Hemangiomas and Vascular Malformations

33

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For decades, pediatric vascular anomalies were classified into two broad categories: hemangiomas and everything else. More specifically, clinicians were taught to distinguish hemangiomas and a handful of other biologically active, proliferative vascular anomalies (Table 33.1) from biologically inactive, non-proliferative vascular malformations (Table 33.2). For the most part, this is still a clinically useful strategy, as the treatment options and timing of intervention sometimes differ drastically. However, with the complete sequencing of the human genome and rapid advances in the identification of mutations associated with many vascular anomalies, targeted medical therapy has dramatically revolutionized the understanding and the approach to vascular anomalies. Table 33.3 shows a partial list of vascular syndromes. Table 33.4 is short list of currently unclassified vascular anomalies. Table 33.5 is a list of vascular conditions with known hereditary influence. Table 33.6 is a sampling of some vascular anomalies and their causal somatic mutations.

Table 33.1 ISSVA (International Society for the Study of Vascular Anomalies) classification. Proliferative Vascular Anomalies

Clinical behavior	Clinical examples
Benign	• Infantile hemangioma (Glut-1 positive) • Congenital hemangioma (present at birth, Glut-1 negative) • Rapidly involuting (RICH) • Non-involuting (NICH) • Partially involuting (PICH) • Tufted angioma • Spindle-cell hemangioma • Epithelioid hemangioma • Pyogenic granuloma (lobular capillary hemangioma) • Other benign vascular tumors
Locally aggressive or borderline	• Kaposiform hemangioendothelioma • Kaposi sarcoma • Other hemangioendotheliomas
Malignant	• Angiosarcoma • Epithelioid hemangioendothelioma • Other malignant vascular tumors

Table 33.2 ISSVA (International Society for the Study of Vascular Anomalies) classification. Vascular Malformations

Lesions	Characteristic clinical manifestations
Capillary malformations (CM)	• Port-wine stains • Cutis marmorata telangiectatica congenita (CMTC) • Hereditary hemorrhagic telangiectasia (HHT)
Lymphatic malformations (LM)	• Macrocystic, microcystic, and mixed • Kaposiform lymphangiomatosis (KLA) • Gorham-stout disease (GSD) • Primary lymphedema
Venous malformations (VM)	• Common venous malformations • Blue rubber bleb nevus syndrome • Glomuvenous malformation (GVM)
Arteriovenous malformations (AVM)	• Sporadic • Hereditary hemorrhagic telangiectasia (HHT) • Capillary malformation/AVM
Arteriovenous fistulas (AVF)	• Sporadic
Combined vascular malformations (2 or more malformations in 1 lesion)	• Capillary venous (CVM) • Capillary lymphatic (CLM) • Capillary arteriovenous (CAVM) • Lymphatic venous (LVM) • Capillary lymphatic venous (CLVM) • Capillary lymphatic arteriovenous (CLAVM) • Capillary venous arteriovenous (CVAVM). • Capillary lymphatic venous arteriovenous (CLVAVM).
Anomalies of major named vessels	• Sporadic

A Complex Vascular Anomalies Team will comprise many disciplines including surgery, interventional radiology, diagnostic radiology, dermatology, physical therapy, pathology, and of increasing importance and dominance, genetics

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Table 33.3 ISSVA (International Society for the Study of Vascular Anomalies) classification. Vascular Malformation Syndromes

Syndrome	Characteristics
Klippel-Trenaunay syndrome	Limb with: • Capillary malformations • Venous malformations • ± Lymphatic malformation • Hypertrophy
Parkes Weber syndrome	Limb with: • Capillary malformations • Arterio-venous fistula • Hypertrophy
Servelle-Martorell syndrome	Limb with: • Venous malformations • Hypertrophy • Bone hypoplasia
Sturge-Weber syndrome	• Facial capillary malformation in V1 distribution • Leptomeningeal capillary malformation • Glaucoma • ± Bone and soft tissue hypertrophy
Maffucci syndrome	• Multiple enchondromas • Venous malformations • ± Spindle-cell hemangioma
CLOVES syndrome	• Congenital lipomatous overgrowth • Venous malformations • Epidermal nevi • Spinal abnormalities • Capillary malformations • ± Arteriovenous malformations
Proteus syndrome	• Asymmetrical somatic overgrowth • Capillary malformations • Venous malformations • ± Lymphatic malformation
Bannayan-Riley-Ruvalcaba syndrome	• Arteriovenous malformations • Venous malformations • Macrocephaly • Lipomatous overgrowth
CLAPO syndrome	• Capillary malformation lower lip • Lymphatic malformation face and neck • Asymmetry • Partial or generalized overgrowth
PHACES	• Posterior cranial fossa abnormalities • Facial hemangioma • Arterial anomalies • Cardiac defects or coarctation of the aorta • Eye abnormalities
Blue Rubber Bleb syndrome	• Multiple dermal venous malformations • Gastrointestinal involvement
LUMBAR	• Lower body hemangioma • Urogenital anomalies and ulceration • Myelopathy • Bony abnormalities • Anorectal and arterial anomalies • Renal anomalies

Table 33.4 ISSVA (International Society for the Study of Vascular Anomalies) classification

Unclassifed vascular anomalies
• Intramuscular hemangioma
• Angiokeratoma
• PTEN (Phosphatase and tensin analog) hamartomas, angiomas of soft tissue, tumors.
• FAVA (fibro adipose vascular anomaly)
• Multifocal lymphangioendotheliomatosis with thrombocytopenia/ cutaneous visceral angiomatosis with thrombocytopenia (MLT/ CAT)

Table 33.5 Inherited vascular anomalies and causal genes

Syndrome	Affected gene
Hereditary hemorrhagic telangiectasia (formerly Osler Rendu Weber)	*ENG, ACVRL1, SMAD4*
Blue rubber bleb nevus syndrome (Bean syndrome)	*TEK (TIE2)*
Familial cutaneous/mucosal venous malformation (VMCM)	*TEK (TIE2)*
Glomuvenous malformations (glomus cell tumors)	*Glomulin*
Primary lymphedema (Nonne-Milroy syndrome)	*FLT4, VEGFR3*

Table 33.6 Sporadic vascular anomalies and causal genes

Syndrome	Affected gene
Capillary malformation (port-wine stain)	*GNAQ*
Capillary malformation with AVM	*RASA1, EPHB4*
Lymphatic malformation	*PIK3CA*
Common venous malformation	*TEK (TIE2), PIK3CA*
CLOVES syndrome	*PIK3CA*
Klippel-Trenaunay syndrome	*PIK3CA*
CLAPO syndrome	*PIK3CA*
Fibro adipose vascular anomaly (FAVA)	*PIK3CA*
Proteus syndrome	*AKT1*
Pyogenic granuloma (lobular capillary hemangioma)	*BRAF, GNA 14*

and oncology. Similar to a tumor board, the multidisciplinary vascular anomalies team can review complex cases that may benefit from a combination of diagnostic and therapeutic options.

Hemangiomas

Hemangiomas are the most common benign neoplasm of infancy, occurring in 10% of full-term babies and as many as 25% of prematures weighing less than a kilogram. Many clinicians still erroneously call all vascular birthmarks hemangiomas, and since all hemangiomas regress spontaneously

and most require no surgical intervention, parents are often advised to wait patiently for 5 years for the hemangioma to "disappear." Unfortunately, 30% of hemangiomas leave significant deformities that cannot be entirely corrected by surgery, and vascular malformations have no ability to regress, leaving a population of children and parents with inappropriate therapy and overly optimistic expectations.

Vascular malformations include abnormally formed capillaries, arteries, veins, lymphatics, or combinations of different vessels that occur in utero, are present at birth (although not always clinically evident), and persist throughout life. More and more of these conditions can now be ascribed to mosaic somatic mutations. Others are clearly hereditary in nature with the dominant genetic transmission. Whereas in the past they were thought to merely exist and slowly dilate, it is now understood that growth can be stimulated by puberty and suppressed by chemotherapeutic agents that block various specific steps of vascular growth.

The typical hemangioma presents in the first few weeks of life as a small strawberry-colored skin lesion that begins to grow out of proportion to the growth of the infant. (Fig. 33.1) The proliferative phase may continue for 6–12 months until the angiogenic factors that stimulate endothelial growth begin to turn off. The first signs of regression include a pale grayish-white color change and a decrease in tissue turgor as the vessels begin to involute. The average hemangioma takes about 5 years to fully regress.

A small subset of *rapidly involuting congenital hemangiomas* (RICH) are present at birth and undergo rapid involution during the first year of life. (Fig. 33.2) Conversely, *non-involuting congenital hemangiomas* (NICH) never seem to involute, are bluish in color with a fine telangiectatic pattern and are warm to the touch, resembling arteriovenous malformations. (Fig. 33.3) Subcutaneous hemangiomas appear blue but are nevertheless composed of proliferating capillary endothelial cells rather than larger vessels; they are still often errone-

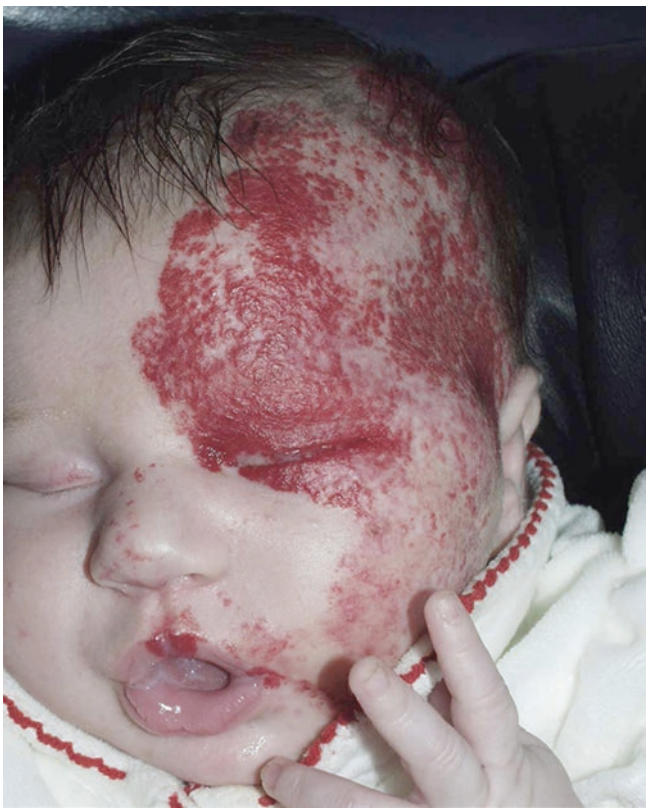


Fig. 33.1 Periorbital hemangioma in the proliferative phase. An ophthalmologist or oculoplastic surgeon is an important part of the multidisciplinary team, as is a dermatologist who can direct oral beta blocker therapy

