Vascular anomalies are lesions seen in all surgical disciplines, particularly in pediatric patients. Specialization in vascular anomalies involves a team effort, with the team consisting of plastic surgeons, general surgeons, neurosurgeons, pediatricians, interventional radiologists, dermatologists, ophthalmologists, otolaryngologists, hematologists, and pathologists. Inconsistent nomenclature in the literature has historically resulted in confusion about classification, diagnosis, and treatment. A biologic classification system has emerged, based on clinical observations, natural history, and cellular features, which separates vascular anomalies into two broad categories: vascular tumors and vascular malformations. For many vascular anomalies, photodocumentation, psychosocial support, and communication are important throughout the treatment course [1].

Classification

Mulliken’s classification system of vascular anomalies was modified and accepted at the 1996 International Society of the Study of Vascular Anomalies workshop, based on the biologic activity of the tumor [2]. This system divides vascular anomalies into two categories based on endothelial activity: vascular tumors and vascular malformations. Vascular tumors, the most common of which are hemangiomas, exhibit rapid growth, endothelial proliferation, and angiogenesis, followed by postnatal regression. Vascular malformations are localized or diffuse errors in embryonic vascular structure that have a normal rate of endothelial cell turnover. Errors can exist in capillary, lymphatic, venous, arterial, or combined structures. Vascular malformations are truly congenital, as they are present at birth and may grow proportionally with the child. They may not be visible at birth, however, because of the small size or deep location of the lesion. Vascular malformations may enlarge with hemodynamic or hormonal changes. Immunohistochemical differences exist between proliferating hemangiomas and vascular malformations, which reflect the biologic differences in these anomalies [3]. They can also be differentiated by imaging studies, such as MRI and ultrasound with color Doppler flow imaging [4]. Antiquated terms, such as “strawberry,” “capillary,” “juvenile,” and “cavernous” hemangioma, are now replaced simply by “hemangioma,” with differences in clinical appearance and color attributable to the depth of the lesion in the dermis, fat, or muscle. Another example of confusing terminology is “port wine stain,” which is a lesion present at birth that does not proliferate or regress. This lesion is now classified as a capillary vascular malformation [2]. Despite the separation in terminology for vascular tumors and malformations, overlap may be seen in certain specific syndromes.

Vascular tumors

Hemangiomas

Epidemiology

Hemangiomas are the most common vascular anomalies of infancy (Fig. 1). They are true neoplasms that grow by rapid endothelial proliferation and are characterized by hypercellularity and an
increased numbers of mast cells and $[^3H]$ thymidine uptake during proliferation [5]. Most hemangiomas appear after birth, grow rapidly during the first year of life, and then predictably regress by ages 5 to 9 years. They occur in approximately 1% to 2% of neonates and in 4% to 12% of term infants by 1 year of age. The incidence is higher in females than in males (3–5:1) and higher in light-skinned than in dark-skinned infants. Studies have shown that hemangiomas are also more common in premature infants, correlating to both decreased gestational age and birth weight [6,7]. A review in 1991 found that hemangiomas are seen only incidentally with rare dysmorphic conditions. Specifically, hemangiomas may be associated with midline clefting, aortic arch coarctation, sacral deformities, and genitourinary (GU) defects [8].

Pathogenesis and natural history: clinical features

Often, hemangiomas are not present at birth but become visible early in the neonatal period. They typically appear as an erythematous pink or red macule, a blanched spot, or a telangiectasia surrounded by a pale halo [9]. Numerous studies have documented that approximately 40% of hemangiomas are present at birth as a small red mark [2,10]. Hemangiomas of the superficial dermis are more likely to be red or crimson, whereas lesions located in deeper tissue tend to have a blue hue. A study of 500 children with hemangiomas revealed four uncommon morphologic variations: deep hemangioma with normal overlying skin, macular hemangioma with port wine stain–like appearance, bossed hemangioma with telangiectasia and peripheral pallor, and hemangioma with persistent fast flow [11]. Hemangiomas demonstrate a rapid proliferation phase, lasting an average of 3 to 5 months [10], followed by a slower involutional phase. They often reach their maximum size by 9 to 12 months or earlier, although there is a subset that continues to proliferate for up to 18 to 24 months [12]. Involution begins as early as a few months after lesion appearance, with the usual onset at 12 to 18 months. The process usually begins centrally in the lesion, spreading peripherally. Complete involution occurs at an estimated rate of 10% per year; a convenient way to remember the rate of involution is to consider that 50% have involuted by age 5 years, 70% by age 7, and 90% by age 9 [12].

The mechanism of involution is not clearly understood. Cellularity, there is a decreased amount of endothelial cell label uptake and decreased number of mast cells, with the tissue being replaced by fibrofatty stroma during this phase [5]. Although most hemangiomas regress spontaneously, 10% to 20% ultimately require some form of treatment. Approximately 14% to 20% of infants have multiple lesions, sometimes in other organ systems, such as the liver, gastrointestinal tract, and brain. Skeletal deformities are very rare with hemangiomas. Infrequently, a “mass effect” may occur on adjacent bone, or there may be associated minor cartilaginous or bony overgrowth, presumably due to local increased blood flow. Cervicofacial and thoracic hemangiomas have a 5% to 10% risk for associated underlying structural abnormalities of the aortic arch and brachiocephalic and intracranial arteries. Hemangiomas of the lumbosacral region have a high incidence of concomitant spinal dysraphism, tethered cord, and anomalies of the pelvic region. Of 178 hemangiomas studied in one series, approximately 60% were located in the head and neck, 24% on the trunk, 7% in the upper limbs, and 10% in the lower limbs [10]. In this same study, neither sex, race, site, size, presence at birth, duration of the proliferative phase, nor clinical appearance of the hemangioma appeared to predict the age at involution. Mild cutaneous abnormalities, such as loose, wrinkled skin, fibrofatty changes, and scarring from ulcers, often remain after involution. Eighty percent of lesions involuting after age 6 result in residual scar, redundant skin, or telangiectasia, whereas only 38% of lesions have an imperfect cosmetic result if they involute before age 6 [10].

