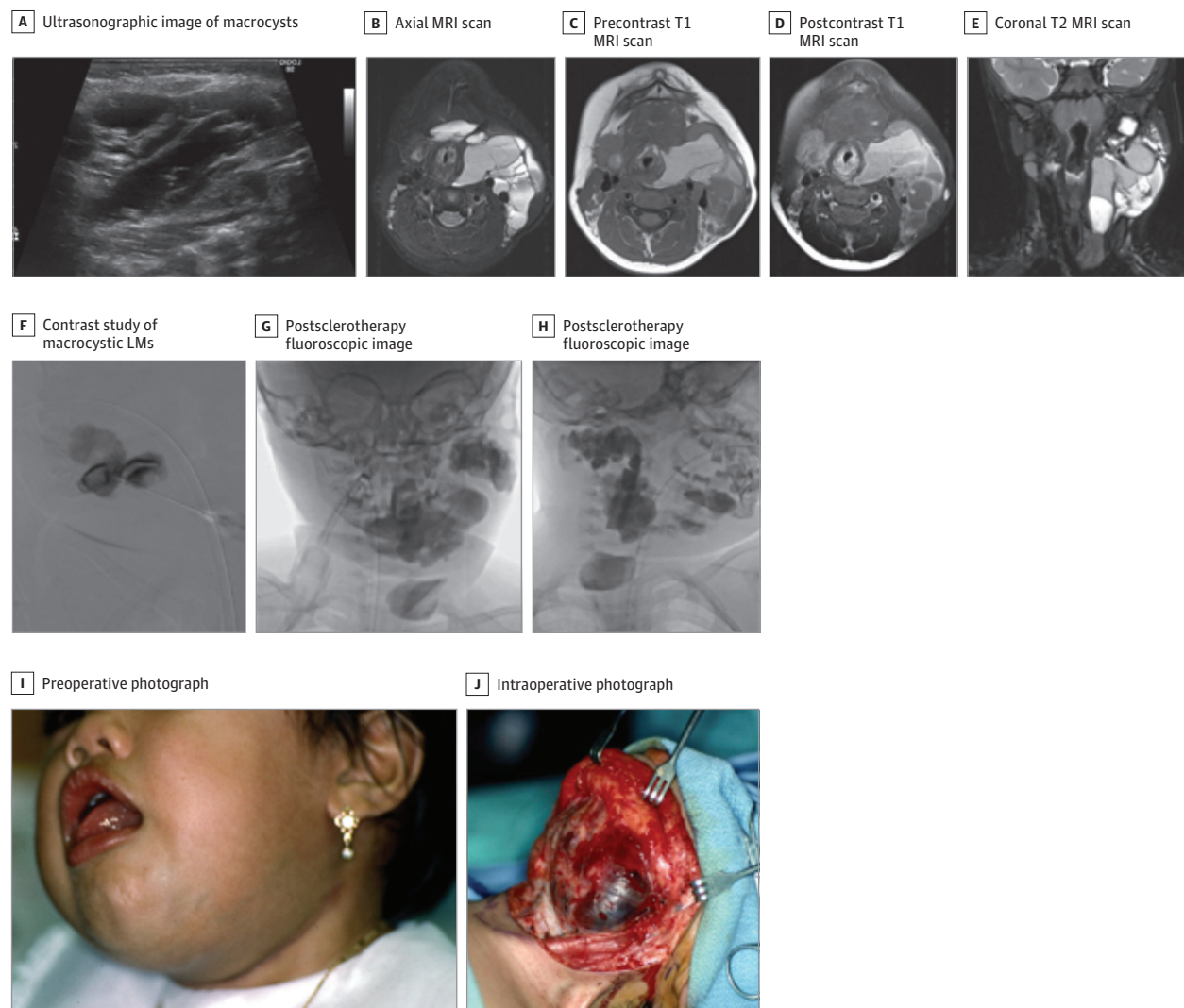
Despite these challenges, the relevance of the proper classification of vascular anomalies and the accuracy of diagnosis continue to expand as genetic sequencing, molecular biology, and radiographic imaging technologies develop. This progress is accompanied by innovations in surgical treatment, advances in sclerotherapy and embolization techniques, and targeted medical therapies.

This review provides an up-to-date overview of the diagnostic and therapeutic management options for congenital vascular malformations of the head and neck. A subsequent article will focus on vascular tumors.