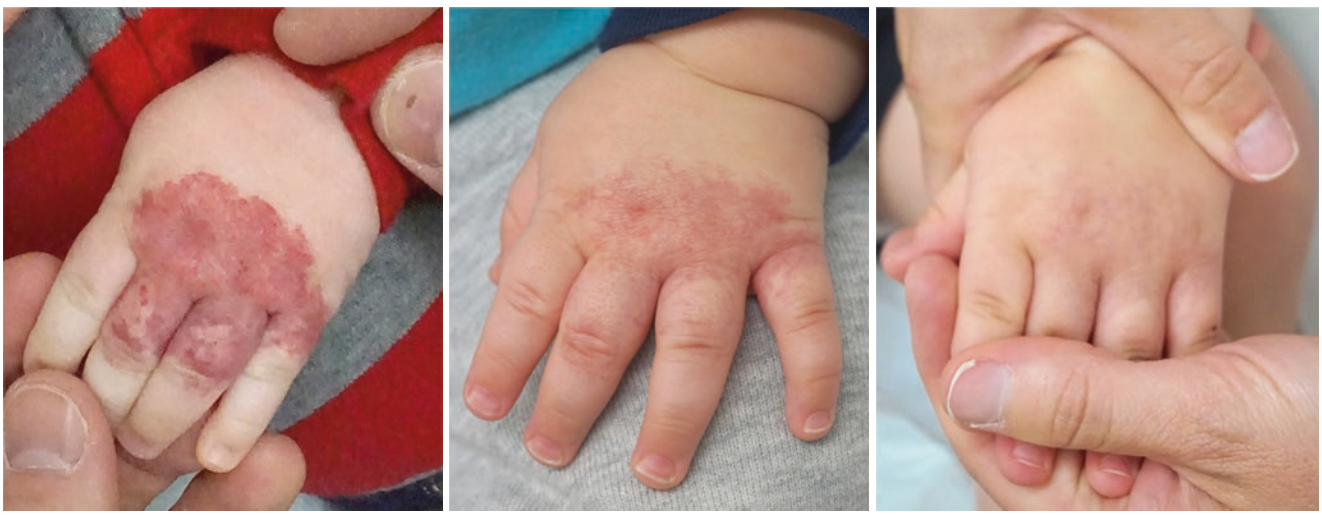


Fig. 33.2 Rapidly involuting congenital hemangioma of the hand (left) with marked improvement after 7 months (center) and near complete resolution after an additional 8 months (right)

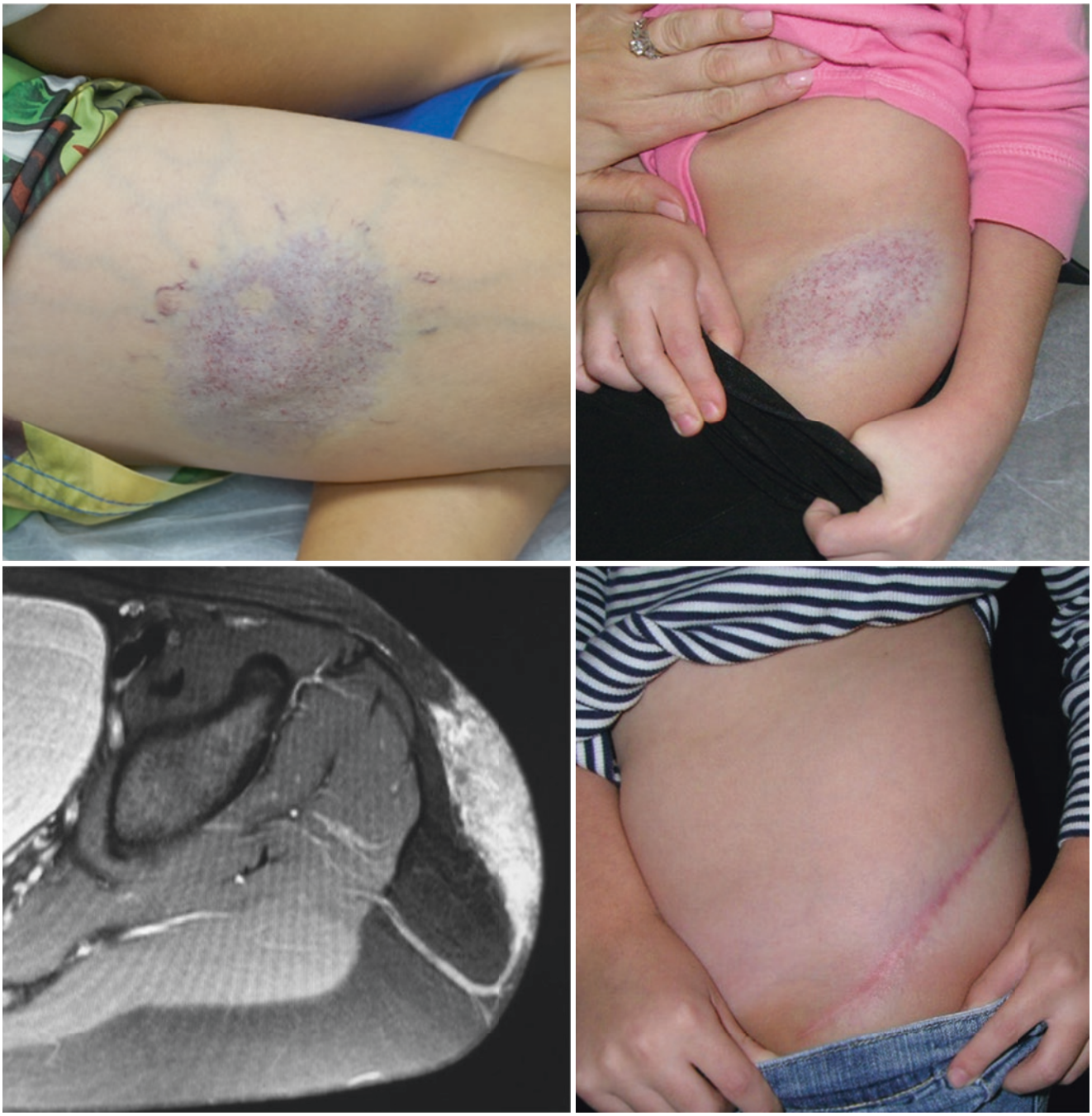


Fig. 33.3 Non-involuting congenital hemangioma of the lateral thigh (top left and top right). NICH of the groin supplied by a single feeding vessel (bottom left), treated by complete excision (bottom right)

ously referred to as "cavernous" hemangiomas. Some hemangiomas have both dermal and subcutaneous components and therefore present with a combination of protruding strawberry and subcutaneous blue bulky soft tissue. (Fig. 33.4).

Although they can occur in any location, 60% of all true hemangiomas are located on the head and neck. Visceral hemangiomas (hepatic and splenic) can also occur. Babies with six or more cutaneous hemangiomas warrant an abdominal ultrasound to rule out this potentially life-threatening condition, which can also be associated with failure to thrive and high-output cardiac failure. In addition, hemangiomas are sometimes part of a syndrome or association. The PHACES association includes posterior cranial fossa abnormalities such as Dandy-Walker cysts, a large facial hemangioma, arterial anomalies, cardiac defects or coarctation of the aorta, eye abnormalities, and sternal clefting or Supraumbilical raphe. Children with the LUMBAR association have a lower body hemangioma, urogenital anomalies

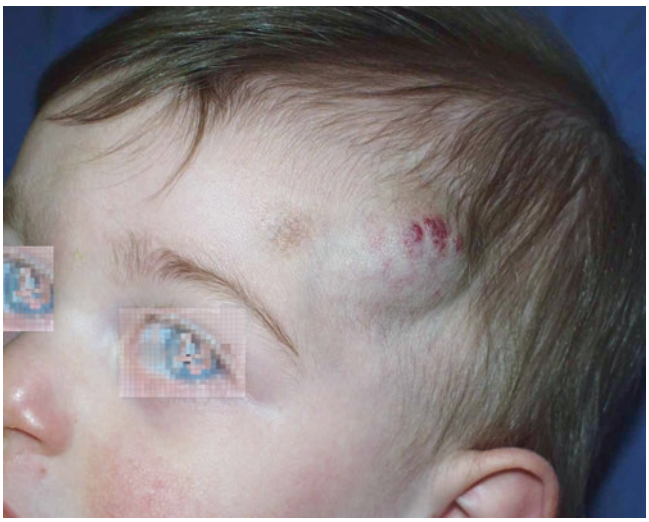
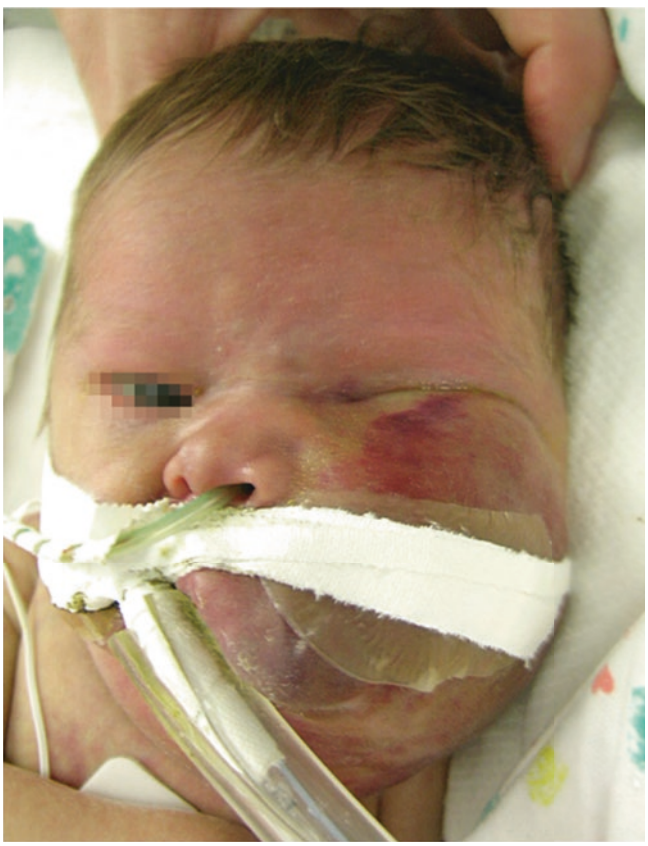


