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Current management of hemangiomas and vascular malformations

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Vascular anomalies is a new, rapidly evolving multidisciplinary field that combines several surgical and medical specialities. The plastic surgeon plays an essential role in the management of affected patients.

The greatest impediment to development of this field has been confusing terminology. This has been responsible for improper diagnosis, illogical treatment, and misdirected research. However, a biologic classification system introduced in 1982 based on studies correlating physical findings, natural history, and cellular features has clarified most of this terminologic disorder [1]. There are two major categories of vascular anomalies: tumors and malformations (Box 1).

Vascular tumors are endothelial neoplasms characterized by increased cellular proliferation. Hemangioma is the most common and is almost exclusive to infants. Other tumors are hemangioendotheliomas, tufted angioma, hemangiopericytomas, and other rare vascular neoplasms, including angiosarcoma. Vascular malformations, on the other hand, are the result of abnormal development of vascular elements during embryogenesis and fetal life. These may be single vessel forms (capillary, arterial, lymphatic, or venous) or a combination. Vascular malformations do not generally demonstrate increased endothelial turnover. They are designated according to the predominant channel type as capillary malformations, lymphatic malformations, venous malformations, arteriovenous malformations, and complex forms such as capillarylymphatico-venous malformation. Malformations with an arterial component are rheologically fast-flow, while the remainder are slow-flow.

There are rare exceptions to this classification scheme. Vascular malformations, while essentially structural disorders, can demonstrate endothelial hyperplasia, possibly triggered by clotting, ischemia, embolization, partial resection, or hormonal influences. Rarely, vascular tumors and vascular malformations can coexist. For example, pyogenic granuloma, a tiny acquired vascular tumor, often appears in the dermis along with a capillary malformation.

History and physical examination can distinguish between vascular tumors and vascular malformations with a diagnostic accuracy of over 90% [2]. The most common error in determining a clinical diagnosis continues to be the inaccurate and imprecise use of terminology. Perhaps the most extreme example is the term *hemangioma*, which is frequently applied generically and indiscriminately to vascular lesions that are entirely different in histology and behavior. *Cavernous hemangioma* is a similar offender, because in reality there is no such entity—a lesion is either a deep hemangioma or a venous malformation.

Vascular tumors

Hemangioma

Pathogenesis

Hemangiomas are endothelial tumors with a unique biologic behavior-they grow rapidly, regress

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Box 1. Vascular anomalies
Tumors
Hemangioma Pyogenic granuloma Kaposiform hemangioendothelioma Other rare tumors
Malformations
Capillary Lymphatic Venous Arteriovenous Combined

slowly, and never recur. The three stages in the life cycle of a hemangioma, each characterized by a unique assemblage of biologic markers and processes, are (1) the proliferating phase (0-1 year of age), (2) the involuting phase (1-5 years of age), and (3) the involuted phase (>5 years of age). These stages are typically clinically apparent and can be distinguished microscopically and immunohistochemically [3].

In the proliferating phase, the hemangioma is composed of plump, rapidly dividing endothelial cells that form tightly packed sinusoidal channels. Even at this early stage, the endothelial cells express phenotypic markers of mature endothelium [3], in addition to markers of activated endothelium. Urinary markers of angiogenesis, such as basic fibroblast growth factor and high molecular weight (MW) matrix metalloproteinases (MMPs) are usually high in infants with proliferating hemangiomas and diminish to normal levels during regression [4,5]. In the involuting phase, there is decreasing endothelial proliferation, increasing apoptosis, and the beginning of fibrofatty replacement of the hemangioma. The net result is loss of volume of the tumor and increasing softness of the overlying skin. During the involuted phase, after regression is complete, all that remains are a few tiny capillary-like feeding vessels and draining veins (some of which can be abnormally large) surrounded by islands of fibrofatty tissue admixed with dense collagen and reticular fibers. The endothelium lining these vessels is flat and mature. Multilaminated basement membranes persist around the residual tiny capillary-sized vessels.

Clinical features

Hemangioma is the most common tumor of infancy and childhood, occurring in 4% to 10% of Caucasian infants. These lesions are three to five times more common in females, with an even higher female preponderance in hemangiomas that are problematic or associated with structural abnormalities. There is an increased frequency of hemangiomas in premature infants with a reported incidence of 23% in neonates who weigh less than 1200 g [6]. Hemangiomas are unusual in dark-skinned infants.

Hemangiomas are generally noted within the first 2 weeks of postnatal life. However, there is wide variability in this timing. Deep subcutaneous lesions, such as in the parotid, may not be noted by until the infant is several months old. Their appearance is heralded, in 30% to 50% of infants, by a premonitory cutaneous mark that may resemble a pale spot, telangiectatic or macular red stain, or a bruise-like pseudoecchymotic patch. Hemangiomas occur most commonly in the craniofacial region (60%), followed by the trunk (25%) and extremities (15%) [2]. Eighty percent of cutaneous hemangiomas are single, while 20% are multiple. Multiple cutaneous lesions often are associated with hemangiomas in other organ systems, particularly the liver.

The presentation of hemangiomas is variable in terms of size, extent and morphology (Fig. 1). When there is superficial dermal involvement, the skin becomes raised, firm and bosselated with a vivid crimson color. If the hemangioma is limited to the deeper dermis, subcutaneous tissue or muscle, the overlying skin may be only slightly raised, warm, and have a bluish hue. All of these structures may be involved with a superficial raised component overlying a deeper tumor. Hemangioma in an extremity may present with a macular, telangiectatic appearance. The adjectives *cavernous* and *capillary*—previously used to describe deep and superficial hemangiomas, respectively—are confusing and inaccurate and should thus be eliminated [1,7].

The three stages of histologic appearance of hemangioma correlate with its clinical course [1]. During the proliferating phase, growth is rapid and frequent observation is needed to document the growth pattern. Few indicators predict the eventual volume of a particular hemangioma or forecast the timing and outcome of involution. Typically, hemangiomas begin to plateau in growth by 10 to 12 months, although some demonstrate growth stabilization earlier or later.