Lymphatic Malformations

Lymphatic malformations (LMs) are low-flow lesions associated with somatic activating variants in *PIK3CA* (Figure 1).⁴ Lymphatic malformations typically manifest in children younger than 2 years, with 50% diagnosed at birth.⁵ Lymphatic malformations may be diagnosed based on antenatal imaging in the second or third trimester, such as in utero ultrasonographic imaging or fetal magnetic resonance imaging (MRI). Ex utero intrapartum treatment (EXIT) procedures to secure the airway may sometimes be indicated, depending on anatomic involvement.⁶ Superficial LMs present as soft bulges, with or without overlying skin discoloration. Mucosal lesions often involve raised white or dark purple vesicles that can leak chyle or blood. Deep lesions abutting the airway may cause airway compromise and deep lesions abutting the esophagus may cause dysphagia. The most com-

Figure 2. Lymphatic Malformations (LMs)



A, Grayscale ultrasonographic image demonstrating multiple anechoic macrocysts. B, Axial T2 fast spin echo inversion recovery magnetic resonance imaging (MRI) scan of left cervicofacial LM. C, Precontrast T1 MRI scan of left cervicofacial LM. D, Postcontrast T1 MRI scan of left cervicofacial LM. E, Coronal T2 fast spin echo inversion recovery MRI scan of left cervicofacial LM. Intrinsic high T1 signal on precontrast T1 image likely reflects blood products from hemorrhage into several cysts. There is only enhancement of the walls and septae of the LM on the postcontrast image. All axial images demonstrate narrowing and rightward deviation of the trachea. F, Negative road-map technique is used for contrast study of macrocystic LMs prior to sclerotherapy. G, Postsclerotherapy spot fluoroscopic image demonstrating opacification of multiple cystic structures that correlate with the lesion seen on MRI scan. H, Postsclerotherapy spot fluoroscopic image demonstrating opacification of multiple cystic structures that correlate with the lesion seen on MRI scan. I, Preoperative photograph of the clinical appearance of cervicofacial LM in a different patient. J, Intraoperative photograph of the clinical appearance of cervicofacial LM.

mon subsites of airway involvement are the oral cavity, oropharynx, and hypopharynx, while glottic, subglottic, and tracheal involvement is comparatively less frequent.⁷

Lymphatic malformations are described as macrocystic, microcystic, or mixed lesions based on imaging characteristics. Macrocystic LMs historically were often termed *cystic hygroma* and microcystic LMs called *lymphangioma*; these terms lack specificity and should no longer be used in the current era of International Society for the Study of Vascular Anomalies classification. A diameter of 1 to 2 cm has been used as a cutoff between macrocystic and microcystic designations, while an alternative practical definition is whether a cyst is amenable to aspiration and, hence, sclero-

therapy. Macrocystic LMs are typically well defined on ultrasonograms with no internal flow on Doppler imaging; microcystic LMs appear as thickened echogenic lesions often infiltrating surrounding tissues (Figure 2A). Lymphatic malformations are hyperintense on T2 MRI sequences; macrocystic lesions may show rim enhancement, while microcystic LMs minimally enhance. Magnetic resonance imaging is best to fully visualize the extent of disease and involvement with adjacent structures (Figure 2B-E). When LM involves the lower cervical region, imaging should include the chest to evaluate for mediastinal extension.⁸

Lymphatic malformation growth is typically commensurate with the child. Episodes of acute enlargement are common and are as-

sociated with infection, inflammation, or intralesional hemorrhage. Suspected infection should be treated with antibiotics, while enlargement associated with inflammation secondary to respiratory or dental infection can be managed with corticosteroids. When lymphocytopenia occurs in patients with LM, there is an association with higher infection and hospitalization rates.⁹ Intralesional hemorrhage can occur with or without trauma and often presents with dependent bruising and painful swelling, which can be managed with nonsteroidal anti-inflammatory drugs, corticosteroids, and occasionally aspiration.

Head and neck LMs can be staged by anatomic location. Most commonly used is the 1995 classification schema by de Serres et al¹⁰ that categorizes LMs by midline and hyoid planes: unilateral infrahyoid involvement (stage I), unilateral suprahyoid involvement (stage II), unilateral infrahyoid and suprahyoid involvement (stage III), bilateral suprahyoid involvement (stage IV), and bilateral suprahyoid and infrahyoid involvement (stage V). Both the risk of complications and recidivism rate increase with advancing stage. An alternative staging system, the Cologne Disease Score, classifies LMs according to degree and progression of disease-specific morbidity with respect to respiration, nutrition, speech, and cosmetic appearance.¹¹ A consensus-based system for LM outcome reporting was developed by the American Society of Pediatric Otolaryngology Vascular Anomalies Task Force and the American Academy of Otolaryngology–Head and Neck Surgery Workgroup for Evidence in Vascular Anomalies in 2015 to facilitate comparison between institutions. This proposed system incorporates de Serres staging plus components of the Cologne Disease Score, as well as quality of life, treatment response, airway obstruction and need for tracheostomy, number of interventions in a given time frame, pain, and LM volume.¹²