Radiographic features

Doppler ultrasound is the most cost-effective, noninvasive means of assessing the difference between hemangiomas and vascular malformations. A proliferating hemangioma will show variable echogenicity, high vessel density, and Doppler shift with low resistance [13]. These lesions may have
high-flow characteristics during the proliferation phase [14]. Hemangiomas with arterial flow can be distinguished from arteriovenous malformations on ultrasound by the presence of solid parenchymal tissue [4]. On contrast CT, hemangiomas appear as well-circumscribed masses of homogenous density, with enhancement during the proliferation phase. Lobular architecture is seen during the involutional phase. Evidence of skeletal change is uncommon. On arteriography, hemangiomas appear with an intense, persistent tumor blush. The well-circumscribed mass appears as lobular organization, with feeding arteries and draining veins [15]. MRI is considered the imaging modality of choice for the work-up of patients with vascular lesions, because it has superior soft tissue resolution and the ability to create arteriograms and venograms [16]. Lesions appear as clearly defined, low-intermediate signal, homogenous parenchymal masses on T1-weighted spin echo images. They demonstrate a high signal intensity on T2-weighted images. Fibrofatty replacement can be visualized during involution. Generally, there are no dilated vascular spaces or flow voids corresponding to visualized vessels [16].

Pathologic features
The endothelial cells from proliferating hemangiomas have been found to be clonal, consistently with the possibility that these tumors are caused by mutations in genes regulating endothelial cell proliferation [17]. The defect may also be due to a response to up-regulation of angiogenic factors or down-regulation of angiostatic factors in the tumor environment. A very distinctive characteristic of hemangiomas compared with vascular malformations and normal tissue is the increased number of mast cells during proliferation, with a return to normal mast cell numbers during involution. Mast cells produce heparin, which is thought to act as an angiogenic stimulator [18]. Another distinctive cellular finding is that hemangiomas demonstrate endothelial hyperplasia during proliferation, and they have a multilaminal basement membrane beneath the endothelium [2]. As these lesions involute, fibrous tissue is deposited, resulting in lobular architecture [12]. Both proliferative and involutional phases can be seen in the same lesion. Characteristic immunohistochemical profiles are seen during each phase of the life cycle. During the proliferative phase, many cellular markers, such as basic fibroblast growth factor (GF), urokinase, and vascular endothelial growth factor (VEGF), have been found to be elevated, whereas increased levels of these specific immunohistochemicals are not present in vascular malformations [3]. Recently, the glucose transporter—1 (GLUT-1) has been described as a specific and reliable marker for hemangiomas in all phases of development [19]. It is absent in vascular malformations, pyogenic granulomas, and granulation tissue, as well as in rapidly involuting and noninvoluting hemangiomas.

Complications
Bleeding usually responds to pressure, although surgical ligation may be needed if bleeding is refractory or voluminous. Ulceration is the most common complication of hemangioma, and it usually occurs during the proliferation phase. A risk exists for secondary infection, bleeding, and scarring. Local wound care must be addressed, as well as treatment of infection and pain control. Large ulcers may need corticosteroid therapy or pulsed-dye laser treatment to decrease lesion size and promote healing.

Visual obstruction with periocular hemangioma is a feared complication. Hemangiomas are the most common orbital tumor of children, and deep orbital tumors may present with only unilateral proptosis [20]. The most susceptible time for deprivation amblyopia is during the first year of life; obstruction for more than a few days can result in amblyopia or anisometropia. More commonly, the pressure of a growing tumor on the cornea may result in astigmatism. Tear-duct occlusion may also result. To prevent potential visual disturbances, any child with a periocular hemangioma should be followed by an ophthalmologist. Earlier and more aggressive treatment may be necessary to prevent visual compromise.

Nasolaryngeal obstruction is common with “beard” area or neck hemangiomas. Airway hemangiomas are rare and typically present in infants 6 to 12 weeks of age with cough and stridor, particularly during feeding or crying. Approximately 60% are associated with a cutaneous lesion of the preauricular region, chin, lower lip, or neck [12,21]. These patients need to be observed closely and evaluated immediately when any signs of airway compromise are noted. Tracheostomy or aggressive treatment of the hemangioma may be warranted. Another associated finding of cervicofacial hemangiomas is the presence of intracranial arterial anomalies [22].

Auditory canal obstruction is associated with parotid hemangiomas. These lesions almost always involve the entire gland and may be bilateral. Obstruction of the external auditory canal can lead to conductive hearing loss, although normal auditory development will occur unless the lesions are bilateral. Large parotid hemangiomas can also cause
airway compromise and ocular impairment. They involute slowly and in the past were thought to be more resistant to medical therapy [23]. A recent study, however, demonstrates that both corticosteroid and interferon therapy are effective in treating parotid hemangiomas. The rates of lesion regression and pharmacologic response are similar to those for hemangiomas at other sites [24].

Tethered spinal cord and genitourinary anomalies are associated with lumbosacral hemangiomas. Radiographic imaging by MRI is warranted in infants with lesions overlying the lumbosacral spine or extending from the anus into the gluteal cleft [12]. Deviation of the supragluteal cleft is a sign worthy of concern. Symptoms of spinal dysraphism may not arise until the child is 3 years of age or older; they include lower extremity paresis, muscle atrophy, and incontinence [23]. Other concomitant syndromic findings have been reported, such as imperforate anus, rectal fistulas, renal anomalies, abnormal genitalia, and other spinal cord defects [12].

Local consumptive coagulopathy can result from large hemangiomas. This entity is different from Kasabach-Merritt phenomenon and is characterized by local intravascular coagulopathy. Thrombocytopenia is usually minimal, with platelet counts between 50,000 and 150,000/mm³, evidence of fibrinolysis (decreased fibrin levels, increased fibrin split products), and elevated prothrombin time (PT) and activated partial thromboplastin time (aPTT) [25].