Fig. 33.4 Hemangioma of the temporal scalp with both subcutaneous and dermal components

and ulceration, myelopathy, bony abnormalities, anorectal and arterial anomalies, and renal anomalies (previously known as PELVIS: perineal hemangioma, external genital abnormalities, lipomyelomeningocele, vesicorenal abnormalities, imperforate anus, and perineal skin tag).

Other proliferative vascular anomalies that occur in infancy include *Kaposiform hemangioendothelioma* (Fig. 33.5) and *angioblastoma* (tufted angioma). Both can cause platelet-trapping and life-threatening thrombocytopenia (Kasabach-Merritt syndrome) and often require a tissue biopsy to make the diagnosis. *Angiosarcomas* are extremely rare malignant tumors that occur mostly in the elderly but have been reported in children.

Pyogenic granulomas, more accurately termed *lobular capillary hemangiomas*, occur at any age, might be caused by minor skin trauma with inappropriate angiogenesis, and are characterized by small vascular lobules. They have a fragile epidermal cover and can bleed profusely (Fig. 33.6).



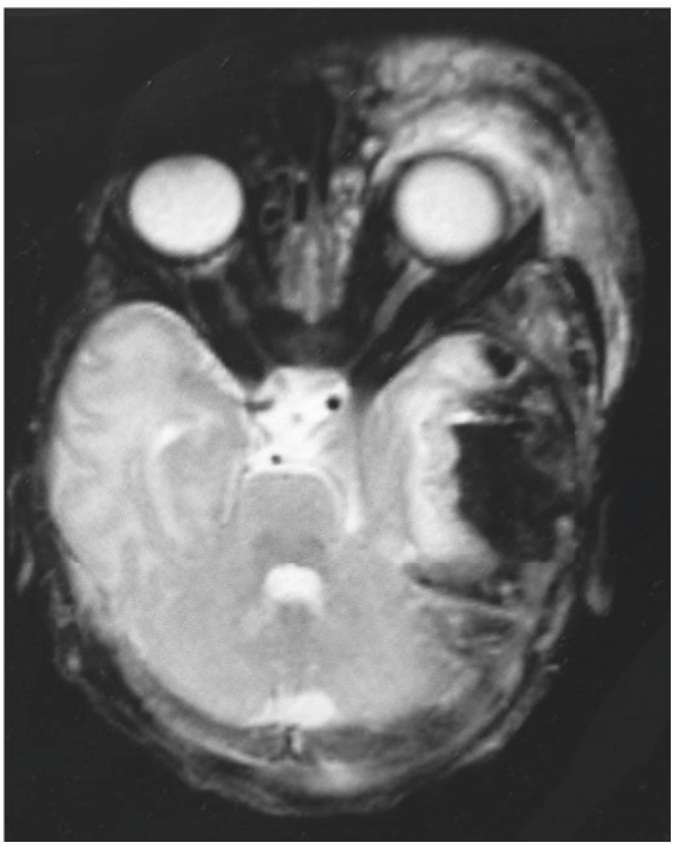


Fig. 33.5 Kaposiform hemangioendothelioma of the left cheek (top left and top right)which was treated with vincristine, steroids, and interferon alpha. He had a left facial palsy (bottom left) that required reanimation with a cross-facial nerve graft and a free gracilis muscle transfer (bottom right)

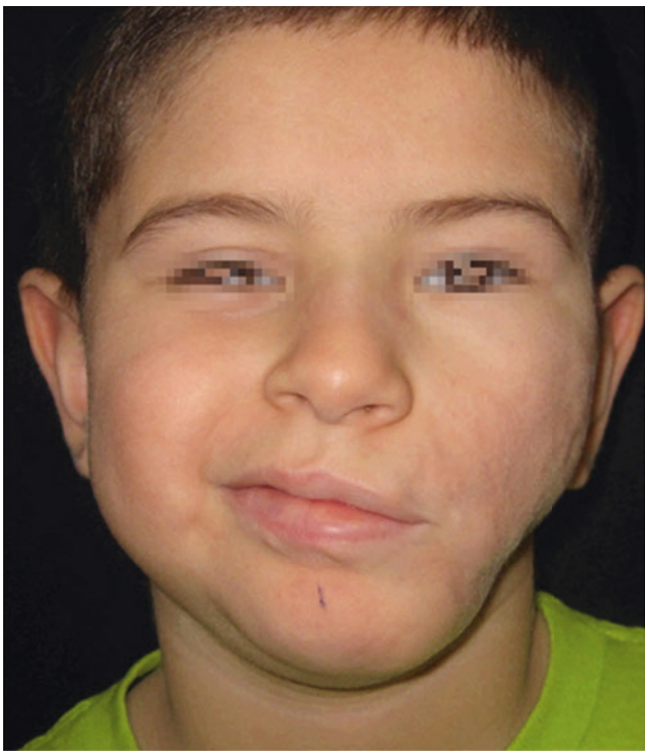


Fig. 33.5 (continued)

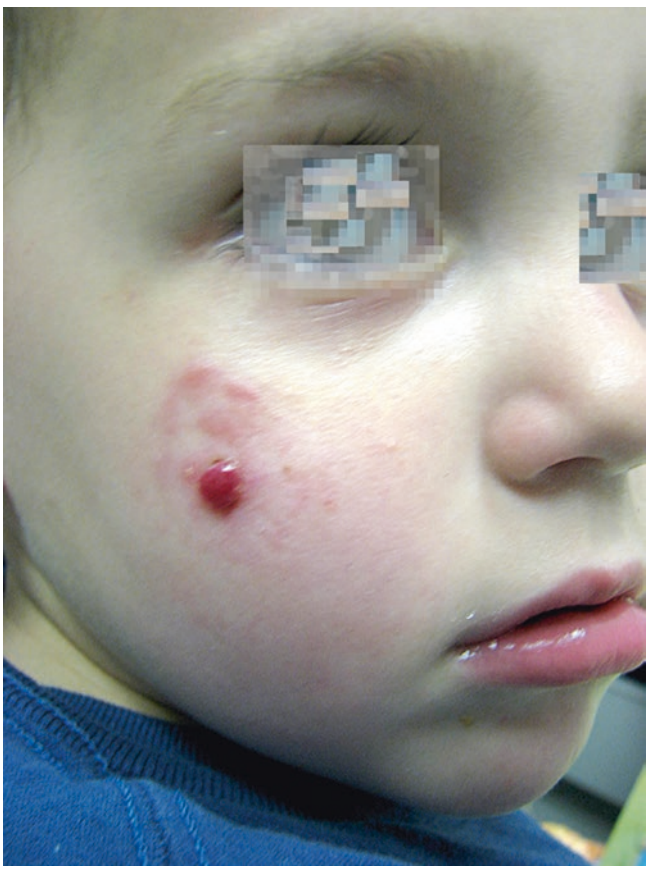


Fig. 33.6 Pyogenic granuloma, often associated with silver nitrate staining and a bandaid from a prior ER visit

Vascular Malformations

Vascular malformations, unlike hemangiomas, are present at birth (although not always clinically evident) and grow proportionately with the child. They are not vascular tumors, do not expand rapidly unless there is intralesional bleeding or lymph accumulation, and they do not regress spontaneously. They may exhibit increased growth and hypertrophy during puberty. They are often associated with overgrowth syndromes.

Capillary vascular malformations (port-wine stains) are usually present at birth as patches of pink or purple skin, often in a dermatomal distribution (Fig. 33.7). If the ophthalmic dermatome (V1) of the trigeminal nerve is involved, there can be simultaneous ocular or CNS involvement (*Sturge-Weber syndrome*), which can cause glaucoma and seizures.

Macular stains (stork bite) resemble port-wine stains in the central forehead and posterior occipital/neck region and have the inexplicable ability to lighten significantly during the first year of life. Persistent vascular pigmentation responds extremely well to pulsed-dye laser therapy, suggesting the vessels are very superficial in the dermis layer of the skin.

Venous malformations appear as clusters of subcutaneous veins that engorge when the affected area is dependent and then empty and soften when the area is elevated (Fig. 33.8).