Patients with LMs require individualized multidisciplinary management. Therapeutic options include surgical resection or debulking, intralesional sclerotherapy, and systemic medical therapy with sirolimus. Prioritization of these options involves anatomic location, radiographic characteristics, clinical manifestations, and the experience of the team providing care. Spontaneous regression of LMs has been reported, but is rare.^{12,13} Aspiration of fluid from lesions may be offered as a stabilizing measure, including at the time of delivery if infant airway stability is compromised.

Tracheostomy and feeding tube placement may be required. Tracheostomy proved necessary during the treatment course in 15% of children in one case series; tracheostomy or feeding tube placement could be permanent if LM intrinsically involves the larynx.^{13,14}

Sclerotherapy performed under ultrasonographic or fluoroscopic guidance is often used as treatment of macrocystic LMs (Figure 2F-H). Optimal timing of sclerotherapy requires weighing the risk of anesthesia associated with young age or comorbidities against timely treatment of urgent or emergency clinical issues. At our institution, it is rare to intervene before 6 months of age. In the absence of an urgent clinical issue, clinicians collaborate with patients' families to select an appropriate age for intervention. Depending on lesion size, more than 1 session of sclerotherapy may be required. If several sclerotherapy sessions are anticipated, medical therapy with sirolimus should be considered, with the goal to delay or lessen the number of procedures requiring anesthesia. Doxycycline is the most frequently used sclerosant drug for macrocystic lesions. Bleomycin is the agent of choice for microcystic lesions and when less swelling is desired after treatment. Combination therapy

is common.¹⁵ Other sclerosing agents such as dehydrated ethanol, sodium tetradecyl sulfate, and OK-432 (picibanil) are less often used. OK-432 is popular outside of the United States for sclerotherapy of macrocystic LMs, with reported response rates of 50% to 95%.^{16,17} Studies are ongoing in the US, as OK-432 is not currently approved by the US Food and Drug Administration.¹⁸ Doxycycline sclerotherapy is quite painful, and coincident prolonged-release local anesthetic injection is recommended to minimize discomfort. Post-sclerotherapy swelling in LMs involving or abutting the orbit or airway can be associated with significant risk of morbidity and mortality. For orbital lesions, measurement of intraocular pressures should be considered given the risk of blindness secondary to optic nerve compression. Postoperative intubation with subsequent intensive care unit observation or endoscopic airway evaluation prior to extubation may be necessary after sclerotherapy of airway lesions.

Superficial microcystic mucosal LMs can be treated by several modalities including laser ablation (most commonly using CO₂ laser), radiofrequency ablation, microdebrider resection, bleomycin sclerotherapy, and systemic sirolimus. Symptomatic reduction in pain and bleeding has been reported with all these options.^{8,19-24}

The role of systemic sirolimus medical therapy in LM management has progressed since its initial compassionate use in a small series of patients with kaposiform hemangioendothelioma.^{25,26} The clinicoradiologic improvement noted led to a phase 2 study of 57 patients with a wider spectrum of vascular anomalies, predominantly lymphatic.²⁷ These patients received sirolimus monotherapy for 48 weeks, with 82.5% partial responses and tolerable toxic effects. A subsequent focused series of head and neck LMs reported that 100% of 19 patients experienced variable improvement with acceptable toxic effects, including no systemic bacterial infections.²⁴ In general, sirolimus appears to reduce fluid content of LM, as demonstrated by improvement of T2 signal on MRI scans and pliability of palpable LM tissues. This reduction of fluid correlates with diminished lymphatic vesicles, decreased pain, fewer episodes of cellulitis, and variable reduction in size. Sirolimus can also be used topically for cutaneous symptoms, specifically drainage and bleeding from lymphatic vesicles.²⁸ Most patients with LMs treated with sirolimus to date have had prior procedures. Considerable institutional variation exists in dose exposure, duration of therapy, and age of initiation of sirolimus, all of which may be associated with therapeutic effect. Although some patients can successfully discontinue sirolimus without recurrence of symptoms, others require ongoing sirolimus treatment for sustained control of symptoms. The optimal integration of sirolimus as adjuvant or first-line therapy into multidisciplinary treatment algorithms is an open question, currently handled on a case-by-case basis.