Kasabach-Merritt syndrome is not a complication of common hemangiomas. This life-threatening complication is related to two vascular neoplasms: kaposiform hemangioendothelioma and tufted angioma. A common clinical indication of Kasabach-Merritt phenomenon is a cutaneous telangiectasia that progresses to confluent ecchymosis [11]. In contrast to local consumptive coagulopathies, petechiae and hemorrhage occur with thrombocytopenia. The mortality is at least 12% and is higher for retroperitoneal locations [25]. Successful interventions are inconsistently reliable; they may consist of systemic steroids, interferon alpha-2a, embolization, pharmacologic agents that affect hemostasis, and surgical excision. Heparin therapy is not indicated [25]. In a study of 21 patients with Kasabach-Merritt phenomenon, all the tumors were single and grew to larger than 5 cm in diameter, and each had a pathognomonic skin change consisting of an advancing rim of ecchymotic, edematous tissue. The average platelet count at presentation was 25,000/mm³. PT and aPTT were normal, fibrinogen levels were decreased, and D-dimer was greater than 1, which may be indicative of a superimposed consumpation of coagulative factors [25]. Residual tumor is common after the resolution of thrombocytopenia and coagulopathy, as the resultant lesions appear to be prominent dormant vascular tumors instead of scars. These residual lesions differ histologically from involuted hemangioma [26].

Congestive heart failure is associated with multiple hemangiomas and visceral involvement. Skeletal changes are rarely associated with hemangiomas. Bony abnormalities may be due to local mass effect. Venous thrombosis can occur with hemangiomas. High-risk anatomic sites include the perineum and genitalia, which easily become ulcerated and infected.

**Treatment**

The management of hemangiomas ranges from simple observation and reassurance to surgical resection. Early intervention may be required to avoid severe complications or psychosocial implications. As the spectrum of the disease is broad, each case must be evaluated and treated on an individual basis. Ocular compromise and life-threatening complications, such as respiratory compromise and congestive heart failure, must be treated aggressively. Less threatening but important outcomes to consider are facial scarring, disfigurement, and social development. Biopsy of any vascular tumor is indicated if there is a suspicion of malignancy.

Observation is the most common initial management, as most hemangiomas regress. Conservative management is often the best treatment. Once the child reaches 4 to 5 years of age and begins school, intervention may be considered for psychosocial reasons. Parental reassurance is an important part of this process; interval photographs may be used to document the lesion’s stability or regression, thereby providing continual reassurance.

Intralosomal steroids are used to stop progression and promote hemangioma involution. Various compounds, such as triamcinolone, betamethasone, and dexamethasone, can be injected into the lesion at 4- to 8-week intervals. In one study of 155 lesions treated with three to six monthly injections of triamcinolone acetonide, 60% to 80% of the hemangiomas showed more than 50% reduction in volume, without subsequent growth. Superficial hemangiomas treated by this method yielded the best results [27]. Caution must be taken when injecting near the eye, because devastating complications include retinal artery occlusion and eyelid necrosis. Other complications include subcutaneous fat atrophy, depigmentation, and systemic absorption.
Systemic steroids are a successful treatment for hemangiomas. A review of 10 case series concluded that treatment of cutaneous hemangiomas with oral corticosteroids results in decrease in size—or cessation of growth in actively proliferating hemangiomas—in 84% of patients [28]. Hepatic hemangiomas are not as responsive to steroid therapy. The recommended initial dose is generally 2 to 3 mg/kg of prednisone daily for a 2-week trial. If there is evidence of regression or stabilization of the hemangioma, the treatment is continued for another 2 weeks and then tapered over several months, with completion by 1 year of age. (Higher doses were not found to be more effective [29].) Cessation of lesion growth is the most common response. The short-term systemic steroid side effects are usually transient and include cushingoid facies, adrenal suppression, personality changes, gastric irritation, fungal infection, hypertension, and diminished height and weight gain. In a study of 62 children taking oral steroids for hemangiomas, 91% returned to their pretreatment height growth curve by 24 months of age after cessation of therapy. Diminished growth was four to five times more likely when children were started on oral corticosteroids before 3 months of age or when they were treated for longer than 6 months [29]. Live virus vaccines should be avoided in children treated with steroids. A study by Akyuz et al [30] found no difference in tumor responsiveness between different steroids (prednisolone and methylprednisolone).

Interferon alpha-2a is an inhibitor of angiogenesis and endothelial cell growth that has been shown to slow the growth of hemangiomas by down-regulating fibroblast growth factor. This process may result in shrinkage of the tumor [31,32]. Interferon alpha-2a is given subcutaneously at a dose of 1 to 3 million U/m2 body surface area (BSA) daily. Results of a large study of 24 patients with life-threatening hemangiomas confirmed that responsiveness was 84%; 42% of patients had complete resolution of the lesion [33]. Common side effects include flu-like symptoms, neutropenia, anemia, leukocytosis, and increased hepatic transaminases. Cortical function and motor system side effects have been reported in adults on interferon alpha-2a therapy. A limiting complication is the occurrence of spastic diplegia in infants. The mechanism is not fully understood, and spastic diplegia appears to be reversible in most instances with cessation of treatment. Interferon alpha-2a is therefore recommended for life-threatening, difficult, or refractory lesions. Careful monitoring of motor and neurodevelopmental status is essential [33,34].

The chemotherapeutic agents vincristine and cyclophosphamide, in low doses, are inhibitors of tumoral angiogenesis and are reported to be effective therapies for hemangiomas [35,36]. Radiation therapy is not widely used, because of the associated risk for cancer, although proliferating hemangiomas are sensitive to it. Radiotherapy may be considered as a last resort for hemangiomas that have not responded to other treatments and are life-threatening or functionally disabling [27].