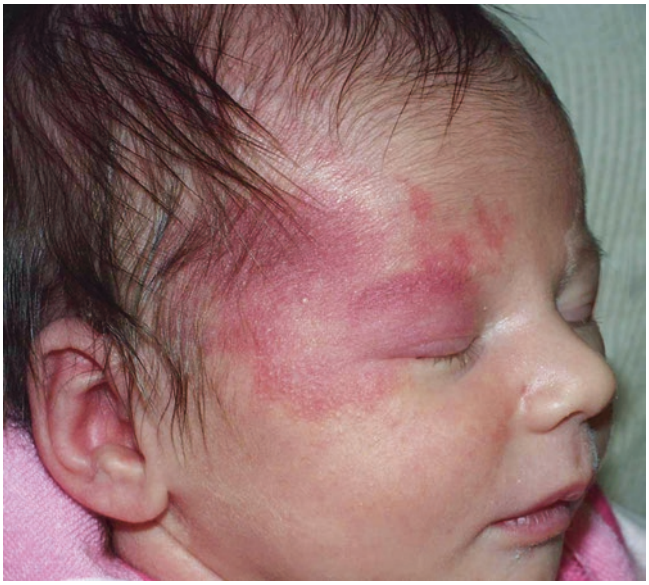


Fig. 33.7 Capillary malformation (port-wine stain). Routine ophthalmologic screening to check for glaucoma, and a possible MRI scan to look for CNS involvement may document the presence of Sturge-Weber syndrome

Rapid enlargement can occur but is more likely due to vascular rupture and hematoma formation rather than the actual growth of the abnormal vessels. Pain and swelling can also be associated with thrombosis of the dilated veins due to sluggish or stagnant flow. They can occur anywhere on the body and sometimes involve underlying subcutaneous tissue, muscle, or viscera. Some can even be transmural: a venous malformation of the cheek might extend from the dermis, through the muscles, and into the submucosal layer. Venous malformations of the head occasionally communicate intracranially with the sagittal sinus.

Blue rubber bleb nevus syndrome (Fig. 33.9) is a genetically transmitted form of venous malformation that occurs in multiple sites all over the body, including the gastrointestinal tract, leading to bleeding and anemia or bowel obstruction due to intussusception. Venous malformations first appear in infancy but the appearance of new malformations continues into adulthood.

Glomuvenous malformations, or glomangiomas (glomus cell tumors) look like small clusters of bluish-purple dermal or subcutaneous vessels and are composed of glomus cells, which normally regulate cutaneous circulation (Fig. 33.10). They are often tender to touch and can be exquisitely tender when located beneath a fingernail in the nail bed. These lesions often have a dominant genetic mode of transmission.

Lymphatic malformations sometimes manifest at birth as obvious soft tissue masses with significant soft tissue hypertrophy (Fig. 33.11). They are composed of thousands of tiny lymphatic cysts or several large macrocysts (in the cervicofacial region these historically have been called cystic hygromas). Dermal or mucosal involvement results in visible lymphatic vesicles. Blood can leak into the dermal lymphatics, resulting in crusty cutaneous lesions (*angiokeratomas*) that might appear to bleed profusely but the discharge is predominantly lymph stained with blood pigmentation. Some large cystic lymphatic malformations appear to have the capacity to regress, which is probably due to repeated episodes of infection or inflammation that gradually cause fibrosis of some of the abnormal lymphatic spaces.

An *arteriovenous malformation* (AVM) presents as a warm, pulsatile mass that can occur anywhere on the body (Fig. 33.12). The AVM may include a patchy cutaneous capillary vascular malformation and hypertrophy of the involved area (Parkes-Weber syndrome). High turbulent flow within the lesion often causes a bruit or thrill to be appreciated on examination. There is sometimes a noticeable increase in size during puberty, presumably due to hormonal stimulation and additional vascular shunting.

Spider angiomas are common dermal vascular malformations with a central feeding vessel and a radiating pattern of tiny telangiectasias (Fig. 33.13). When compressed, the lesions blanch, then readily refill from the center to the periphery when pressure is released.

Klippel-Trenaunay syndrome describes a patchy capillary vascular malformation overlying a low-pressure, low-flow venolymphatic malformation, usually with local tissue hypertrophy (Fig. 33.14). In the lower extremity, a markedly dilated lateral vein is sometimes noted and represents a remnant from fetal development. The skin sometimes exhibits multiple angiokeratomas scattered diffusely over the areas of the port-wine stain.

Proteus syndrome is an overgrowth condition that affects the entire body to varying degrees, creating vascular malformations, lipomas, epidermal nevi, and thickened, wrinkled plantar surfaces. John Merrick, the Elephant Man, is thought to have had Proteus syndrome, not neurofibromatosis.

CLOVES syndrome patients (Congenital Lipomatous Overgrowth, Vascular malformation, Epidermal nevi, and Spinal or Skeletal abnormalities) may have massive soft tissue overgrowth of the trunk (Fig. 33.15). Genetic analysis typically reveals a somatic PIK3CA mutation.

Maffucci's syndrome includes enchondromas of the hands, vascular malformations in unrelated areas, rare angiosarcomas, and a 15–20% lifetime risk of developing chondrosarcoma.

Fig. 33.8 Venous malformation of the upper lip (top left and top right). The application of vascular clamps decreased the intraoperative blood loss during surgical debulking (bottom left). The improvement in contour was significant, and in this case most likely more effective than sclerotherapy alone (bottom right)

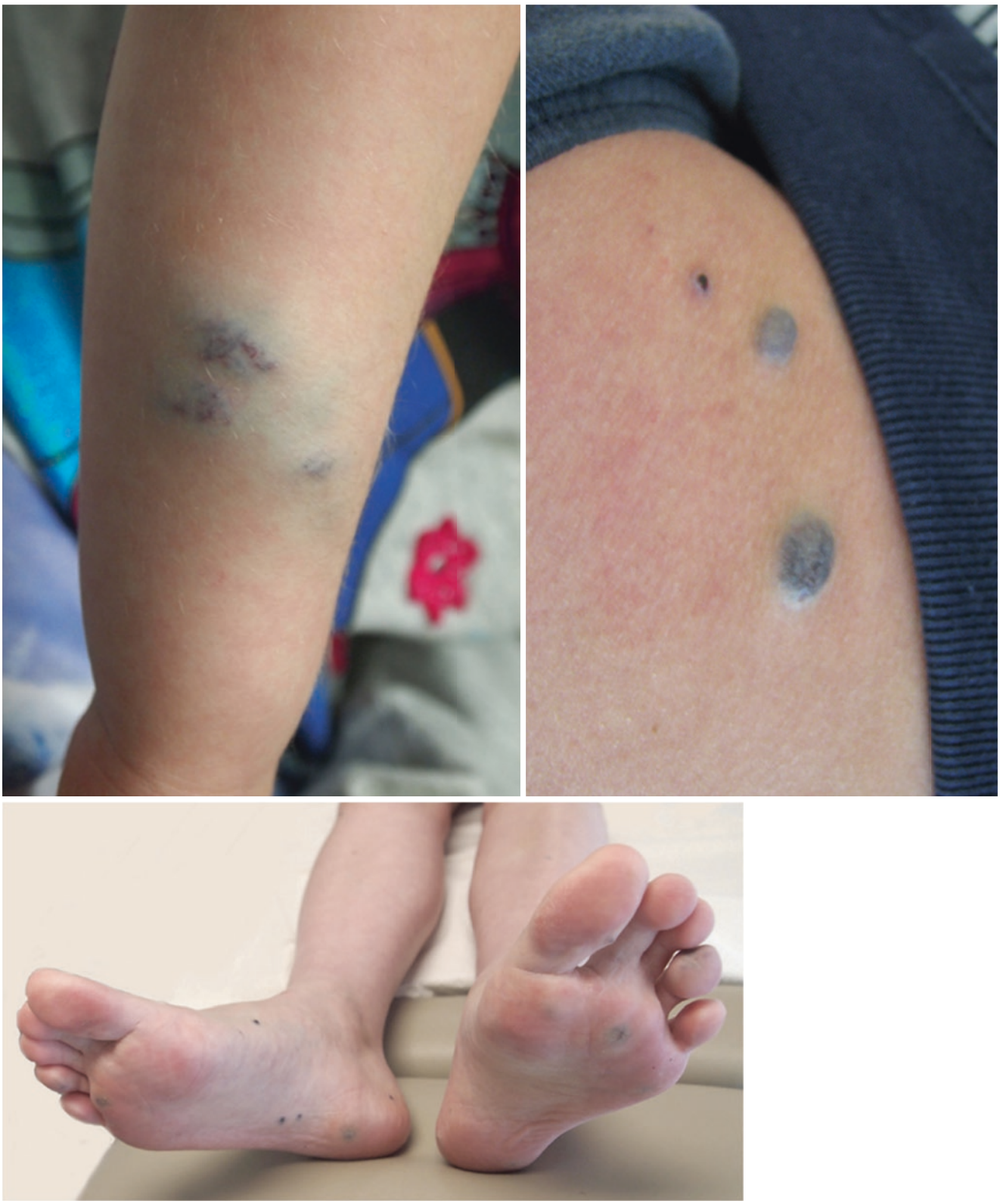


Fig. 33.9 Blue rubber bleb nevus syndrome (acquired venous malformations) of the arm, shoulder, and feet