Surgical treatment remains appropriate in specific clinical scenarios (Figure 2I-J). Surgical resection outcomes are best with macrocystic lesions involving a single anatomic site, particularly the infrahyoid neck.^{14,29} Intraoperative macrocyst decompression may enhance dissection. Suprahyoid lesions are more prone to crossing tissue planes, thus complicating resection with higher rates of recurrence and morbidity.^{30,31} Subtotal resection may be necessary if critical structures are at risk.³² Staged resections can be planned, but have the disadvantage of scar formation and anatomic distortion, which may complicate future procedures. When multiple anatomic sites are involved, there is heterogeneity among clinicians with respect to the order in which sites should be surgically addressed.³²

Depending on location, intraoperative facial nerve electromyography monitoring is useful as LMs may displace or alter facial nerve anatomy.³³ Preoperative mapping of the facial nerve via percutaneous stimulation, recording the motor responses as measured by electromyography, can be used to outline the nerve's course on the skin.^{32,34}

Nasotracheal intubation for postoperative airway stabilization should be considered for lesions involving the upper aerodigestive tract, particularly suprahyoid lesions involving the tongue and floor of the mouth, as significant postoperative swelling is anticipated. Postoperative pooling of lymphatic fluid is likely and can challenge wound healing, dictating suction drain placement.³⁵ There is emerging experience that preprocedural and periprocedural sirolimus may minimize lymphatic leak and shorten the duration of postoperative drain requirement.³⁶

The effectiveness of surgery vs sclerotherapy as the primary mode of treatment for select macrocystic LMs is debated. One multicenter study documented equal effectiveness as measured by the likelihood of requiring no further treatment within 1 year, as well as the comparative resource use between the 2 treatment methods.³⁷

Venous Malformations

Venous malformations (VMs) are low-flow lesions composed of ectatic, dysmorphic venous channels. Approximately 40% of VMs occur in the head and neck.³⁸ Most VMs (>90%) are sporadic and unifocal. An association of sporadic VM with somatic variants in the *TIE2* (OMIM 600221) and *PIK3CA* (OMIM 171834) genes has been established (Figure 1).^{39,40}

The most commonly involved sites of VM in the head and neck are the muscles of mastication, the lip, and the tongue. However, any mucosal surface of the aerodigestive tract can be involved, with the potential for airway compromise and dysphagia.⁴¹⁻⁴³ Venous malformations typically present as soft nonpulsatile masses with purple or blue skin discoloration. They differ on physical examination from other vascular lesions with respect to their compressibility and tendency to fluctuate in size with gravity or increased central venous pressure.

Ultrasonography of VMs demonstrates dilated compressible channels with or without phleboliths (Figure 3A). Flow in the channels may be too slow to appear on color Doppler imaging, but compression and decompression of the lesion may elicit color. Venous malformations are hyperintense on MRI T2-weighted scans, and fat suppression is helpful in delineating the extent of the lesion (Figure 3B-E). On postcontrast MRI and computed tomography scans, there is initially inhomogeneous enhancement, with progressive increased enhancement. Venous malformations typically enhance more avidly than LMs, with the latter usually enhancing solely at the periphery; this difference can be helpful in clarifying diagnosis.

As with other vascular malformations, trauma, infection, hormonal fluctuations, and incomplete treatment can spur lesion expansion.⁴⁴ Venous malformations differ in their proclivity toward progressive dilation with pooling and stasis of blood. More than 60% of VMs reportedly progress in adolescence, which supports consideration of earlier treatment of even asymptomatic VMs.⁴⁵

Venous malformations can cause disfigurement owing to discoloration and contour irregularity. They may also cause intermittent pain and inflammation owing to venous stasis and localized intravascular coagulation with thrombus or phlebolith development. Nonsteroidal anti-inflammatory drugs and warm compresses are helpful in pain management. For patients with mild to moderate thrombophlebitic pain, low-dose aspirin (2-5 mg/kg/d up to 81 mg daily) can prevent or lessen the severity of pain episodes. When aspirin use proves insufficient, anticoagulation with low-molecular-weight heparin can be administered for thrombus prevention and improvement of pain associated with venous stasis.⁴⁶ Medical therapy with sirolimus has recently been used for refractory pain, swelling, and coagulopathy associated with VMs.^{47,48}

Endovascular sclerotherapy is the mainstay of therapy for VMs (Figure 3F-I). Sodium tetradecyl sulfate is the most commonly used agent; dehydrated ethanol and bleomycin are alternative options. Sodium tetradecyl sulfate is prepared as a foam with air and ethiodized oil agitated in various ratios. The foam preparation slows transit time through the malformation and increases contact of the sclerosant agent with the endothelium. Venous malformations typically swell more than LMs after sclerotherapy; thus, airway protection is paramount. The treated area will become swollen and firm for 1 to 2 weeks after treatment. Because both sodium tetradecyl sulfate and ethanol are caustic agents, care should be taken to minimize the risk of extravasation of the sclerosant agent into adjacent tissues or egress into normal veins.