Lasers can be used successfully to treat proliferating hemangiomas, ulcerated hemangiomas, and residual discoloration or telangiectasias remaining after involution. Multiple treatments are usually required. Flashlamp pulsed dye lasers can be used to treat ulceration, telangiectasia, and erythema. This technique offers a minimal depth of penetration, and the beam does not allow the laser energy to reach the deep portion of the lesion [12,37]. Flashlamp pulsed dye laser treatment is most successful for complete remission in small, superficial hemangiomas and is recommended as an early treatment [38]. The Q-switched neodymium:yttrium-aluminum-garnet (Nd:YAG) laser is the treatment of choice for deep hemangiomas with subcutaneous components [31, 39]. Clymer et al [40] report pleasing results with minimal associated complications in all of their patients with hemangiomas or vascular malformations treated with the Nd:YAG laser. The carbon dioxide and argon lasers have also been described for treatment of hemangiomas.

Endovascular interventional therapy of large hemangiomas is indicated when their location and behavior interfere with the airway or vision, or when the hemangioma causes a consumption coagulopathy [14]. Persistent bleeding and infection are other considerations in treatment decisions. Embolization before surgical resection may be needed to improve outcomes. Often, multiple modalities must be used to treat hemangiomas successfully when they are life- or function-threatening lesions. Surgical excision is a consideration for hemangiomas that are life-threatening or are likely to have a deforming residual scar, cause psychosocial impairment, bleed, ulcerate, or result in airway or visual obstruction. The goals are function preservation (eg, sight, smell, hearing) and good cosmesis. Combination therapy may be needed for large, refractory lesions. Circular excision with a single intradermal purse-string closure has been demonstrated to result in a smaller, more favorable scar during any stage of the tumor’s life cycle [41].

**Associated syndromes**

PHACE syndrome is associated with large, plaque-like segmental facial hemangiomas. The acronym PHACE(S) stands for posterior fossa...
malformations (most commonly Dandy-Walker syndrome), hemangioma, arterial anomalies, coarctation of the aorta and cardiac defects (patent ductus arteriosus (PDA), ventricular septal defect (VSD)), eye abnormalities (microphthalmia, cataracts, optic nerve hypoplasia), and occasional sternal defects. Intracranial hemangiomas have also been found in association with this syndrome [42]. Nearly 90% of patients with PHACE syndrome are female [12]. Many other central nervous system lesions have been described, such as aneurysms and anomalous branches of the internal carotid and vertebral arteries. Seizure disorders and developmental delays are common [12]. Any infant with a large segmental facial hemangioma needs to be followed closely with brain and great vessel imaging, blood pressure in all four extremities to evaluate for aortic coarctation or right-sided aorta, ophthalmology referral for eye abnormalities, and developmental milestone monitoring.

Anatomic anomalies
Hemangiomas are associated with other anatomic malformations but rarely are found with dysmorphic conditions [8]. In these instances, female preponderance is the rule. The hemangiomas are often in midline structures. In addition to the PHACE syndrome, cervicothoracic hemangiomas may be associated with midabdominal raphe, sternal nonunion, and right-sided coarctation of the aorta. Lumbosacral hemangiomas can signal underlying spinal lipomeingocele, tethered spinal cord, or diastematomyelia. Pelvic and perineal hemangiomas can be associated with urogenital and anorectal anomalies, such as anterior or vestibular anus, hemilitoris, atrophy, or absence of the labia minora and hypospadias [43,44].

Hemangiomatosis

Definition
Eighty percent of hemangiomas occur as single lesions, whereas 20% of patients will have multiple hemangiomas. Benign or disseminated, this disease consists of the presence of a few to hundreds of small hemangiomas, with or without extracutaneous involvement. Often there is visceral involvement, which has been described as “disseminated hemangiomatosis.”

Pathogenesis and natural history
Benign hemangiomatosis is a condition that typically presents at birth or in the early neonatal period with numerous small, red to purple papulonodules. Visceral involvement, although rarely present, is usually asymptomatic. These tumors often completely regress by 2 years of age [45]. Disseminated hemangiomatosis often carries a poor prognosis for the affected infant, because of the involvement of numerous organ systems and associated complications. Virtually any organ system can be affected, but the liver is the most common extracutaneous site. Like cutaneous hemangiomas, hepatic hemangiomas are more common in females. Most infants with significant hepatic hemangiomas exhibit a triad of symptoms, consisting of hepatomegaly, congestive heart failure, and anemia. These symptoms usually become apparent by 1 to 16 weeks of age [23,46]. Multiple hepatic hemangiomas are usually heralded by concurrent cutaneous lesions [46]. Solitary hepatic hemangiomas and hepatic arteriovenous malformations may not be easily differentiated, because they are both fast-flow lesions that exhibit arteriovenous shunting. Arteriovenous shunting within hemangiomas can cause increased cardiac output and congestive heart failure. Other complications include hemorrhage and consumptive coagulopathy.

Treatment
A multidisciplinary team effort is important in evaluating and treating these patients. Any child with five or more cutaneous hemangiomas should be evaluated for extracutaneous tumors, such as those of the liver, brain, gastrointestinal tract, and lung. Doppler ultrasonography and MRI are useful screening and diagnostic tools. Cardiac failure must be treated with the goal of decreasing blood flow through the hemangioma. Laser treatments, systemic corticosteroids, interferon alpha-2a, chemotherapeutic agents, and surgical interventions compose the treatment. Embolization, hepatic artery ligation, hepatic resection, and even liver transplantation have been performed in severe cases. Early, aggressive treatment can lower mortality from 77% (if untreated) to as low as 27% [47].

Rapidly involuting congenital hemangioma and congenital nonprogressive hemangioma
These are “hemangiomas” that present fully developed at birth and remain static or rapidly involute. They have been found to be histologically, radiographically, and immunohistochemically distinct from common hemangiomas, tufted hemangiomas, and kaposiform hemangioendotheliomas [48]. These lesions are distinguished from common hemangiomas in that no central feeding vessels are seen on histology, and the lesions are GLUT-1 negative and have normal mast cell counts. In addition, radiographic imaging shows evidence of hemosiderin
deposition and thrombosis, absence of central arterial flow voids, and large, irregular feeding arteries in disorganized patterns [48,49].