During the involuting phase, after 1 year of age, the growth of the hemangioma slows, and, for a time, is commensurate to that of the child. The



Fig. 1. Variable morphologic appearances of hemangioma, illustrated in patients (A-F). Patient C has associated PHACES syndrome with carotid and aortic arch abnormalities. Note the sternal cleft.

telltale signs of regression appear. The skin begins to pale, typically beginning at the center of the lesion and a patchy grayish discoloration becomes discernable. The hemangioma is softer on palpation. The involuting phase extends from 1 year until 5 to 7 years of age. The rate of regression is unrelated to the appearance, depth, gender, site, or size of the hemangioma [2]. Typically, the final traces of color disappear by 5 to 7 years of age.

Nearly normal skin is restored in at least 50% of children. The involved skin may have telangiectasias and a crepe-like laxity (anetoderma), a result of the destruction of elastic fibers. Yellow discoloration or scarred patches persist if ulceration occurred during the proliferating phase. If the tumor was once large and protruding, there is frequently a fibrofatty residuum with redundant skin. Hemangioma of the scalp or eyebrow often destroys hair follicles with resulting alopecia.

It is important to recognize that even a large and bulky subcutaneous hemangioma can regress totally, while a flat, superficial hemangioma can irreversibly alter the cutaneous texture, resulting in an atrophic patch. This variable outcome makes it difficult to predict outcome in infancy. Hemangiomas rarely cause major skeletal distortion or hypertrophy. A large facial hemangioma can, however, be associated with minor bony overgrowth, likely a result of increased blood flow. Hemangiomas can also produce a mass effect on the local facial skeleton, the nose, an ear, or the mandible.

There are two recognized subsets of hemangioma that demonstrate patterns of histologic and biologic behavior different from typical infantile hemangioma. They are both called congenital hemangiomas because they develop during prenatal life and present fully developed at birth. One type, known as rapidly involuting congenital hemangioma, involutes rapidly during the first few weeks or months of life [8]. These tumors are often raised with a characteristic redviolaceous color and coarse telangiectasias, often with a peripheral pale halo or central pallor. There is often superficial ulceration and, occasionally, signs of rapid arteriovenous shunting that can simulate an arteriovenous malformation. Their distribution more commonly involves the trunk and extremities. A second, less common type of congenital hemangioma termed noninvoluting congenital hemangioma persists into late childhood. These lesions are typically ovoid, macular, or slightly raised; pale gray in color with prominent telangiectasiae; and warm to palpation [9].

Differential diagnosis

There are two maxims to remember in the differential diagnosis of a cutaneous vascular lesion in infancy: not all hemangiomas look like strawberries, and not all strawberries are hemangiomas [7,10]. Hemangiomas are often misdiagnosed. A deep hemangioma, particularly in the cervical or axillary regions, can be mistaken for a lymphatic malformation. A macular hemangioma can have the appearance of a capillary malformation. Other infantile vascular tumors can be misdiagnosed as hemangioma, such as fibrosarcoma [11]. If there is any question about the clinical diagnosis, radiologic examination is mandated. Biopsy is essential if history, physical examination, or radiologic imaging create any suspicion of malignancy.

Clinical evaluation

Essential components of a first visit with the family of a hemangioma patient include:

- establishment of a rapport and open dialog with the parents or care providers;
- 2. confirmation of the diagnosis;
- 3. photographic documentation;
- consideration of the need for pharmacologic or surgical intervention;
- 5. determination of the need for other studies to

establish the extent of the hemangioma or to rule out associated anomalies; and

6. referral to reputable sources of information and parental support.

Parents with an affected infant, no matter how small or large the hemangioma, are understandably frightened. In general, hemangiomas arise postnatally in previously unblemished infants. Concerns include guilt over possible actions during pregnancy that may have incited this event and frustrations about how other individuals react to the child, as well as other fears of associated anomalies and of further growth of the lesion.

Reassurance is a mainstay, with open discussion of all of these issues. Parents are often afraid to raise these concerns, so a systematic review of hemangioma etiology, misinterpretation by the public, and relationship to other abnormalities is essential. It is helpful for the surgeon to openly recognize that the cause of hemangiomas remains entirely speculative and that there are no known linked factors. Parents should be told explicitly that having an affected child does not predispose them to having other affected children, but that this is a common enough entity that having another child with a hemangioma is not out of the realm of possibility.

Photographs are essential-they will provide a basis of reassurance for documented regression at subsequent visits. Many parents will present with a full set of photos documenting their emotional trial. It may be helpful to sit down and review photographic series of previous patients, documenting the course of regression or surgical results when an operation is indicated. Parents should also be referred to reputable information sources. The internet, an unedited modality, is replete with alarming Web sites, so it is helpful to guide families to respectable authorities. One particularly helpful Web site is the hemangioma newsline (www.hnnewsline.org), which is maintained by the National Organization for Vascular Anomalies. Depending on the level of concern, it may also be helpful to refer new parents to parents of previous patients who have indicated a willingness to speak with others.

The physical examination is generally detailed. Key questions to consider are:

- Is there dermatomal involvement, jeopardy to vision, a bearded involvement, or stridor in the head and neck?
- Is there ulceration?
- Are there multiple cutaneous lesions?
- Is there a lumbosacral or perineal involvement?

Dermatomal head and neck involvement. If there is a dermatomal distribution in V1/V2/V3, consideration must be made of PHACES syndrome (Posterior fossa malformations, Hemangiomas, Arterial anomalies, Coarctation of the aorta and cardiac defects, and Eye abnormalitieS) [12-14]. These hemangiomas tend to be macular with superficial skin involvement and a seeming paucity of subcutaneous tissue. In these cases, it is important to look for associated sternal notching or a midline raphe. If this is suspected, a full radiologic workup is mandated, including head and neck MRI/magnetic resonance angiography to visualize the carotids and circle of Willis, along with ophthalmologic evaluation. Reported ocular associations include micropthalmia, increased retinal vascularity, congenital cataract, and optic nerve hypoplasia. There may be persistent embryonic intra- and extracranial arteries, hypoplasia or absence of the ipsilateral carotid or vertebral vessels, aneurysmal dilatation of the carotid artery [12], coarctation and right-sided aortic arch, or dilatation of the carotid siphon.