Long-pulse Nd:YAG laser therapy ameliorates discoloration and lesion size of superficial mucosal VMs and has been used to treat mucosal lesions within the oral cavity, pharynx, and larynx.^{49,50} Joint Nd:YAG laser and sclerotherapy at the same anesthetic setting has been used.⁴⁹

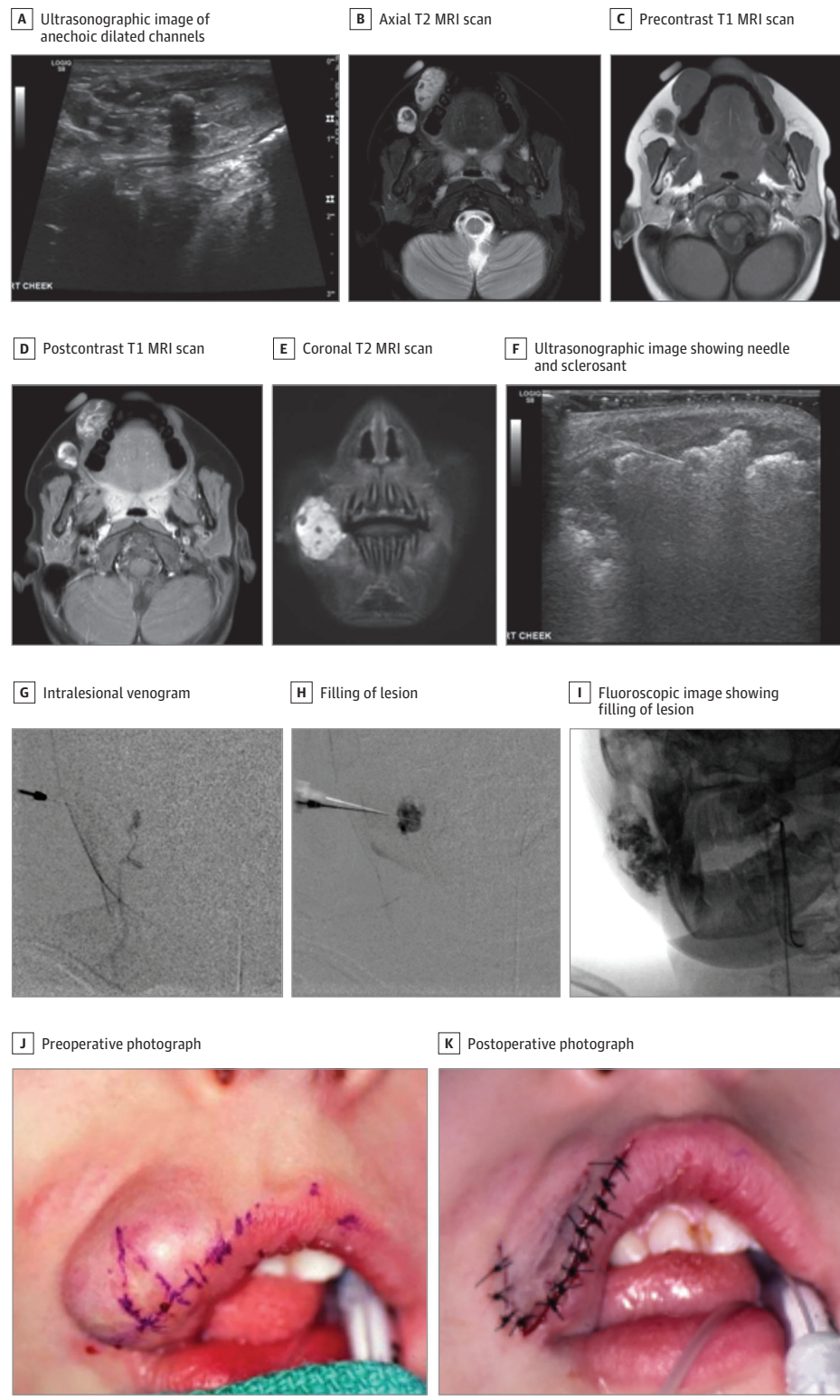
When critical structures such as a facial nerve or an optic nerve are in close proximity to the lesion, surgical excision alone may be favored to lessen the risk of neural injury.³⁸ Surgical excision is also a treatment consideration for patients with persistent pain or cosmetic disfigurement. Surgical planning for VMs varies according to depth of the lesion, proximity to vital structures, and presence of mucosal involvement. Localized well-defined VMs that spare vital structures are amenable to complete surgical resection (Figure 3J-K).⁴⁴ More complex lesions often require a combination of sclerotherapy and surgical debulking for symptom control.⁵¹ Lesions treated by sclerotherapy may be easier to subsequently resect because of the development of fibrosis within several months.⁵²