Noninvoluting congenital hemangioma

Noninvoluting congenital hemangioma is a rare, congenital cutaneous vascular anomaly that grows proportionally with the child and does not regress. No gender predominance exists. Clinically, these lesions typically are well delineated, round or oval, and pink, blue-red, or purple in color, with a central or rim pallor and telangiectasia (Fig. 2). Radiologically, they are almost indistinguishable from common hemangiomas. They demonstrate increased numbers of mast cells and lobules of small vessels. Unlike common hemangiomas of infancy, these lesions do not test positive for the GLUT-1 marker. Because these lesions are fast-flow on Doppler evaluation, they have been treated as arteriovenous malformations in the past. Noninvoluting congenital hemangiomas do not exhibit early venous drainage, ruling out the diagnosis of arteriovenous malformation or arteriovenous fistula. Excision is the recommended treatment [50].

Tufted angioma

Tufted angioma is also known as “progressive capillary hemangioma” or “Nakagawa’s angioblastoma.” It is a rare, benign tumor with a slow rate of growth, predilection for the trunk, and absence of spontaneous involution. Most develop within the first year of life. The lesion is typically a dusky red to blue subcutaneous plaque or nodule, 2 to 5 cm in diameter. It is said to resemble a “doughnut,” with an annular shape and central depression. Many

Kaposiform hemangioendothelioma

Kaposiform hemangioendothelioma is a rare, locally aggressive, endothelial-derived neoplasm. These lesions are commonly associated with Kasabach-Merritt syndrome. They most commonly affect children younger than 2 years and are often present at birth. The incidence is similar in both genders, and there is a high mortality if the anomaly is left untreated. The lesions are typically on the trunk, extremities, or retroperitoneum. Mature lesions are violaceous, with a nodular growth pattern and surrounding telangiectasias or ecchymosis, which is associated with underlying Kasabach-Merritt syndrome. MRI will identify ill-defined tumor margins, with only a few small feeding and draining vessels. Histologically, kaposiform hemangioendotheliomas appear as lobular infiltrates of benign endothelial cells and are similar in appearance to Kaposi’s sarcoma [23].

Pyogenic granuloma (lobular capillary hemangioma)

Pyogenic granuloma, or lobular capillary hemangioma, is a common acquired vascular lesion of the skin and mucous membranes. It is usually seen as a solitary, bright red papule with a rapid growth rate. It frequently becomes pedunculated and usually measures 0.2 to 2 cm in diameter. Most lesions are located in the head and neck area (Fig. 3). The cause is unknown, but hypotheses include a hyperproliferative vascular response to viral infection, trauma, or an underlying dermatologic disorder or vascular anomaly. Pyogenic granulomas often occur within capillary malformations. Commonly, skin breakdown and bleeding prompt visits to the emergency room or physician’s office. Unlike common hemangiomas, pyogenic granulomas have a normal number of mast cells. In a review of 178 cases, pyogenic granulomas were found to occur most commonly within the first 5 years of life, with a male to female ratio of 3:2. Most patients (74%) had no history of pre-existing cutaneous disease or trauma [51]. Regression of pyogenic granulomas is uncommon. Lesions treated with cautery or tangential excision tend to recur, and surgical excision is the treatment of choice. Treatment with carbon dioxide laser or sclerotherapy has also been efficacious, with careful
Vascular malformations

Definition

Vascular malformations are present at birth and typically do not regress. They grow with the child or in response to hemodynamic changes secondary to trauma or hormonal influence. Unlike hemangiomas, vascular malformations have a normal rate of endothelial cell turnover and normal mast cell counts and \[^{3}\text{H}]\text{ thymidine uptake}\ [5]. They are considered to be true structural anomalies that result from an error in vascular morphogenesis between 4 and 10 weeks of gestation. They are usually firm, compressible, and not tender. They may distend with exertion, emotion, Valsalva’s maneuver, hot weather, or illness. Vascular malformations are subdivided into “high-flow” and “low-flow” lesions. High-flow lesions include arterial malformations, arteriovenous malformations, and arteriovenous fistulas. Malformations that are high flow often have palpable pulsatility. Low-flow lesions include venous, capillary, and lymphatic malformations. Skeletal deformities are common with low-flow lesions, causing body distortion, hypertrophy, or hypoplasia. Skeletal abnormalities associated with high-flow lesions are bony destruction, distortion, and hypertrophy. As with hemangiomas, vascular malformations can have local complications, such as orbital obstruction, and cosmetic consequences [14]. In general, low-flow lesions are treated with transcatheter sclerotherapy, whereas high-flow lesions are treated with embolization, sclerotherapy, or surgical excision [16].

Epidemiology

Unlike common hemangiomas, vascular malformations exhibit no gender predilection [10]. Most are sporadic errors in development, but some are inheritable in an autosomal dominant pattern. Vascular malformations—most commonly, macular stains—are reported to occur in approximately 40% of newborns [55]. Macular stains usually vanish within the first year of life.

Pathogenesis and natural history

Clinical features

Vascular malformations are present at birth and grow proportionally with the child. They do not typically involute and may expand with hormonal changes, such as puberty, exogenous hormone administration, pregnancy, and trauma. They usually remain the same color and are soft and compressible. Cervicofacial vascular malformations may have associated intracranial malformations.

Radiographic features

MRI is the best method for defining internal structure and flow characteristics of vascular malformations. They are heterogenous on contrast CT, and skeletal changes are commonly seen as bony destruction or remodeling [14,16]. Venous malformations have pathognomonic calcifications called “phleboliths.” Lymphatic malformations have cystic architecture and septae. On arteriography, vascular malformations appear as purely abnormal vessels without a dense mass [15]. Although ultrasound is useful to delineate superficial lesions, it is not able to evaluate intraosseous involvement or large, deep lesions [56].