Visual interference. In the neonate, assessment of any hemangioma that has the potential to increase pressure on the visual globe should include evaluation by a pediatric opthalmologist. Periorbital hemangioma can block the visual axis, causing deprivation amblyopia, or extend into the retrobulbar space, leading to ocular proptosis. More often, a small hemangioma involving the upper eyelid or supraorbital area can distort the growing cornea, producing astigmatic amblyopia. The results of the ophthalmic evaluation will help guide therapy.

Airway involvement/stridor. Subglottic hemangioma is a common life-threatening lesion. The symptoms are typically hoarseness and, later, biphasic stridor, generally manifesting between 4 and 12 weeks of age. Approximately 50% of these infants have a cutaneous cervical hemangioma, often in the "beard distribution" [15]. Evaluation of an infant with a cervicofacial hemangioma should include assessment of the airway. If pharmacologic therapy fails, a tracheostomy may be necessary.

Ulceration. Spontaneous epithelial breakdown, crusting, ulceration, and necrosis occur in 5% of cutaneous hemangiomas. Ulceration can arise at any anatomic site, but is most frequent in lesions involving the lips, perineum, anogenital area, and extremities (Fig. 2). The infant becomes tremendously irritable from the pain, often feeding and sleeping poorly. Ulceration may destroy an infant's eyelid, lip, or nose. Ulcerated sites may become secondarily infected, leading to cellulitis, septicemia, and, in some cases, death [16].

Cleansing, along with a daily application of hydrated petrolatum, such as Aquaphor or a topical antibiotic, is useful for small or superficial ulcerations. Topical viscous lidocaine may be applied intermittently to relieve pain. DuoDERM, Tegaderm, or Mepilex may be applied. Dressings are often

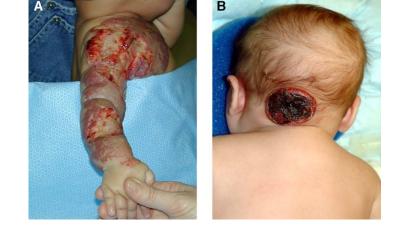


Fig. 2. Hemangioma ulceration. Ulceration may be (A) extensive or (B) localized. Surgical resection of localized, ulcerated lesions should be considered.

difficult to secure in anatomic locations where ulcerations are common.

Superficial ulceration usually heals within days to weeks, although deep ulceration can take weeks to reepithelialize. Pharmacologic treatment with corticosteroid can accelerate healing and minimize recurrence. Flashlamp pulsed-dye laser may also alleviate pain and promote healing. If possible, total resection of an ulcerated hemangioma should be contemplated if primary closure is possible and if the resulting scar would be predictably the same following surgical removal of the regressed hemangioma later in childhood. Resection in infancy is most often indicated for ulcerated tumors of the scalp, trunk, or extremity, and rarely for facial lesions. Following involution of hemangioma, scarring is predictably worse in areas of ulceration compared with previously nonulcerated areas.

Multiple cutaneous lesions

Multiple hemangiomas in a single patient have been called "disseminated hemangiomatosis." In these infants, the cutaneous lesions are usually tiny (<5 mm in diameter), firm, and dome-like. Any infant with five or more cutaneous tumors should be suspected to harbor visceral hemangiomas (most commonly in the liver, followed by the brain, gastrointestinal tract, and lung) and screened by way of ultrasonography or MRI as indicated.

Lumbosacral disease

Lumbosacral hemangiomas are recognized to be associated with an underlying tethered spinal cord. Ultrasonography is useful for screening infants less than 4 months of age for occult spinal dysraphism. MRI is generally needed to identify spinal cord abnormalities. There are rare instances in which pelvic or perineal hemangiomas may be associated with urogenital and anorectal anomalies, such as anterior or vestibular anus, hemiclitoris, atrophic or absent labia minora, and hypospadius [17].

Treatment

Observation. Most hemangiomas are small, banal tumors, which should simply be allowed to undergo proliferation and involution. These will leave normal or slightly blemished skin. Usually, however, an infant with hemangioma is referred to a plastic surgeon because of the hemangioma's large size, rapid growth, dangerous location, ulceration, or potential for other complications.

Pharmacologic therapy for complications. The precise frequency of endangering and life-threatening complications, such as tissue destruction, distortion and obstruction, caused by hemangiomas has been estimated to be 10% [18]. The first line of medical treatment is corticosteroid, either topical, intralesional, or systemic. If the lesion does not respond to corticosteroid, second-line pharmacologic agents include vincristine or interferon alfa-2b.

- 1. Topical or intralesional corticosteroid. Intralesional injection of corticosteroid should be considered for a small, well-localized cutaneous hemangioma located on the nasal tip, cheek, lip, or eyelid to slow the growth of the tumor and minimize distortion of surrounding structures. Triamcinolone (25 mg/mL), at a dosage of 3 to 5 mg/kg, is injected slowly at a low pressure with a 3-mL syringe and fine gauge needle. If possible, the periphery of the lesion should be compressed (using the ring of an instrument) to concentrate the colloidal particles within the lesion. Subcutaneous atrophy can result, but this is usually temporary. Typically, 3 to 5 injections are needed at 6- to 8-week intervals with a response rate similar to that for systemic corticosteroid. Intralesional injection for periorbital hemangioma should be used cautiously. Blindness and eyelid necrosis are reported complications. Potent topical corticosteroid resulted in improvement in one small series of patients with periocular lesions [19].
- 2. Systemic corticosteroid. The first-line treatment for problematic, endangering, or life-threatening hemangiomas is orally administered corticosteroid (Fig. 3). Prednisone or prednisolone is prescribed at a dosage of 2 to 3 mg·kg·d. The dosage is then tapered slowly, typically every 2 to 4 weeks, and the steroid is generally discontinued entirely when the child is 10 to 11 months of age. Occasionally, there is some minor rebound growth after corticosteroid is discontinued, which may mandate another 4 to 6 weeks of therapy. Rebound growth can happen if the dose is tapered too quickly or administered on alternate days. Live vaccines should be avoided during steroid treatment. The patient should also be started on an oral histamine receptor blocker (eg, omeprazole) because of corticosteroid-related gastric irritation. Side effects do occur with corticosteroid. A Cushingoid appearance is expected, such that parents should be forewarned. This subsides as the dose is tapered toward the end of therapy. There may be diminished weight and height gain, but a period of "catch up" growth has

been documented to occur following cessation of therapy [20].