Intraoperative hemorrhage may hinder surgical resection as thin VM vessel walls are easily damaged during dissection. A potentially useful preventive measure in this setting is preoperative embolization with *n*-butyl cyanoacrylate. This substance polymerizes on exposure to blood or water, creating a firm mass within the VM that facilitates complete resection while minimizing blood loss.⁵³ Its use potentially facilitates a single-stage procedure for localized VM of the head and neck, with surgery performed immediately after embolization.⁵⁴

Arteriovenous Malformations

Arteriovenous malformations (AVMs) are high-flow lesions with abnormal connections between dysplastic arteries and draining veins

Figure 3. Venous Malformations (VMs)

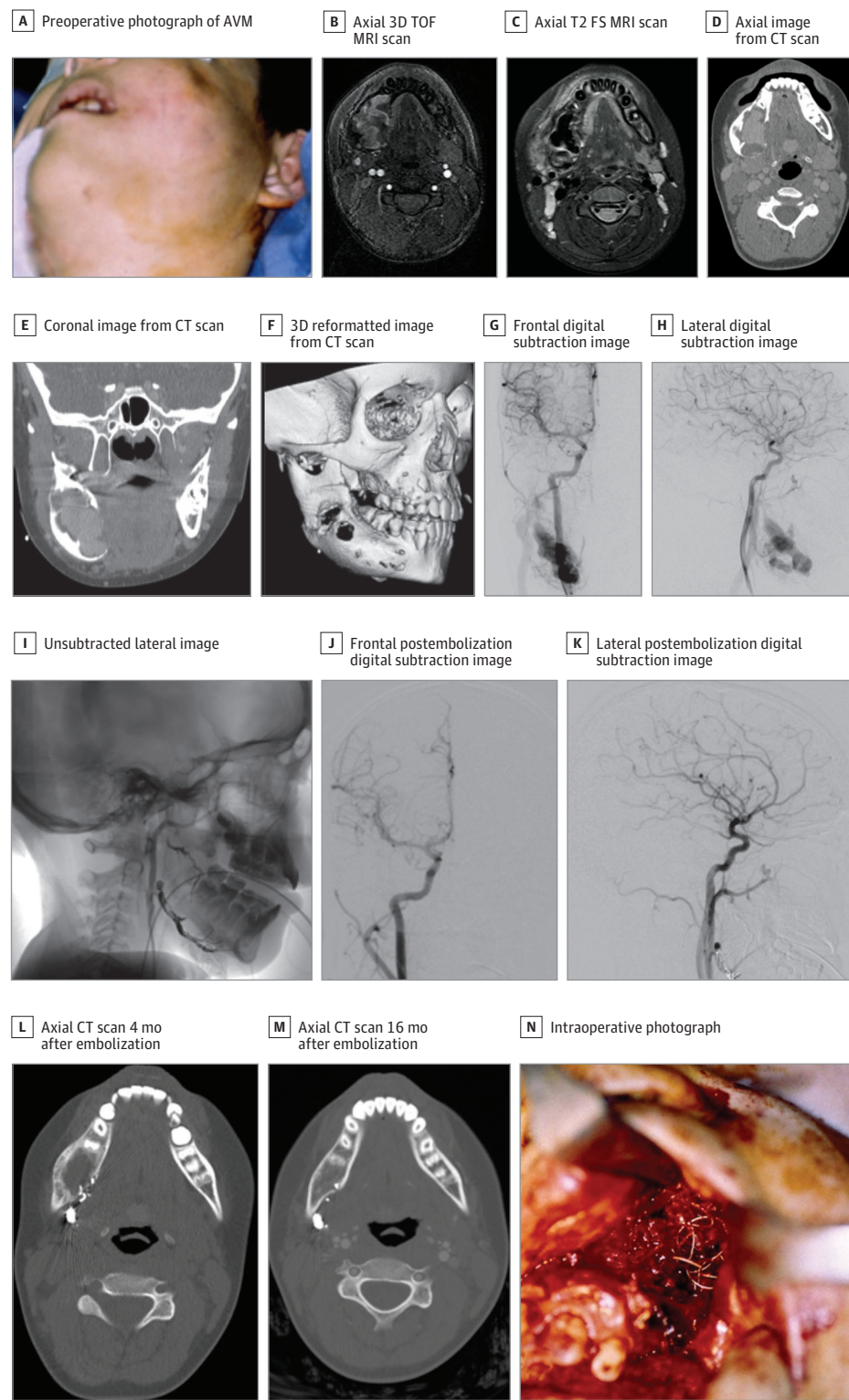


A, Grayscale ultrasonographic image demonstrating anechoic dilated channels, one of which contains an echogenic, shadowing phlebolith. B, Axial T2 fat-suppressed magnetic resonance imaging (MRI) scans of right facial VM. C, Precontrast T1 MRI scans of right facial VM. D, Postcontrast T1 MRI scans of right facial VM. E, Coronal T2 fat-suppressed MRI scans of right facial VM. Note the rounded signal voids on T2 sequences reflecting phleboliths, an imaging hallmark of VMs, and heterogeneous enhancement of the lesion. F, Ultrasonographic image showing access needle and echogenic sclerosant foam filling the channels of the VM. G, Negative road-map intralesional venogram shows filling of a portion of the VM and contrast opacifying small draining vein. H, Negative road-map image during sclerotherapy shows filling of the lesion with no extravasation or egress into draining veins. I, Spot fluoroscopic postsclerotherapy image shows filling of the lesion with no extravasation or egress into draining veins. J, Photograph of the clinical appearance of right lip VM in a different patient immediately prior to excision. K, Photograph of the clinical appearance of right lip VM after excision.

via intervening nidus vessels, bypassing normal capillary beds. Extracranial head and neck AVMs occur much less frequently than intracranial AVMs.⁵⁵ Arteriovenous malformations may occur sporadically in isolation, or within a genetic syndrome such as hereditary

hemorrhagic telangiectasia, *PTEN* hamartoma tumor syndrome, CLOVES (congenital lipomatous overgrowth, vascular malformations, epidermal nevi, spinal/skeletal anomalies/scoliosis) syndrome, and capillary malformation-AVM. The molecular and