Pathologic features

Vascular malformations exhibit normal endothelial cell turnover. In contrast with hemangiomas, they generally contain large vascular channels lined by flat endothelium and a unilamellar basement membrane. They have normal mast cell counts and do not demonstrate increased endothelial \[^{3}\text{H}]\text{ thymidine uptake}\ [2,18].

Complications

Skeletal hypertrophy is often associated with vascular malformations. In a study of 580 patients with vascular anomalies, there were 224 vascular malformations, 34% of them with bone changes (whereas only 1% of the patients with hemangiomas...
demonstrated bony involvement) [57]. In this study, bony hypertrophy and distortion were typical of lymphatic malformations. Hypoplasia and demineralization were common in extremity venous malformations. Destructive and intraosseous changes were found more often in arterial or other high-flow lesions. Another potential problematic complication of vascular malformations is visual obstruction, resulting from lesions that occur near the eyelids and orbit. Malformations affecting the upper extremity may interfere with finger dexterity and worsen with dependent positioning. Local consumptive coagulopathy can occur with vascular malformations.

Treatment

Depending on the type of lesion, possible methods of treatment include observation, compression garments, laser treatment, embolization, surgical debulking, and excision.

Capillary vascular malformation (port wine stain or naevus flammeus)

Pathogenesis and natural history

Capillary malformations occur in 0.3% to 0.5% of newborns and frequently involve the face and neck. They are typically flat, cutaneous lesions that change from pink to purple and become more cobblesstoned with age (Fig. 4). In contrast to common macular stains (eg, “salmon patch,” “angel’s kiss,” “nevus flammeus neonatorum,” and “nevus flammeus nuchae”), capillary malformations do not disappear with age but actually thicken and darken. Although the lesions occur spontaneously, there is an increased incidence of lesions in first-degree relatives, so that genetic analysis has been attempted.

One study found strong evidence that capillary malformations are linked to chromosome 5q [58].

Treatment

An ophthalmology consultation is essential for any patient with a facial port wine stain, because of the high incidence of glaucoma, most commonly associated with malformations in the supraorbital branch of the trigeminal nerve (V1) and infraorbital branch of the trigeminal nerve (V2) distributions. These lesions can be successfully treated, with minimal associated risks of scarring or complications, with a pulsed-dye yellow laser light [52].

Complications

The complications of capillary malformations may result from the underlying disorders that they herald. Similar to hemangioma, a lumbar midline capillary malformation can signal possible spinal dysraphism, lipomeningocele, or tethered spinal cord. A facial or occipital port wine stain can indicate a retinal arteriovenous malformation or meningoencephalocele, respectively. Treatment with lasers can be incomplete and result in scarring or pigmentation abnormalities.

Associated syndromes

Sturge-Weber syndrome is characterized by a facial port wine stain involving the area innervated by the first branch of the trigeminal nerve, although it can also involve V2 and V3 distributions. It is commonly associated with overgrowth of the facial skeleton, leptomeningeal malformations, choroidal angioma, and glaucoma. The patients usually suffer from seizures within the first year of life. Only 10% of individuals with the typical V1 port wine stain have Sturge-Weber syndrome. Klippel-Trenaunay syndrome is characterized by a cutaneous capillary malformation of the trunk or extremities, with underlying venous and lymphatic malformations. Associated skeletal overgrowth occurs. Parkes-Weber syndrome is another combined vascular disorder with capillary malformations, similar to Klippel-Trenaunay, with the addition of multiple arteriovenous fistulas or arteriovenous malformations.

Lymphatic malformation

Definition

Lymphatic malformations are often referred to as “lymphangiomas.” This terminology is confusing, because the suffix “-oma” stands for “tumor,” and these malformations do not proliferate and have a low rate of endothelial cell turnover. Lymphatic mal-
formations are low-flow or no-flow distended lymphatic channels that are usually present at birth and become more prominent with age. Microcystic lymphatic malformations may permeate the skin and muscle and can be associated with tiny, clear cutaneous vessels, commonly referred to as “lymphangioma circumscriptum.” This superficial aspect of the malformation can be misleading, because there is often an extensive intradermal and subcutaneous component.

Pathogenesis and natural history

Lymphatic malformations may appear as cool, soft, smooth, translucent masses that are located beneath normal or bluish skin. They are single or multiple cysts that can be separate or interconnected. Hypertrophy of soft tissue, fat, and bone often occurs. The most common sites of lymphatic malformations are the neck, axilla, and chest. These malformations generally do not regress spontaneously, and they occur equally in both genders. They usually are sporadic but may occur as part of a syndrome. Deep lymphatic malformations are the most difficult to distinguish from subcutaneous hemangiomas. Clinical differentiation may be possible, because lymphatic malformations are soft and compressible, whereas hemangiomas are firmer. Some authors comment on the tendency of lymphatic malformations to change in size, thus mimicking hemangiomas. This phenomenon may be due to the presence of infection or the opening of lymphatic venous anastamoses; it does not represent the involution and regression that occur with hemangiomas [2]. “Cystic hygroma” has been the common term for lymphatic malformations occurring at the base of the neck or shoulder. Radiologically, these are multiloculated cystic lesions with fibrous septae. Lesions in the head and neck can unexpectedly enlarge with infection and cause airway obstruction.

Treatment

Spontaneous resolution is thought to occur only in a small percentage of lymphatic lesions, usually by the age of 5 years. Resolution may be due to changes in the lymphatic and venous connections or to repeated inflammation and subsequent scarring. Expectant treatment is feasible for the first few years of life, unless complications occur. Compression garments can be used to control swelling in the extremities. Complete or staged partial excision may be performed successfully and is the treatment of choice. Transient enlargement should not trigger surgical intervention, because it is often a response to infection. Another treatment option is intralesional sclerotherapy under fluoroscopic or ultrasound guidance with bleomycin or picibanil (OK-432) [59–62]. Carbon dioxide or Nd:YAG lasers are used for treatment of small lesions and palliation of large ones.