 Second-line pharmacotherapy: vincristine, interferon alfa. In general, the sensitivity of hemangioma to corticosteroid is as high as 90%, with stabilized growth or accelerated regression. Indications for second line therapy are: (1) failure of response to corticosteroid; (2) contraindications to prolonged systemic corticosteroid; (3) complications of corticosteroid; and, rarely, (4) parental refusal to use corticosteroid.

Previously, recombinant interferon alfa-2a or -2b was considered as the second-line drug for endangering hemangiomas [21]. However, the side effects of this agent in infants (eg, spastic diplegia) can be serious [22], leading to the adoption of vincristine as an alternative for the treatment of corticosteroidresistant hemangiomas by several vascular anomaly centers [23]. There is no role for irradiation in the management of cutaneous hemangiomas.

Laser therapy. Pulsed-dye laser is reserved for ulcerated hemangiomas or for treatment of persistent telangiectasias following involution. Previously, some investigators advocated prompt lasering of nascent hemangioma in the belief that this would diminish growth of the tumor [24]. However, a comprehensive prospective study has now conclusively demonstrated that when infants with newly diagnosed hemangiomas were randomized to laser or control groups, there was no positive effect of laser on reducing subsequent hemangioma proliferation [25].



Fig. 3. Hemangioma regression in two patients who received corticosteroids. The first patient is depicted in (A) and (B), the second patient in (C) and (D).

Operative management. Excision can be considered during each of the three stages of the hemangioma life cycle for select circumstances.

- 1. Infancy (proliferative phase). Relative indications for excision of hemangioma during the proliferative phase include: (1) obstruction, usually visual or subglottic; (2) deformation, such as periorbital distortion with secondary astigmatic amblyopia; (3) bleeding or ulceration unresponsive to medical or laser therapy; and (4) anticipated scar from ulceration that would be more pronounced than that following surgical resection. Obstructive hemangiomas of the upper eyelid or brow that do not respond to pharmacologic therapy can be excised or debulked. Other respectable lesions include those that are well-localized or pedunculated, particularly those that bleed or are ulcerated. Ulcerated scalp hemangiomas generally lead to alopecia. The scalp is lax in an infant, facilitating excision and primary closure.
- 2. Early childhood (involuting phase). Typically, excision of a large or protruberant involuting phase hemangioma is done during the preschool period. Children generally become aware of physical differences at approximately three years of age. Excision of a hemangioma in early childhood is indicated if (1) it is obvious that resection is inevitable; (2) the scar would be the same were excision postponed until the involuted phase, or (3) the scar can be easily hidden. Unique consideration must be given to every child's hemangioma. Conventional resection techniques are not always applicable. Although lenticular excision and linear closure is a traditional method for the removal of a spheroidal lesion, a circular excision with intradermal purse-string closure may yield preferable results for resection of residual protruberant fibrofatty tissue following hemangioma involution [26].
- 3. Late childhood (involuted phase). When possible, resection of affected tissue should be postponed to this phase. The involuted skin can look quite normal, particularly if the hemangioma involved only the superficial dermis. Often, though, the skin is atrophic with tiny telangiectatic vessels. Previously ulcerated areas may manifest as a hypopigmented or yellowish-tan scar. Indications for resection during late childhood include (1) damaged skin, (2) abnormal contour, and (3) distortion. Resection may be possible in a single stage, but staged

excision may be required, particularly for involuted lesions of the lips, cheek, glabela, and scalp.

Pyogenic granuloma

Pyogenic granuloma is an extremely common acquired vascular tumor in the pediatric population. These lesions can occur anywhere but usually arise in the face. Pyogenic granulomas can grow rapidly, evolving from sessile papules into pedunculated tumors connected to the underlying dermis by a narrow stalk. They generally remain small (average diameter: 6.5 mm). Frightened parents will frequently bring their child to a physician's office following a bleeding episode. The treatment of pyogenic granulomas is either curettage, shave excision and laser phototherapy, or full-thickness excision.

Kaposiform hemangioendothelioma

Kaposiform hemangioendothelioma is a vascular tumor associated with profound thrombocytopenia, petechia, and bleeding—a constellation known as *Kasabach-Merritt syndrome*. Only recently has it been recognized that this tumor is entirely distinct from hemangioma of infancy (which is not associated with thrombocytopenia) [27]. Furthermore, the coagulopathy is more appropriately referred to as *Kasabach-Merritt phenomenon*, rather than a syndrome, because the mechanism for platelet trapping is not yet understood.

The tumor is generally present at birth, although it can also appear postnatally. The sexes are equally affected. They are unifocal and commonly involve the trunk, shoulder girdle, thigh, perineum or retroperitoneum, and, less commonly, the head and neck region. The overlying skin is a brawny deep redpurple in color, tense, edematous, and warm, with ecchymosis present over and around the tumor. Thrombocytopenia is profound (<10,000/mm³) with decreased fibrinogen, elevated fibrin split products, and generalized petechiae. In rare cases, kaposiform hemangioendothelioma can present without thrombocytopenia or coagulopathy.