Figure 4. Arteriovenous Malformations (AVMs)



A, Immediate preoperative photograph of AVM in one patient. B, Axial 3D time-of-flight (TOF) magnetic resonance imaging (MRI) scan of a different patient. C, Axial T2 fat-suppressed (FS) MRI scan. D, Axial image from contrast-enhanced computed tomography (CT) scan. E, Coronal image from contrast-enhanced CT scan. F, 3D reformatted image from contrast-enhanced CT scan, demonstrating enlarged vascular lesion causing marked expansion and erosion of the right mandibular body. G, Frontal digital subtraction angiogram image with right common carotid injection showing opacification of large venous varix with early visualization of the right maxillary and external jugular veins. H, Lateral digital subtraction angiogram image. I, Unsubstracted lateral image demonstrates embolic material in inferior alveolar artery and facial artery feeding branches. J, Frontal postembolization digital subtraction angiogram image with right common carotid injection. K, Lateral postembolization digital subtraction angiogram image with right common carotid injection. There is no longer filling of the varix, nor is there visualization of early venous drainage. L, Axial CT scan at 4 months postembolization. M, Axial CT scan at 16 months postembolization shows progressive remodeling of the mandible. N, Intraoperative photograph of arteriovenous malformation in a different patient.

genetic basis for AVM development remains incompletely understood; several signaling pathways—transforming growth factor beta, Ras and MAPK, and PI3K and Akt—have been implicated.⁵⁶ The most common variants in extracranial AVMs are in *MAP2K1* (OMIM 176872)

(Figure 1),⁵⁷ distinct from *KRAS* (OMIM 190070) or *BRAF* (OMIM 164757) variants in intracranial AVMs.⁵⁸

Approximately 50% of extracranial AVMs affect the head and neck, with predilection for the midface and oral cavity.^{59–61} The natu-

ral history of AVMs is detailed by the Schobinger classification system.⁶² The first stage is characterized by skin discoloration and warmth. Progression to stage II includes lesion enlargement with palpable pulsations (Figure 4A). At stage III, there is ulceration due to venous hypertension and stasis, local tissue destruction, pain, and the risk of profuse bleeding. Stage IV is defined by high-output congestive heart failure, rarely seen with head and neck AVMs.