Complications

Lymphatic malformations often enlarge secondarily to infection, and recurrent Beta-streptococcus infection is a common complication requiring treatment [63]. Bleeding may occur into the malformation. Cervicofacial lymphatic malformations represent a particularly difficult clinical entity, because complete resection is a challenge. Abnormal speech, airway compromise, mandibular bony overgrowth, and cranial nerve damage during resection are some of the complex sequelae that may need management [64].

Associated disorders and syndromes

An association exists between lymphatic lesions of the midline posterior cervical region and chromosomal abnormalities. Turner’s syndrome is a highly lethal chromosomal anomaly that involves lymphatic malformations of the head or nuchal region and fetal hydrops. Venous malformations of the gastrointestinal tract can also occur, leading to hemorrhage. Other associated syndromes include trisomy 13, 18, and 21, Roberts syndrome, and Noonan syndrome [55]. Klippel-Trenaunay and Parkes-Weber syndromes involve combined capillary, venous, and lymphatic malformations.

Venous malformation

Definition

Venous malformations are low-flow lesions that occur both sporadically and in a familial form [65]. They may consist of well-circumscribed, sponge-like

Fig. 5. Recurrent venous malformation of the wrist following remote surgical resection.
vascular spaces or poorly marginated collections of veins and present as a faint blue patch or a soft mass (Fig. 5). They may occur alone or as combined malformations.

Pathogenesis and natural history

Venous malformations are frequently noted at birth and may cause pain when swollen [66]. They occur in any body tissue, including internal organs and bone. Venous malformations may swell with exertion or when in a dependent position and contract with elevation. They may be asymptomatic or cause symptoms secondary to compression or bleeding (Fig. 6). Venous malformations may be localized to skeletal muscle, most often in the head and neck region or the extremities. Radiologic evaluation reveals a compressible soft tissue swelling with low velocity and monophasic blood flow. Osseous deformities and phleboliths may be present. These calcifications seen on CT are pathognomonic of slow-flow venous malformations [14].

Treatment

Treatment of venous malformations includes conservative management, because a great number of these are asymptomatic. Compressive garments and aspirin are used to minimize thrombotic events, whereas embolization, surgical excision, and sclerotherapy are used alone or in combination to treat lesions. Percutaneous sclerosis has been performed successfully with tetracycline, doxycycline, OK 432, bleomycin, dextrose, ethanol, ethanolamine oleate, and polidocanol microform [14,67–69]. This procedure should be done under fluoroscopic visualization or Doppler ultrasonography guidance to limit tissue necrosis and systemic effects. The sclerosant damages the endothelial cells, causing thrombosis and subsequent fibrosis. Because some recanalization occurs, a series of injections spaced 2 to 3 months apart is frequently needed.

Complications

Small areas of the venous malformation may spontaneously thrombose, causing pain and a palpable nodule. Large venous malformations may be associated with chronic consumption of fibrinogen and release of fibrin split products, with normal or slightly decreased platelets. Skeletal abnormalities are common with venous malformations. Trauma to the affected area may cause bleeding, infection, or thrombosis.

Associated disorders and syndromes

Turner syndrome patients may have venous malformations of the gastrointestinal tract. Blue-rubber bleb nevus syndrome consists of diffuse cutaneous and gastrointestinal venous malformations [8]. Other organ systems may be affected as well. The lesions tend to enlarge with time and may be painful. They are typically bluish in color, dome-shaped, firm, and rubbery in consistency. Blue-rubber bleb nevus syndrome consists of multiple venous malformations of the skin, mucous membranes, muscle, and viscera and may be a particular manifestation of an autosomal dominant familial venous malformation disorder [65]. Maffucci syndrome consists of venous and lymphatic malformations with bony shortening and deformity. Patients also have enchondromas of the fingers, toes, and proximal extremities. Malignant degeneration occurs in up to 20% to 30% of cases.

Klippel-Trenaunay and Parkes-Weber syndromes involve combined capillary, venous, and lymphatic malformations.

Arterial malformation

Definition

Arterial malformations fall into a broad spectrum of abnormal vessels, including tortuous, anomalous, hypoplastic, duplicated, stenotic, ectatic, and aneurysmal arteries. They are usually asymptomatic until later in life.

Pathogenesis and natural history

These high-flow lesions are unusual but exhibit warm skin with an associated thrill or bruit. Patients frequently present with a history of previous trauma to the involved area.
Treatment

Attempts at proximal vessel ligation have been unsuccessful. They often cause redirection of flow into other channels of lower resistance, resulting in more severe symptoms. Partial staged excision, with revascularization if needed, has been more successful [63]. Selective embolization is useful, depending on the location of the lesion. Irradiation and steroids are not indicated.

Complications

Consumptive coagulopathies may develop with extensive arterial malformations, as well as shunting and congestive heart failure. Limb hypertrophy and skeletal overgrowth are common. Pain and distal ischemia, secondary to proximal steal phenomenon, are associated [63].

Arteriovenous malformation

Definition

Arteriovenous malformations (AVMs) are fast-flow lesions composed of direct vascular connections between arteries and veins, bypassing the capillary network. Symptoms associated with AVMs include pain, hyperhidrosis, hypertrichosis, hyperemia, thrill, trophic changes, ulceration, and bleeding. Differentiating between AVM and hemangiomas is critical, given that their prognosis and treatment are different.

Pathogenesis and natural history

AVMs may present at birth, during infancy, or in conjunction with hormonal changes. They are commonly believed to arise during fetal development. They may be the result of failure of regression or apoptosis of primitive arteriovenous channels or of a failure of capillary bed formation in the primitive retiform plexus, perhaps related to local ischemia. It is thought that these abnormal communications persist, but they may not conduct fast blood flow for many years [70,71]. AVMs typically present with a cutaneous blush or increased local warmth. An associated bruit, redness, pain, and swelling may coexist, with possible tissue edema and ischemia. Puberty and pregnancy have an effect on the onset and progression of AVMs. In one study, 69% of head and neck AVMs were located in the middle face [70]. The surgical management of craniofacial AVMs has been historically problematic, because of significant blood loss and incomplete resection with multiple recurrences [71]. Ultrasound, MRI, and angiography are important imaging modalities for assessing the extent of AVMs and soft tissue involvement. Ultrasound with color Doppler flow imaging has been found accurate in differentiating AVMs from hemangiomas with arterial flow [4].