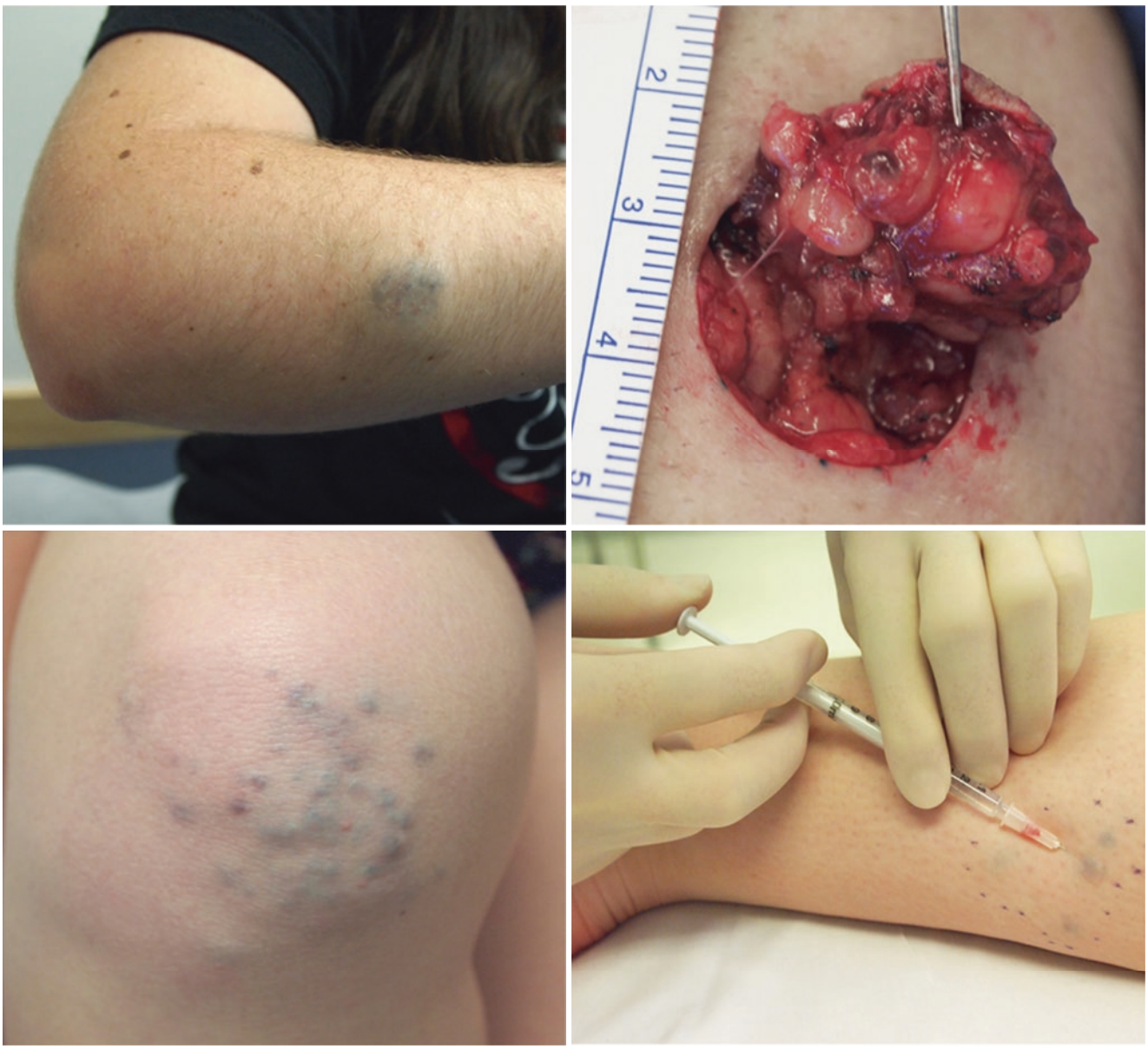


Fig. 33.10 Glomuvenous malformation. Solitary nodular lesions can be excised (top left and top right), but diffuse lesions (bottom left) often respond to sclerotherapy with 1% polidocanol (bottom right). General anesthesia may be necessary, particularly with diffuse involvement, due to the intense pain associated with injection into these pressure-sensitive lesions

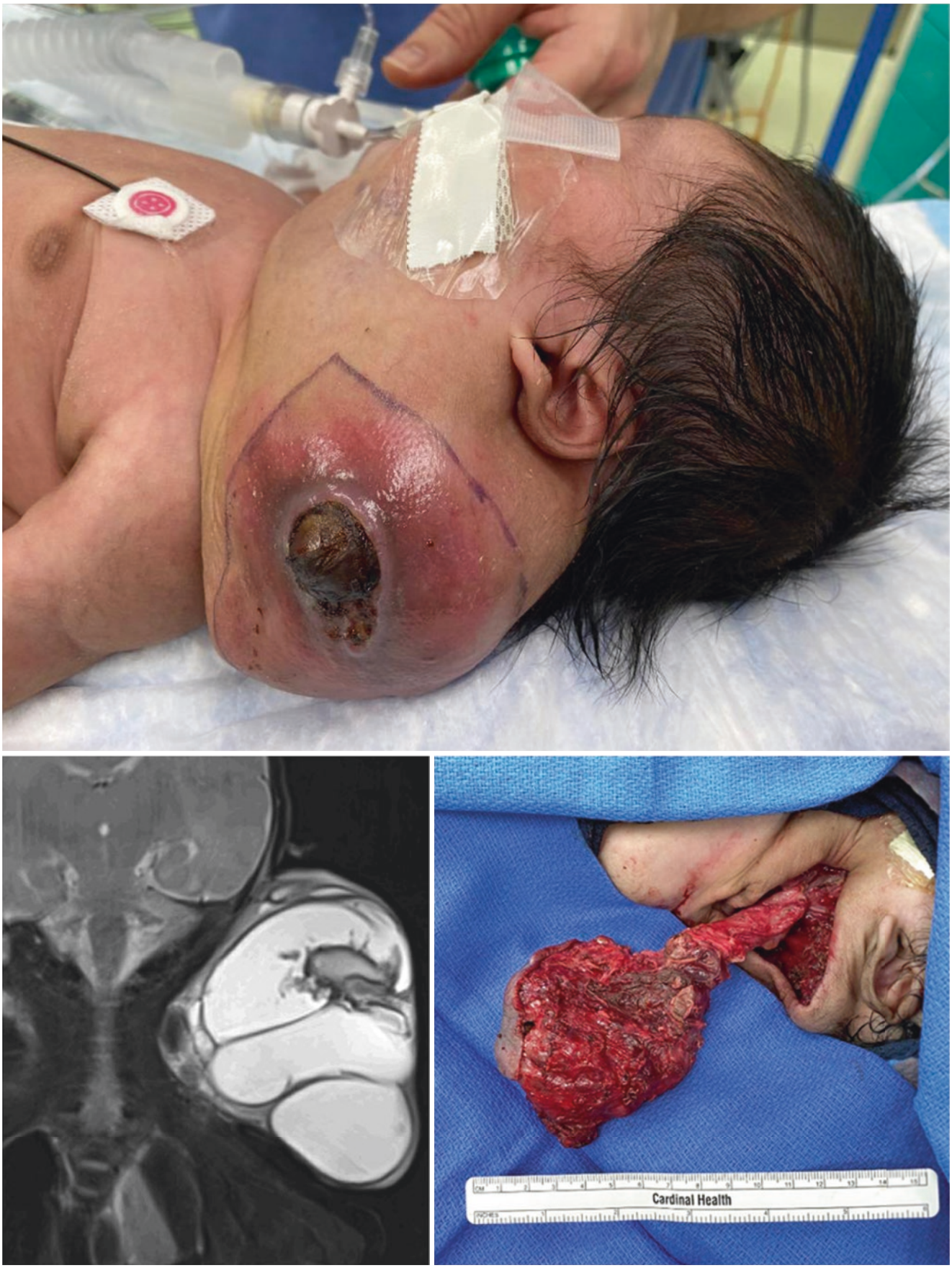


Fig. 33.11 Lymphatic malformation of the neck in a newborn (top). The corresponding MRI study demonstrates a multicystic, macroscystic vascular anomaly (bottom left). After an initial attempt at several days of doxycycline sclerotherapy and catheter drainage by interventional radiology, surgical debulking was necessary because of the problematic ulcerated wound (bottom right)

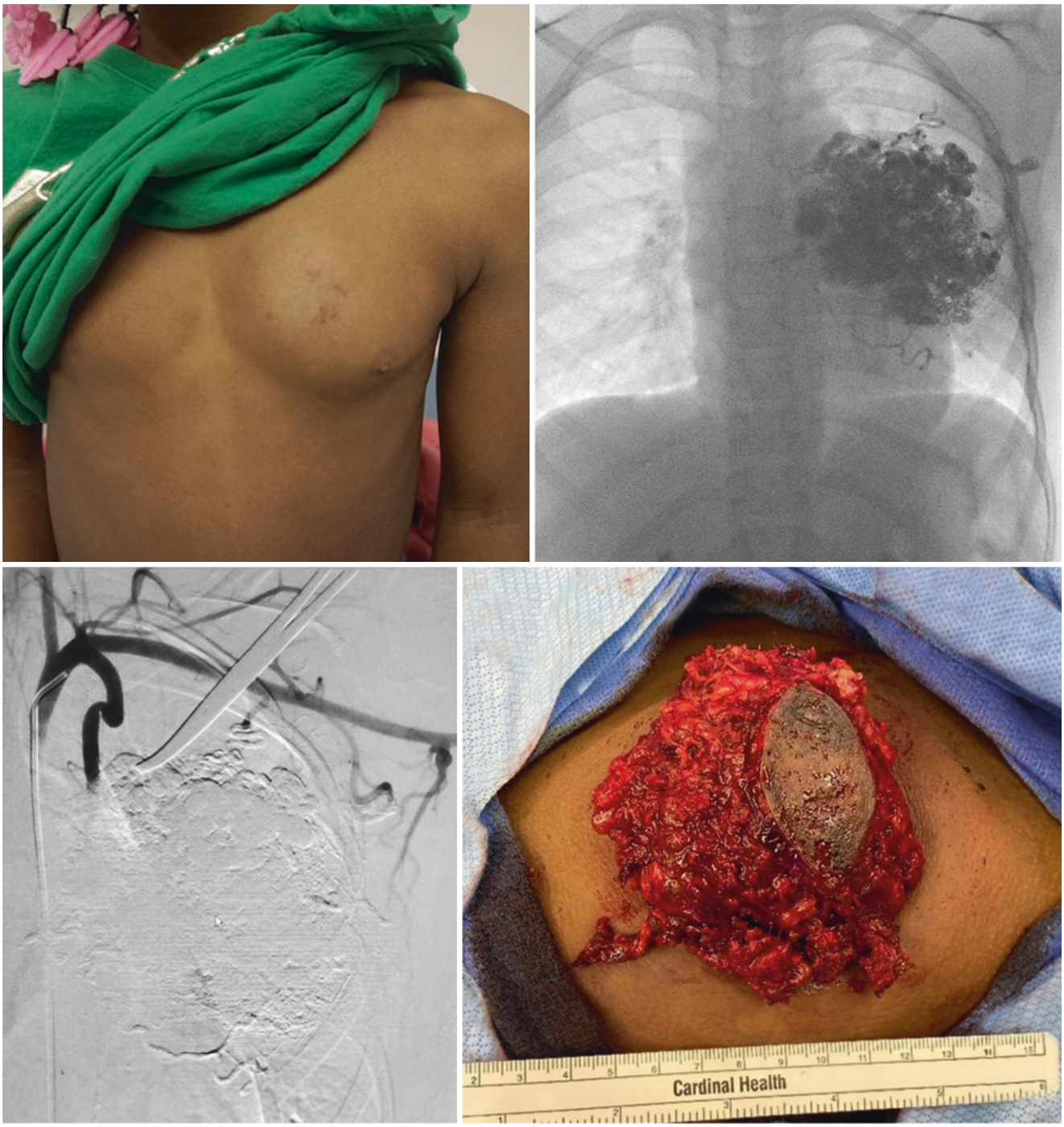


Fig. 33.12 Arteriovenous malformation of the left chest wall (top left). Preoperative embolization of the feeding branches from the left internal mammary artery with glue (top right and bottom left) permitted surgical excision with minimal blood loss (bottom right)