Treatment is pharmacologic. First-line therapy is systemic corticosteroid; second-line treatment is vincristine or interferon. All of these therapies are less effective in treating kaposiform hemangioendothelioma than hemangioma. The mortality rate remains high, 20% to 30%, particularly for the retroperitoneal tumor. Kaposiform hemangioendothelioma often continues to proliferate into early childhood with some regression in mid-childhood. Even when therapy is successful in regressing the tumor, long-term follow-up often demonstrates persistent (although usually asymptomatic) tumor.

Vascular malformations

Classification

Vascular malformations result from errors of embryonic and fetal development. The classification of these anomalies is based on the clinical, radiologic, and histologic appearance of the abnormal channels, which may be either hematic or lymphatic in nature. A vascular malformation can be slow-flow (ie, capillary, lymphatic, or venous) or fast-flow (ie, arterial). If there are combinations of these elements, the malformation is called an arteriovenous malformation (AVM), lymphatico-venous malformation (LVM), or capillary-lymphatico-venous malformation (CLVM).

Capillary malformations

The pathogenesis of capillary malformations (CMs) is not understood. CMs occur anywhere on the body and can be localized or extensive. Historically, they have been referred to as port-wine stains-a term that is now outdated. CMs have an equal sex distribution; the birth prevalence is reported to be 0.3% [28]. The cutaneous discoloration is often, but not always, evident at birth; the stain may be disguised by the erythema of neonatal skin. Facial CMs often occur in a dermatomal distribution. Fortyfive percent of facial port wine stains are restricted to one of the three trigeminal dermatomes, while 55% of facial CMs overlap sensory dermatomes, cross the midline, or occur bilaterally [29]. The mucous membranes are often involved. With age, facial CMs generally become darker and can develop nodular expansion (Fig. 4). In the lower and mid-face, there can be maxillary or mandibular overgrowth with labial hypertrophy and gingival hyperplasia. In all patients with an upper facial CM, a diagnosis of Sturge-Weber syndrome should be considered on initial presentation. Cutaneous CM in the trunk and limbs is also associated with soft tissue and skeletal overgrowth, both axially and circumferentially; these, however, rarely demonstrate the textural and color changes seen in facial CMs.

CMs are often associated with developmental defects of the central neural axis. An occipital CM, frequently with an associated hair tuft, can overlie an encephalocele or ectopic meninges. A capillary stain

on the posterior chest can signify an underlying AVM of the spinal cord (Cobb syndrome). A CM over the cervical or lumbosacral spine may signal occult spinal dysraphism, lipomeningocele, tethered spinal cord, and diastematomyelia [30]. There may be subtle signs of neurogenic bladder dysfunction or lower extremity weakness, and therefore, careful neurologic examination, spinal radiographic imaging, and bladder function studies are indicated [31].

Sturge-Weber syndrome

Sturge-Weber syndrome consists of a facial CM with ipsilateral ocular and leptomeningeal vascular anomalies. The capillary stain can be ophthalmic (V1) extending into the maxillary (V2), or involve all three trigeminal dermatomes [29]. The leptomeningeal anomalies can be CM, VM, or AVM. Small foci can be silent, but extensive pial vascular lesions can cause refractory seizures, contralateral hemiplegia, and variably delayed motor and cognitive development. Anomalous choroidal vascularity can lead to retinal detachment, glaucoma, and blindness. Therefore, periodic fundoscopic examination and tonometry are essential in following children with Sturge-Weber syndrome with ophthalmic examination mandated every 6 months until age 2 and then yearly.

Current management of CM is cosmetic camouflage and laser photocoagulation, but there is still a place for excision and grafting. Timing of therapy with tunable flashlamp pulsed-dye laser is controversial. In general, significant lightening occurs in approximately 80% of patients. The outcome is better on the face (lateral moreso than medial) compared with the trunk. Multiple sessions may be required. The lesion darkens again in up to 50% of patients between 3 and 4 years following treatment.

Small fibrovascular nodules can be easily excised. Resection and resurfacing with split or full thickness skin grafts patterned to fit the esthetic facial units may be required in patients with extensive fibronodular hypertrophy. Contour resection can effectively correct macrochelia and labial ptosis [32]. Orthognathic procedures are indicated when there is occlusal canting, a result of hemimaxillary vertical overgrowth, or for mandibular prognathism.

Lymphatic malformations

The pathogenesis of lymphatic malformations (LMs) is unknown. LMs manifest in various forms, from a localized sponge-like lesion to diffuse involvement of an anatomic region or multiple organ systems (Fig. 5). Radiologically and histologically, they are characterized as microcystic, macrocystic, or

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Fig. 4. Appearances of facial capillary malformation are illustrated by patients (A-D). Note dermatomal distribution and increasing nodularity and tissue distortion in older individuals.

combined. In the nineteenth century, microcystic LMs were called *lymphangiomas* and macrocystic LM were called *cystic hygromas*; however, these terms are outdated and should be avoided.

LMs are usually noted at birth or within 2 years of life. Prenatal ultrasonography can detect relatively large lesions as early as the second trimester, although LMs are frequently misdiagnosed as other pathologic entities [33]. LMs most commonly occur in the cervicofacial region, axilla/chest, mediastinum, retroperitoneum, buttock, and perineum. The overlying skin is usually normal, but may have a bluish hue. Dermal involvement can manifest as puckering or tiny pathognomonic vesicles, which resemble minute blisters that become a dark-red color as a result of intravesicular bleeding.