Treatment

AVMs may be considered one of the most difficult and frustrating lesions to treat. Methods of treatment include complete excision of the nidus and feeding vessels, combined embolization before excision of a large AVM, and complete embolization of the lesion. Embolization alone can be used for symptom palliation. Painful or rapidly enlarging lesions warrant early intervention because of the risk of progression and serious hemorrhage. Soft tissue reconstruction may be necessary after resection. In a study of 81 patients with head and neck AVMs, successful outcome was not significantly related to gender, age at treatment, clinical stage, or treatment method. In the same study, several malformations underwent rapid expansion in the time interval between embolization and resection, so the authors advocate resecting the lesion within 24 to 48 hours following embolization [70]. Proximal ligation of feeding vessels is contraindicated because of subsequent recruitment of adjacent vessels to supply the nidus, which may make future resection or highly selective embolization by means of the proximal artery more difficult.

Complications

As AVMs progress, pain, pruritus, ulceration, infection, and bleeding episodes may occur, as well as massive hemorrhage or congestive heart failure. Bony involvement may occur, with resultant skeletal deformities.

Associated disorders and syndromes

Rendu-Osler-Weber syndrome, or hereditary hemorrhagic telangiectasia, is an autosomal dominant disorder characterized by mucocutaneous telangiectasia and visceral AVMs.

Combined malformation

Definition

Any combination of vascular malformations may occur, such as capillary-lymphatic, capillary-venous, and capillary-lymphatico-venous malformations. Combined venous-lymphatic malformations often occur as a dorsal hand low-flow malformation with skeletal hypertrophy [63].

Associated disorders and syndromes

Many syndromes exhibit a combination of vascular malformations. The more common syndromes
include Maffucci syndrome (lymphatico-venous malformation), Klippel-Trenaunay syndrome (capillary-lymphatico-venous malformation), Parkes Weber syndrome (capillary-lymphatico-venous malformation with arteriovenous shunting, which distinguishes it from Klippel-Trenaunay syndrome), Solomon syndrome (capillary malformation, venous malformation, AVM), Riley-Smith syndrome (lymphatico-venous malformation), Bannayan syndrome (A VM, lymphatico-venous malformation), and Proteus syndrome (capillary malformation, venous malformation) [8].

Arteriovenous fistula

Arteriovenous fistulas are typically thought to be acquired through penetrating or blunt trauma, although they may be found in the absence of trauma. They consist of a single or few arteriovenous connections or side-to-side anastamoses. Because of the steal effect, the distal arterial circulation may become ischemic. Decreased cardiac output and ultimate failure may occur. Embolization may be used to occlude the arterial trunk [14].

Miscellaneous vascular malformations

Macular stain

Naevus flammeus neonatorum ("stork bite," "salmon patch," "angel kiss") and naevus flammeus nuchae are common macular stains found in up to 60% of infants. They are transient, flat, pink, irregular lesions that blanch with pressure and engorge with patient agitation. They occur in the glabellar region, eyelids, nape of the neck, and nasal alae. These lesions typically fade and disappear within the first year of life, which distinguishes them clinically from capillary vascular malformations. They are commonly associated with rare dysmorphic syndromes, such as Beckwith-Wiedemann syndrome [8]. This syndrome consists of omphalocoele, macroGLOSSIA, and a facial macular stain. Abnormalities of the liver, pancreas, and kidneys may also occur.

Telangiectasia

Telangiectasias are vasodilatations of the venous or arteriolar system. Spider veins of the lower extremities are common and are primarily related to venous dilatation. Facial telangiectasias are arteriolar dilatations that are thought to result from sun exposure. Sclerosing agents, such as polidocanol and laser therapy, are the mainstays of treatment. Cutis marmorata is a normal cutaneous vascular pattern seen in fair-skinned children when placed in a low-temperature environment.

Associated syndromes

Cutis marmorata telangiectatica congenita is a severe, pathologic version of cutis marmorata in which the cutaneous marbling may become apparent at normal temperatures and involve dark, depressed areas of skin. Local ulceration, scarring, and skin atrophy may occur. Rendu-Osler-Weber syndrome, or hereditary hemorrhagic telangiectasia, is an autosomal dominant disorder that is most common in the white European population. It consists of discrete, spider-like red maculopapules on mucosal surfaces, face, fingers, and nail beds. These lesions are also found in solid organs. They commonly become apparent after puberty and are prone to ulceration and bleeding. Louis-Bar syndrome, or ataxia-telangiectasia, is an autosomal recessive disorder characterized by cerebellar ataxia and cutaneous and ocular telangiectasias. Frequently, a severe immunologic deficiency is associated, and patients may have recurrent severe respiratory tract and sinus infections. Essential telangiectasia is an acquired, generalized, idiopathic disorder that occurs almost exclusively in females and usually becomes apparent in adulthood. The lesions are predominantly on the lower extremities, and they progress into serpiginous patterns or sheets of telangiectasias. They usually do not bleed.

Angiokeratoma

Angiokeratoma is a localized vascular malformation of the dermis that occurs with associated hyperkeratosis. These lesions usually present as dark red to black papules that tend to bleed when traumatized. They occur in different anatomic groups, such as the hands and feet, genitalia, or trunk and thighs. Fabry’s disease is a sex-linked recessive metabolic disorder associated with angiokeratomas of the hips, buttocks, and perineum.

Summary

Vascular anomalies are a group of lesions that are technically and intellectually challenging to diagnose and treat. They may have a profound psychosocial impact on the patient and family, and the natural course of the lesion may be life- or function-threatening. Improved classification systems, diagnostic modalities, and treatment options have made the study and therapy of these anomalies
References