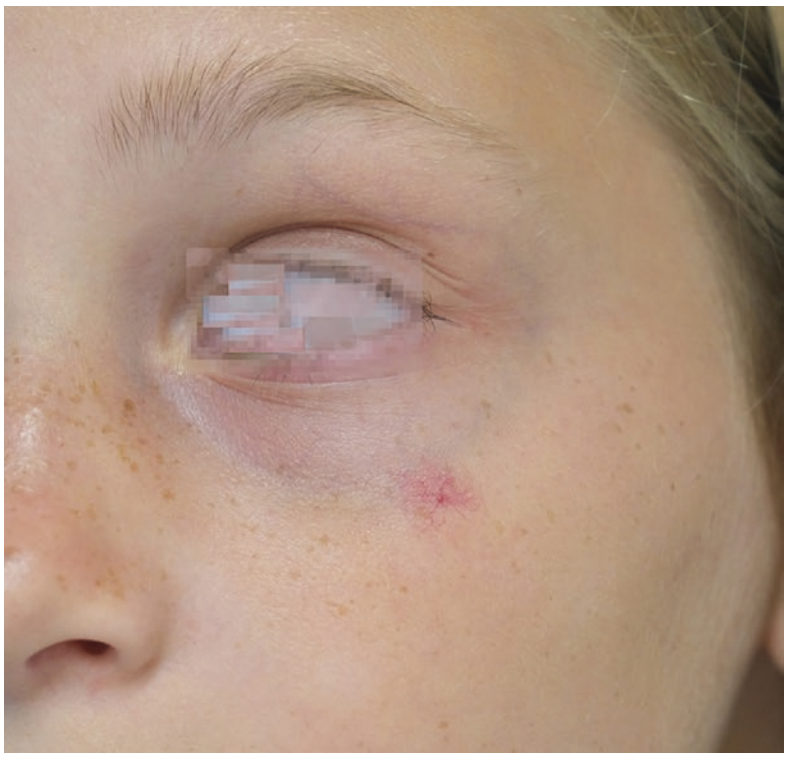


Fig. 33.13 Spider angioma commonly seen on the face. The pulsed dye laser is the treatment of choice

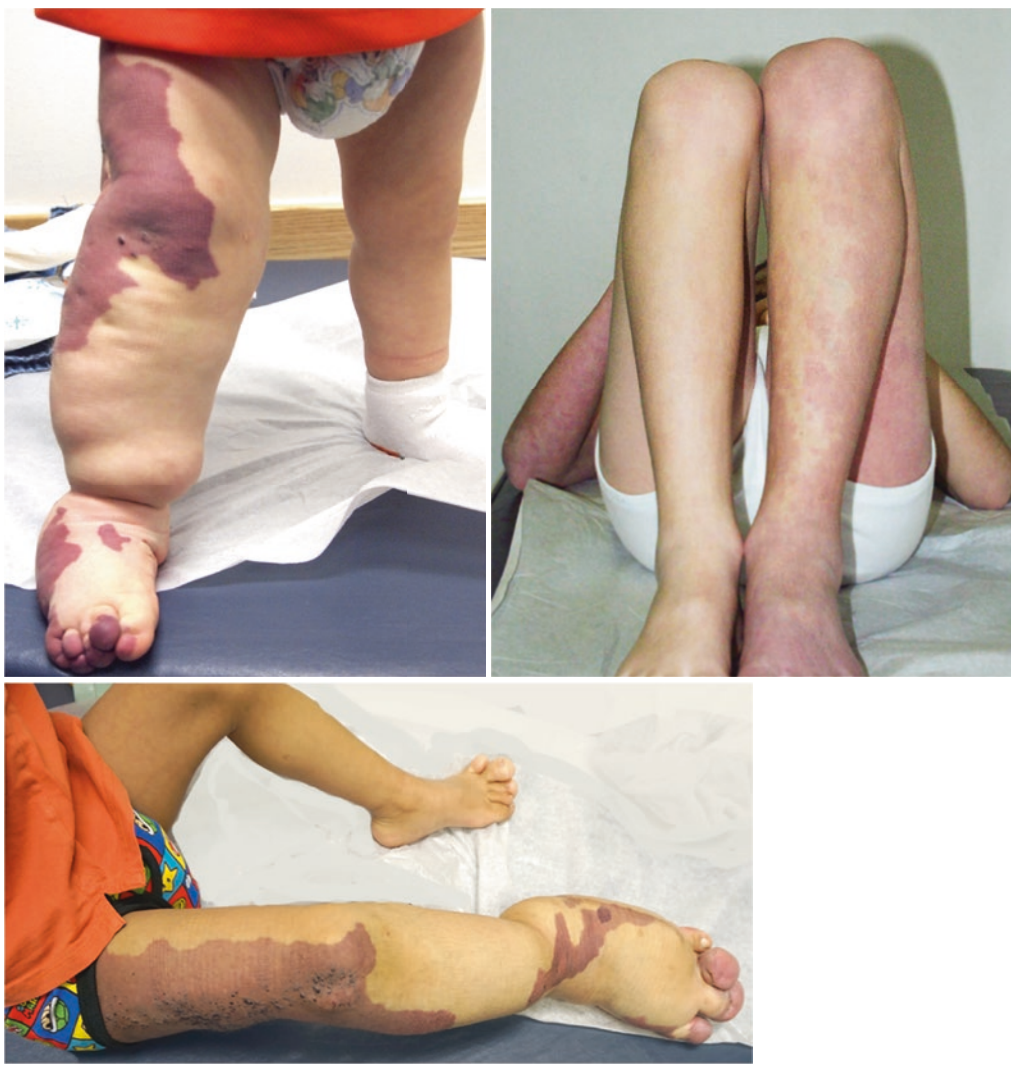


Fig. 33.14 Klippel-Trenaunay syndrome demonstrating the patchy port-wine stain, hypertrophy, and significant deformity that can occur in these three patients

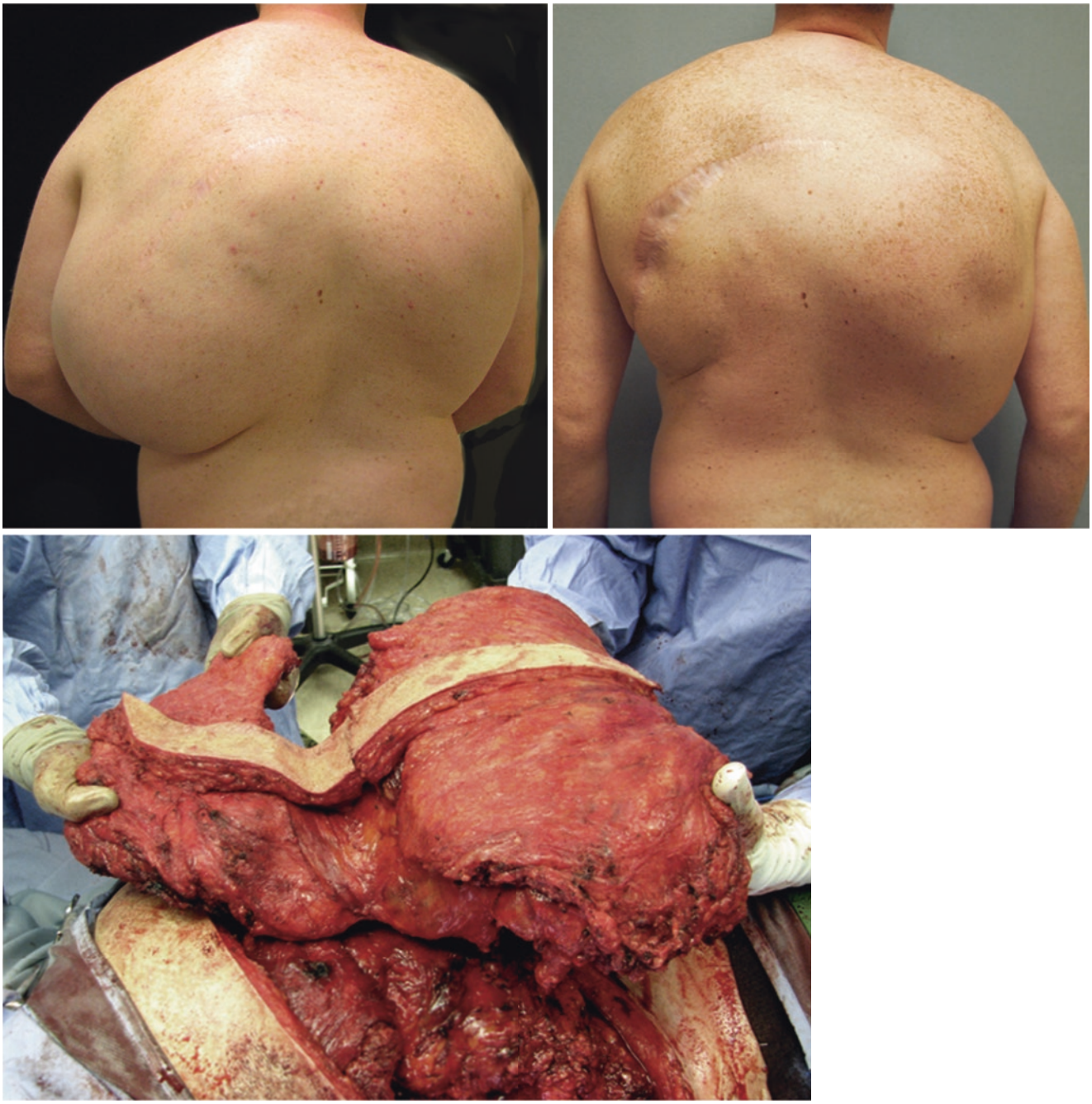


Fig. 33.15 The large truncal masses associated with CLOVES syndrome present a surgical challenge as significant blood loss and need for transfusion is common. A cell saver and a postoperative compression garment may help limit blood loss. Pre-surgical treatment with rapamycin and sclerotherapy may decrease the magnitude of the surgical resection, or perhaps avoid the need for surgery. (Preop appearance, top left, postop appearance after debulking, top right. Intraop photo of the resected specimen, bottom)