Facial LMs are localized or diffuse, and may associated with skeletal overgrowth. Orbital LMs are reported to cause proptosis in 85%, ptosis in 73%, and restrictive eye movements in 46% of patients [34]. LM in the lower face is the most common etiology for macrochelia, macrotia, and macromala [7]. Cervicofacial LM may be unilateral or bilateral, with variable degrees of mandible involvement. LM in the floor of the mouth and tongue presents as macroglossia, vesicles, and intermittent swelling. An HEMANGIOMAS AND VASCULAR MALFORMATIONS

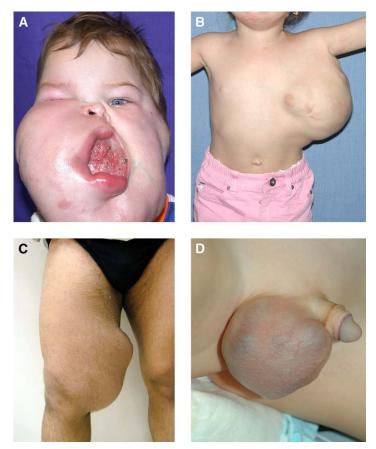


Fig. 5. Variable appearances of lymphatic malformation are noted in patients (A-D).

open-bite deformity generally results. In the neck, LMs most frequently occur in the anterior cervical triangle. Speech and swallowing may be impaired, and the possibility of oropharyngeal obstruction is a concern. Tracheostomy may be necessary in early infancy. The mediastinum is often involved in cervical LM.

Management of LM is directed at treating sequelae such as bleeding and recurrent infection, correcting contour, and improving function.

LMs can enlarge abruptly secondary to intralesional hemorrhage; this has been documented in 8% to 12.6% of lesions [35]. When this occurs there is sudden swelling and ecchymosis. Intralesional bleeding is a predisposing factor for infection, and antibiotics should be initiated. Cellulitis is common in LMs, particularly those in the head, neck, and perineum. This typically results in rapid expansion of the lesion with erythema, fever, and tenderness. Prompt initiation of antibiotic therapy is mandated. The clinical course may be lengthy. The involved area often remains indurated for months. Prophylactic antibiotics are generally not indicated for patients with LMs, although parents can be given a prescription to administer the drug at the first signs of infection. Dental hygiene is an important prophylactic measure in children with facial LMs.

Sclerotherapy may be an effective therapy for macrocystic lesions. Intralesional bleomycin has a reported success rate of greater than 80% in patients with LMs of the head and neck [36]. OK-432, a lyophilised mixture of attenuated group A *Streptococcus pyogenes* of human origin, has also been reported to have dramatic results reported [37]. Its mode of action is not fully understood. It is recognized to be significantly less effective in diffuse or microcystic cervicofacial LMs [37]. Argon, neodynium:YAG, or carbon dioxide laser can be used to coagulate lymphatic vesicles on the surface of the tongue or oral mucosa [38], although these usually recur.

Surgical procedures are indicated for respiratory obstruction, nutrition, and distortion caused by LMs.

A newborn with an extensive cervicofacial LM frequently presents with respiratory obstruction secondary to involvement of the tongue and floor of mouth, which may warrant immediate tracheostomy. Resection, the mainstay of treatment for LM, can usually be deferred until later infancy or early childhood (Fig. 6). Older infants are better able to tolerate prolonged anesthesia and the dissection of delicate neurovascular structures is often easier in an older child.

Although the operative goal is complete resection, this is rarely possible because the LM involves structures that must be preserved. For a diffuse malformation, staged excision is recommended, limiting each procedure to a defined anatomic area. Reoperation on a previously resected area is teduous, because LMs frequently develop venous flow following prior surgical interventions. Postoperative wound complications are common, including prolonged drainage, swelling, seroma, and infection. An elastic compression garment should be available immediately after the procedure with refitting of more custom garments planned following the resolution of postoperative edema.

Certain surgical considerations relate to the affected region. Coronal incisions are indicated for fronto-temporal-orbital LMs. Upper eyelid LMs are removed through upper tarsal fold incisions. Hemifacial LMs are generally resected through preauricular incisions, with meticulous dissection of the facial nerve in continuity with the superficial portion of the parotid gland. Facial LMs may also be directly excised through a melolabial incision or transoral route. Labial LMs are resected through a transverse mucosal incision without violation of the vermilion border. Surgical reduction of macroglossia may be required to restore the tongue in the oral cavity or because of an open bite deformity. Skeletal contour correction with osteotomies and orthognathic procedures are usually saved for adolescence, although they can be considered earlier [39]. Cervical LMs require a radical-neck type of dissection with identification of all nerves. If the cervical LM involves the axilla, excision of these areas should be done as a separate procedure. Axillary LMs may extend into the upper extremity, necessitating staged excision; if the brachial plexus is involved, all components must be identified and preserved [40].

Lymphangioma circumscriptum is the Latin term for a superficial cutaneous-subcutaneous lymphatic anomaly, which usually manifests in the posterior cervical area, shoulder, axilla, or lower extremity as multiple vesicles that bleed repeatedly and drain clear fluid. These communicate with blind-ended lymphatic cisterns deep in the subcutaneous plane. Definitive treatment necessitates excision of both skin and subcutaneous tissue down to fascia with subsequent graft or flap closure. There is a marked tendency for recurrence.

Venous malformations

Pathogenesis

Venous malformations (VMs) are the most common type of vascular malformation. They are composed of thin-walled, dilated, sponge-like channels of variable size and mural thickness with normal endothelial lining and deficient smooth muscle. In general, they are bluish, soft, and compressible and

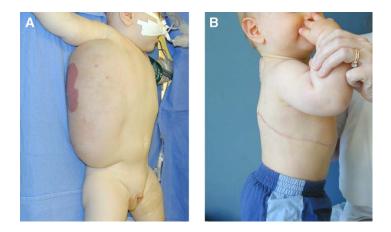


Fig. 6. Surgical resection of an extensive lymphatic malformation. (A) Preoperative view. (B) Postoperative view. (courtesy of Dr. Steven J. Fishman, Boston, MA).

tend to slowly expand with time. They principally occur in skin and subcutaneous tissues, but can also involve muscle, viscera, joint structures, and the central nervous system. They range in appearance from small varicosities to extensive lesions of the face, extremities or trunk (Fig. 7). Most VMs are solitary, though multiple cutaneous and visceral lesions also occur. The multifocal forms can be inherited.