Ultrasonography of AVMs demonstrates enlarged vascular channels with low-resistance arterial waveforms. Magnetic resonance imaging and computed tomography typically demonstrate dilated and tortuous feeding arteries with early filling of ectatic draining veins on postcontrast images (Figure 4B-F). Angiography can be helpful in assessing flow dynamics and further defining lesional anatomy prior to endovascular or surgical procedures (Figure 4G-H).⁶³

Schobinger stage I lesions are typically asymptomatic. Cosmetic deformity and possible functional compromise become apparent with stage II lesions. Treatment becomes mandatory for stage III and IV lesions. Most AVMs are complex and involve multiple tissue planes. Complete cure is often unrealistic; rather, lesion control to reduce symptoms and preserve vital functions is the goal. Treatment options include embolization, surgical excision, or a combination thereof. There is no established medical therapy for AVMs; genotype-guided therapy to target *MAP2K1* activation has reportedly been successful in 2 cases refractory to other measures.^{57,64}

Embolization can be performed via a transarterial approach or by direct percutaneous puncture of either the nidus or a perinidal vessel (Figure 4I-K). Transvenous or percutaneous approaches to obliterate draining veins have also been described.⁶⁵ Potential embolic agents include dehydrated ethanol, several forms of acrylate glue, or ethylene-vinyl alcohol copolymer (Onyx; EV3 Neurovascular). These liquid agents are able to penetrate the AVM nidus and the immediate draining veins. Proximal arterial embolization with coils or other similarly large implants may be associated with ischemia-related angiogenesis and further growth of the AVM.^{65,66} Thus, treatment of the nidus and/or outflow veins is paramount. Moreover, blockage of these large arterial feeding vessels may limit future treatment options. Temporary occlusive agents such as polyvinyl alcohol particles, embolic spheres, or gelatin sponge slurry may be used as preoperative embolic agents to decrease intraoperative blood loss or to control spontaneous bleeding in the acute setting. Recently, interstitial injection of bleomycin has been reported as an effective treatment for early-stage AVMs.⁶⁶

Surgical resection alone is typically reserved for small lesions or for lesions refractory to embolization. The morbidity of completely resecting large diffuse AVMs often outweighs the benefits; in such situations, the focus is on symptom palliation with partial or staged resection targeting the most problematic areas. Resection margins

are challenging to establish as AVMs can blend into surrounding tissues (Figure 4N). Operative blood loss mitigation options include preoperative embolization within 24 to 48 hours of surgery, hypotensive anesthesia techniques, topical administration of epinephrine and coagulation-enhancing factors, and ensuring the availability of multiple electrocautery devices that can be used simultaneously if needed.^{67,68}

The difficulty of reconstruction after resection increases proportional to the size and complexity of the lesion. Both regional and free tissue transfer grafts may be necessary, but can be compromised by abnormal local tissue perfusion and aberrant blood supply associated with the AVM.⁶⁷ Postoperative healing is likewise impeded by such abnormal perfusion. Hematoma risk is high owing to the vascular nature of these lesions. Recurrence rates after embolization, surgical resection, and the combination thereof vary widely, with recurrences documented up to 10 years after treatment.⁶⁰

Local Tissue Hypertrophy

Progressive hypertrophy of adjacent soft tissue and osseous structures is often noted as children with head and neck vascular malformations grow into adolescence. Oral cavity mucosal and submucosal overgrowth can cause bleeding as well as dysarthria and dysphagia. Aberrant maxillary and mandibular overgrowth are associated with malocclusion and cosmetic disfigurement.⁶⁹ Some cases of local tissue hypertrophy, such as facial infiltrating lipomatosis, are associated with somatic activating variants in *PIK3CA* (Figure 1).⁷⁰

Surgical intervention may be necessary to restore functional anatomy and preserve symmetry in facial contour. A staged zonal approach to soft tissue excision should be used, taking into account aesthetic subunits and relaxed skin tension lines when designing incisions, and using local or free tissue flaps for reconstruction as needed.^{71,72} Orthognathic surgery to address facial bony overgrowth is ideally delayed until skeletal maturity.⁷³

Conclusions

Most vascular malformations of the head and neck require a multidisciplinary approach. Available medical, interventional radiologic, and surgical interventions are constantly evolving. Optimization of function and cosmesis must be balanced with minimization of treatment-associated morbidity. Otolaryngologists-head and neck surgeons must remain up to date regarding options for diagnosis and management of these lesions.

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Drafting of the manuscript: Gallant, Chewning, Orbach, Trenor.

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