Diagnosis

In the majority of cases, history and physical examination will allow an accurate diagnosis, but in the modern era, genetic testing is becoming increasingly important as it may offer future targeted treatment. In some patients, serial clinical examinations will make the diagnosis, based upon the growth or lack of growth of the vascular anomaly. For example, a flat patch of vascular pigmentation initially thought to be a capillary vascular malformation (port-wine stain) might become strawberry red and raise and increase its area of involvement, which is indicative of a hemangioma.

An MRI with and without contrast will usually distinguish the true etiology of most vascular anomalies and is indicated for atypical hemangiomas when the diagnosis is in doubt, for lesions involving the head and neck (to assess the extent of periorbital, parotid, and airway involvement or posterior cranial fossa abnormalities), and for those overlying the spine to rule out lipomyelomeningocele with spinal cord tethering. An ultrasound to exclude hepatic or splenic involvement is indicated in patients who have more than six cutaneous hemangiomas, while an echocardiogram is sometimes needed to rule out cardiac abnormalities if the lesion is thought to be part of a syndrome.

Although an MRI can usually demonstrate the extent of vascular malformations, particularly if they have muscular or visceral involvement, it is only truly indicated if it will change therapy. An MRI scan of the head for port-wine stains involving the V1 distribution may indicate CNS involvement in Sturge-Weber syndrome. Baby aspirin might be recommended to decrease the risk of seizures. Historically the best treatment for Klippel-Trenaunay syndrome with obvious involvement of the leg was conservative compression therapy (physical therapists can provide decongestive massage as well as tailored compression garments), and an MRI was not needed to make the diagnosis or to recommend therapy. However, if one is contemplating sclerotherapy or venous ligation and removal of abnormal veins, an MRI/MRV will not only document the course of the anomalous veins, it will also confirm the presence of normal draining veins. A biopsy of the involved tissue will typically confirm the presence of a causal somatic PIK3CA mutation, making patients candidates for Rapamycin suppression. A baseline MRI scan preceding therapy can be compared with subsequent follow-up scans to document a response to medical suppression.

For a suspected AVM, an MRI/MR-angiogram is a better initial screening test, reserving an angiogram for those cases that require additional diagnostic and potentially therapeutic arteriography. An ultrasound-guided needle can facilitate injection of lymphatic and venous malformations for sclerotherapy.

For clinically atypical hemangiomas that remain ambiguous on US and MRI and which do not respond to beta-blocker suppression, a needle or incisional biopsy may be indicated. Infantile hemangiomas will stain glucose transporter protein (Glut-1) positive at all stages of development and involution. Thyroid function tests are indicated in patients with hepatic hemangioma, as the active form of thyroid hormone can be inactivated by increased levels of type 3 iodothyronine deiodinase, resulting in hypothyroidism.

Tissue biopsy in the form of skin punch biopsy if superficial, a needle biopsy by interventional radiology if deep, or a surgical incisional biopsy can provide a combination of pathological and genetic information. The tissue should be sent in saline rather than formalin, with instructions for the pathologist to snap freeze a portion in liquid nitrogen for genetic testing. The genetic mutations listed in Table 33.6 (a much longer list is available through the ISSVA) may help guide which genetic panels are desirable. At Children's Hospital of Philadelphia, we are fortunate to have the Center for Applied Genomics, which collects all vascular tissue samples for advanced genetic research, including deep exome sequencing on vascular malformation tissue samples to identify novel candidate genes and variants that cause vascular malformations.

Treatment of Hemangiomas

Pediatricians advise the vast majority of parents whose infants have hemangiomas to be patient and wait for eventual cessation of growth and gradual involution. Half of all hemangiomas will finish involuting by 5 years of age and 70% will have involuted by age seven. Approximately 70% of all hemangiomas will involute satisfactorily without requiring any further intervention; however, at least 30% will leave a residual deformity in the form of redundant skin, dermal scarring, bulky fibrofatty tissue, or facial disfigurement. Hemangiomas of the lips, nose, and cheeks commonly leave behind redundant and distorted tissue that will require surgical attention and result in some kind of surgical scar.

With the advent of the internet, parents are increasingly eager to take an active role in the management of their child's hemangioma. Rather than watch them become progressively more deformed, they desperately hope to abort the natural history of hemangioma. They seek early laser therapy or surgical excision and some will shop around until they find a surgeon who will take an aggressive approach. A balanced approach is necessary and the surgeon must always weigh the risks and benefits of a surgical scar and operative complications against the possibility that natural involution will leave a better final result. Our personal philosophy is that

because surgery leaves a scar 100% of the time, before proceeding with surgery one should be reasonably confident that natural involution will leave a worse deformity. Also, the decision to operate before complete involution increases the risk of bleeding and decreased intraoperative visibility may increase the risk of damage to nerves and other key anatomic structures.

Life-threatening subglottic hemangiomas and vision-threatening periorbital hemangiomas cannot be managed conservatively. Previously, steroid therapy was the treatment of choice for problematic hemangiomas, despite its many side effects that included irritability, change in appetite, temporary and reversible growth suppression, hypertension, and Cushingoid appearance. The beta blocker propranolol has now replaced corticosteroids as first-line therapy at most institutions. First reported in 2008 to have the ability to suppress the growth as well as speed the involution of hemangiomas, beta blocker therapy appears to have far fewer side effects. Initially, beta blocker therapy obligated the infant to several days of inpatient observation and cardiology consultation for side effects such as hypoglycemia, hypotension, and bradycardia. However, propranolol and related beta blockers have proven to be so safe that office initiation and home therapy no longer obligate a hospital stay. Small hemangiomas have also been treated with topical beta blocker (timolol eye drops) twice daily, but similar to topical steroid cream or intralesional steroid injections, the rate, distribution, and amount of medication delivered is much less predictable.

Laser photocoagulation with a pulsed yellow dye laser is sometimes useful for small, flat hemangiomas, but because the light can only penetrate about 1 mm into the dermis it is generally not useful for bulky or subcutaneous lesions. Most parents will describe a couple weeks of regression after laser therapy followed by some rebound growth, therefore repeated treatments are often necessary to suppress the hemangioma until permanent involution occurs. Topical or oral beta blocker between laser treatments is commonly utilized. The laser is also useful for painful or ulcerated hemangiomas. Although somewhat unpredictable, in many cases laser therapy appears to be able to suppress pain within 24–48 h, possibly by photocoagulation of the sensitive nerve endings in the lesion, and accelerate healing, perhaps by suppressing inappropriate vascular proliferation.

In most situations, surgical excision or debulking is similar to the excision of a nevus or cyst. Hemangiomas that leave redundant skin or excess fibrofatty scar tissue will often benefit from elliptical excision, trading the hemangioma for a linear scar. The timing of excision is a judgment call which will be influenced by the degree of deformity, the size of the hemangioma, the amount of residual vascularity, the location (less cosmetically important hemangiomas tend to carry less urgency), the anxiety level of the parents, and the experience of the surgeon. Large hemangiomas might require staged excision, particularly if debulking surgery is elected prior to complete involution, increasing the potential for significant operative bleeding. Large hemangiomas in the lip or nasal regions benefit from early debulking to facilitate feeding and social acceptance, with the understanding that a secondary surgical revision will be necessary in the future.

Nasal tip hemangiomas commonly splay apart paired tip cartilages and leave behind excess skin and bulky fatty tissue after the vessels have involuted. Correction commonly requires judicious trimming of nasal skin and hemangioma, and suturing of the tip cartilages together (Fig. 33.16). Lip hemangiomas are usually asymmetric and surgical debulking or removal of a hemangioma essentially creates a cleft lip deformity. Techniques for cleft lip repair, often with minor adjustments to individualize the procedure for a given patient, provide a strategy for addressing these very challenging deformities. Subcutaneous hemangiomas that leave excess fibrofatty tissue will occasionally be amenable to debulking by liposuction if enough time is allowed for complete vascular involution. Scalp hemangiomas will often cause dermal scarring and damage the hair follicles, leaving a patch of alopecia. Excision (alopecia reduction) is the treatment of choice, rather than punch or micro hair grafting.

Cheek hemangiomas can leave problematic deformities in an area that is normally very smooth. Surgical scars in the middle of the cheek are often equally noticeable, and therefore one must be fairly certain that natural regression will leave a worse result than a surgical scar before proceeding with excision. Options for surgical intervention include standard elliptical excision, excision with a purse-string closure, carbon dioxide laser skin resurfacing, or pulsed dye laser with sclerotherapy for residual vessels. Excision of redundant skin and subcutaneous tissue caused by a parotid hemangioma must be undertaken very carefully to avoid injury to branches of the facial nerve.