VMs grow commensurately with the child and expand slowly, but may enlarge rapidly with thrombosis. They are easily compressed, expanding when the affected area is dependent, or following a Valsalva maneuver if the VM is in the head and neck region. Phlebothrombosis is common, leading to distention, firmness, and frequently pain in affected soft tissues. Pain and stiffness, particularly in head and neck lesions, is often most pronounced on awakening in the morning, presumably because of stasis and swelling. Phleboliths, diagnosed as radio-opaque nodules on plain radiography, can be seen in children as young as 2 years of age.

Cervicofacial VMs are often unilateral. They can produce a mass effect resulting in facial asymmetry and progressive distortion of features. Intraorbital VMs expand the orbital cavity and may communicate with VMs of the infratemporal fossa and cheek through the sphenomaxillary fissure. As a result, the patient can have exophthalmia when the head is dependent and enophthalmia when standing upright [30]. Oral VMs tend to cause dental malignment due to a mass effect. A buccal VM can involve the tongue, palate, and oropharynx but rarely impedes speech or swallowing. Pharyngeal, tracheolaryngeal, and deep cervical-oropharyngeal VMs may compress and deviate the upper airway to cause insidious obstructive sleep apnea.



Fig. 7. Variable morphologies of venous malformation are depicted in patients (A-D). The patient in C has a supraclavicular VM that becomes evident following the Valsalva maneuver.

VM in an extremity may be limited to the skin and subcutis, or extend into underlying muscles, joints and bone, or both. Limb length discrepancy can occur, or there can be hypoplasia of the affected side due, in part, to chronic disuse secondary to pain. Intraosseous VM causes structural weaking of the bony diaphysis predisposing to pathologic fracture.

Coagulation studies should be obtained in any patient with an extensive VM, because these can be associated with coagulopathy (distinct from Kasabach-Merritt phenomenon). MRI is the most informative imaging technique for documenting the nature and extent of a VM. Venography may be required for a complete assessment in patients with extensive VM.

Indications for treatment of VM include appearance, functional problems, and pain. The principal therapeutic modalities are elastic compression, sclerotherapy, and surgical resection or a combined approach. Elastic compression aids in reducing swelling and pain in an involved extremity. A custom garment can be worn while the patient is upright and removed during recumbency. A baby aspirin taken daily provides some prophylaxis against painful thromboses.

Sclerotherapy, the mainstay of treatment, is the injection of an agent to induce inflammation and obliteration of affected veins. For small cutaneous or mucosal lesions, local injections may be effective. For large VMs, sclerotherapy should be done under general anesthesia by an experienced interventional radiologist with real-time fluoroscopic, and often ultrasonographic, monitoring. Absolute ethanol is the most common sclerosant. Local complications of sclerotherapy include blistering, full-thickness cutaneous necrosis, and nerve injury [41]. Multiple sclerotherapeutic sessions, generally done at bimonthly intervals, are often necessary to shrink a VM because of recanalization of venous channels



Fig. 8. Variable appearances of arteriovenous malformation are seen in patients (A, B and D). The intraosseous mandibular AVM in patient A is subtle on physical examination, but can be visualized as quite extensive in a Lucite skull model (C) reconstructed through medical modeling of a MRI. (courtesy of Medical Modeling, Golden, CO).

following initial obliteration. The success rate is reasonably high; in one series, 76% of patients had marked improvement or cure [41].

In general, it is preferable to shrink a VM by sclerotherapy before scheduling surgical resection. Excision of a small, well-localized VM is usually successful in these cases. In some locations, such as the hand and forearm, staged subtotal resection can be accomplished without preoperative sclerotherapy.

Arteriovenous malformations

The pathogenesis of AVMs is not understood. Intracranial AVM is the most common, followed by extracranial head and neck, extremity, truncal, and visceral sites (Fig. 8). AVMs are usually noted at birth but are frequently misdiagnosed. Usually, they are mistaken for a CM or hemangioma. Fast-flow typically becomes evident during childhood. The cutaneous stain becomes more erythematous and develops local warmth, a palpable thrill, and a bruit. A mass may expand beneath the capillary stain, occasionally with rapid enlargement following trauma or during puberty.

Later consequences of arteriovenous shunting include ischemic signs and symptoms and indolent ulceration. Intractable pain and intermittent bleeding may ensue. In the lower extremity, dry brownviolaceous plaques, known histologically as *pseudo-Kaposi sarcomas*, may appear. An extensive AVM can cause increased cardiac output and, ultimately, congestive heart failure.

A clinical staging system, introduced by Schobinger in 1990, is useful for documenting the presentation and evolution of an AVM [42]:

- Stage I (quiescence): pink-bluish stain, warmth, and arteriovenous shunting by way of Doppler examination
- Stage II (expansion): same as stage I, plus enlargement, pulsations, thrill, bruit, and tense/ tortuous veins
- Stage III: same as stage II, plus dystrophic skin changes, ulceration, (destruction) tissue necrosis, bleeding, or persistent pain
- Stage IV: same as stage III, plus cardiac failure (decompensation)

Clinical diagnosis is confirmed by ultrasonography and color Doppler examination. MRI best documents the extent of the vascular malformation. AVM is characterized by the presence of feeding and draining vessels. Angiography shows variable degrees of arterial dilatation and tortuosity, arteriovenous shunting, and dilated draining veins. Feeding arteries may have aneurysms in older patients. Discrete fistulae can sometimes be visualized within diffuse AVM. In young children with diffuse AVM, a discrete nidus may not be identifiable.

The mainstays of management are embolization, sclerotherapy, surgical resection, and reconstruction. Ligation or proximal embolization of feeding vessels should never be done. Such manuevers deny access for embolization, and result in the rapid recruitment of new vessels from adjacent arteries to supply the nidus. Angiography precedes interventional or surgical therapy to precisely outline feeding and draining vessels. Embolization can be with coils or glue, either accessing the malformation from proximal arterial or retrograde venous approaches. Sclerotherapy is another approach that may be used if there are tortuous arteries or feeding vessels have been ligated. This involves direct puncture of the nidus during local arterial and venous occlusion.

Often complete resection is not possible or would result in severe disfigurement, particularly in a young patient. In these instances, embolization or sclerotherapy may be used to control symptoms, such as pain, bleeding, or congestive heart failure. Typically, embolization provides only transient improvement because of recruitment of new vessels by the nidus.

When surgical intervention is undertaken, embolization is done 24 to 72 hours before resection to provide temporary occlusion of the nidus and facilitates the surgical procedure. Extremity lesions may, in certain circumstances, be excised without preoperative embolization. The surgical goal is complete resection, unlike staged resection applicable to slow-flow vascular malformations, to minimize the chances of recurrence. The nidus, and usually involved skin, must be widely excised. Study of MRI scans, angiograms, and, occasionally, models made from MRI scans, is helpful in planning the excision. The pattern of bleeding from the wound edges is the best way to determine whether or not the resection is adequate. Intraoperative frozen sections from the resection margins may be helpful. Linear wound closure is sometimes possible. Often, primary closure requires skin grafting or tissue transfer. If there is any concern about the adequacy of resection, temporary coverage with a split-thickness skin graft can be an interim measure.

Combined embolization and surgical resection is most successful for stage I or II well-localized AVMs [43]. Follow-up evaluation is necessary for years with clinical examination supplemented by ultrasonography or MRI. The chances of recurrence are high, and experienced surgeons recognize that a "cure" can only be judged after many years. Interestingly, recurrence has been observed to involve free flap tissue used to reconstruct a defect, following incomplete excision of an AVM.

Unfortunately, many AVMs are not localized. They permeate deep craniofacial structures, infiltrate the pelvic tissues, or penetrate all tissue planes of an extremity [40]. In these cases, surgical resection is rarely indicated, and embolization for palliation is the only course.

Complex/combined malformations

Malformations not infrequently incorporate different combinations of vascular elements, such as lymphatic and venous endothelium in a lymphaticovenous malformation, and cannot be identified as purely one or the other. One example is "Klippel-Trenaunay syndrome" where patients have lesions that incorporate abnormal capillary, lymphatic and venous structures. This should, more correctly, be referred to a "capillary-lymphaticovenous malformation" or "CLVM". This malformation presents with unilateral or bilateral soft-tissue and skeletal hypertrophy of an extremity and may also be truncal. There is tremendous variability in the presentation of this disorder, from a slightly enlarged extremity with a capillary stain to a grotesquely enlarged limb with malformed digits (Fig. 9). There may be pelvic or visceral involvement. Coagulopathy is common in patients with extensive lesions. They may be hypoor hypercoagulable.

Treatment is aimed at the sequelae of this complex malformation, such as overgrowth, consequences of venous anomalies, and weeping from lymphatic vesicles. Overgrowth is both axial and circumferential. Limb length should be followed by an orthopedic colleague. A shoe lift may be required in early childhood with later epiphysiodesis of the femoral growth plate if there is a significant discrepancy. Grotesque congenital enlargement of the foot requires selective amputation. Massive circumferential enlargement of the calf, thigh, or buttock can be improved by staged contour resection. Hand involvement may necessitate procedures to improve function, such as digital or palmar debulking or ray resection of a massively enlarged digit. Before any surgical intervention for a CLVM, the anatomy of the deep venous system must be thoroughly evaluated. Unless a deep system is present and functioning, any intervention will predispose the patient to venous congestion in an affected extremity. An elastic compressive stocking is recommended for patients with symptomatic venous insufficiency. Treatment options for these problems include sclerotherapy, excision, and selected venous ligation.

An additional complex combined malformation is Parkes Weber syndrome, which denotes a complex high-flow AVM throughout a limb. This malformation is evident at birth with enlargement and

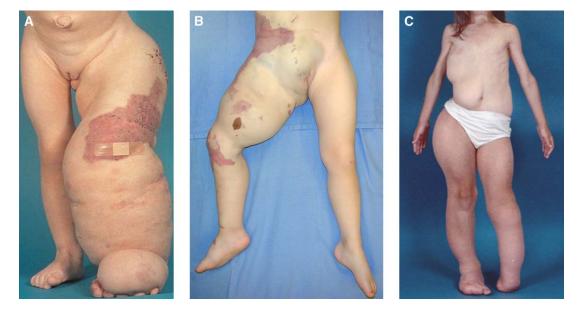


Fig. 9. Examples of CLVM, also known as *Klippel Trenaunay syndrome* are seen in patients (A-C).

confluent erythematous staining of the involved limb. The lower limb is more frequently involved than the upper limb. Detection of a bruit or thrill confirms the diagnosis. Overgrowth in an affected extremity is subcutaneous, muscular, and bony with diffuse microfistulae. Treatment is generally conservative, again with orthopedic involvement for the leg length discrepancy. Embolization may help with pain or cutaneous ischemic changes.

Vascular anomalies with syndromic associations

It is important for the plastic surgeon to be aware that a number of vascular anomalies fall into this category - syndromes that include both vascular malformations and other abnormalities. A full discussion is beyond the scope of this article. This includes Bannayan-Riley-Ruvalcaba syndrome, Proteus syndrome, and Maffucci's syndrome. In Bannayan-Riley-Ruvalcaba syndrome, patients have a PTEN tumor suppressor gene mutation, and develop vascular malformations and early malignancies. Proteus syndrome refers to a sporadic, progressive vascular, skeletal, and soft tissue condition that lies at the interface of vascular anomalies and overgrowth syndromes. Maffucci syndrome includes exophytic cutaneous venous malformations, bony exostoses, and enchondromas. There is a high rate of malignant transformation in these patients.

Summary

Patients with vascular anomalies were previously outcasts in the medical system. The internet has facilitated patient family communication and the advent of far-reaching support groups. With the advent of multidisciplinary clinics, physicians have found new ways to combine therapies for these complex patients. The plastic surgeon plays an essential role in defining this care.

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