Ear hemangiomas can cause significant skin and subcutaneous excess, but the subcutaneous component often involutes dramatically. To avoid a soft tissue deficiency, it is often safer to postpone debulking until the ear hemangioma has almost completely involuted.

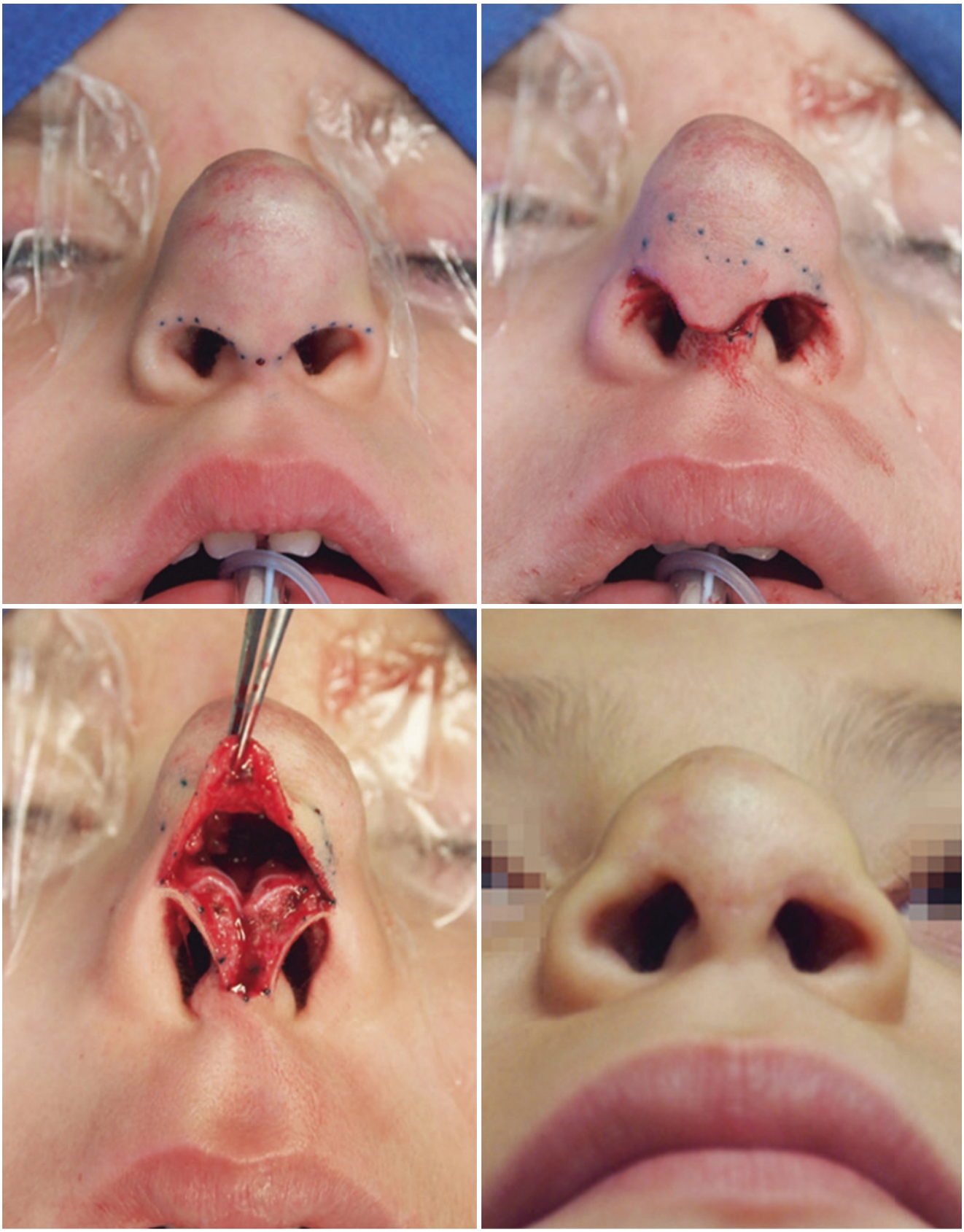


Fig. 33.16 Nasal tip hemangioma (top left) debulking involves judicious trimming of excess skin and subcutaneous fat (top right), as well as centralization of the nasal tip cartilage (bottom left). Postop appearance (bottom right)

Treatment of Vascular Malformations

The treatment of *capillary vascular malformations* (port-wine stains) most commonly involves the use of a pulsed yellow dye laser. The wavelength can vary with the type of laser, but currently, the three most recent generations of pulsed yellow dye lasers use a 595-nanometer wavelength, which is absorbed by oxyhemoglobin. The handpieces most often deliver circular pulses of variable width and power density. A cryogen cooling spray to accompany each laser pulse decreases the pain of the laser pulse and protects the skin from thermal injury. Protective goggles for all personnel and protective goggles or corneal shields for the patient are essential. Depending upon the age of the patient and the location of the lesion, topical anesthetic cream or general anesthesia may be necessary. Clinicians must inform parents that despite multiple laser treatments (at least 6–8, and often more) it is highly unlikely that the birthmark will ever completely fade. Furthermore, the laser typically leaves extremely dark bruises for 2–3 weeks and, if the power density is too high or the pulses are delivered too close together, scarring can occur. Because it can take 2–3 months to see the full benefit of each treatment, laser treatments are separated by at least 2 months. The laser is not equally effective on all areas of the face and it is less effective as one moves distally on the extremities towards the hands and feet. Parents and patients should be made aware that results are sometimes disappointing. Additionally, despite successful laser treatment, some will darken with age as residual vessels further dilate. In this situation, laser treatment can be resumed and might offer additional benefits.

Facial capillary vascular malformations, particularly those on the lips, can also cause significant hypertrophy, which often necessitates surgical debulking. Plastic surgical techniques for cleft lip repair or reconstruction can be applied to obtain cosmetically acceptable results after major debulking (Fig. 33.17).

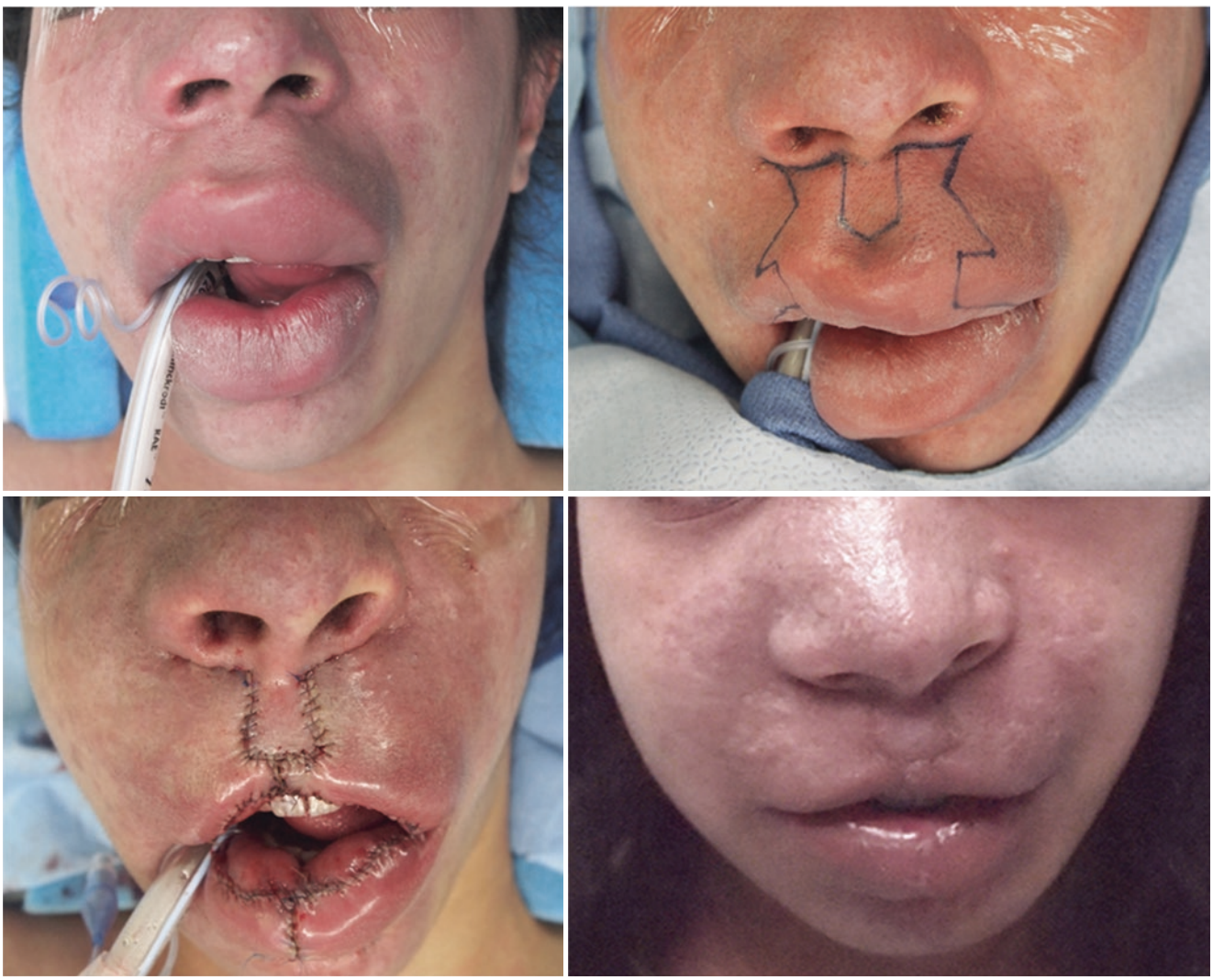


Fig. 33.17 Debulking strategy for a markedly hypertrophied upper and lower lip associated with a capillary vascular malformation: Preop appearance (top left), upper lip markings demonstrating lip tissue to be excised (top right), immediate appearance after debulking of the upper and lower lip (bopttom left), and appearance 6 weeks later (bottom right)

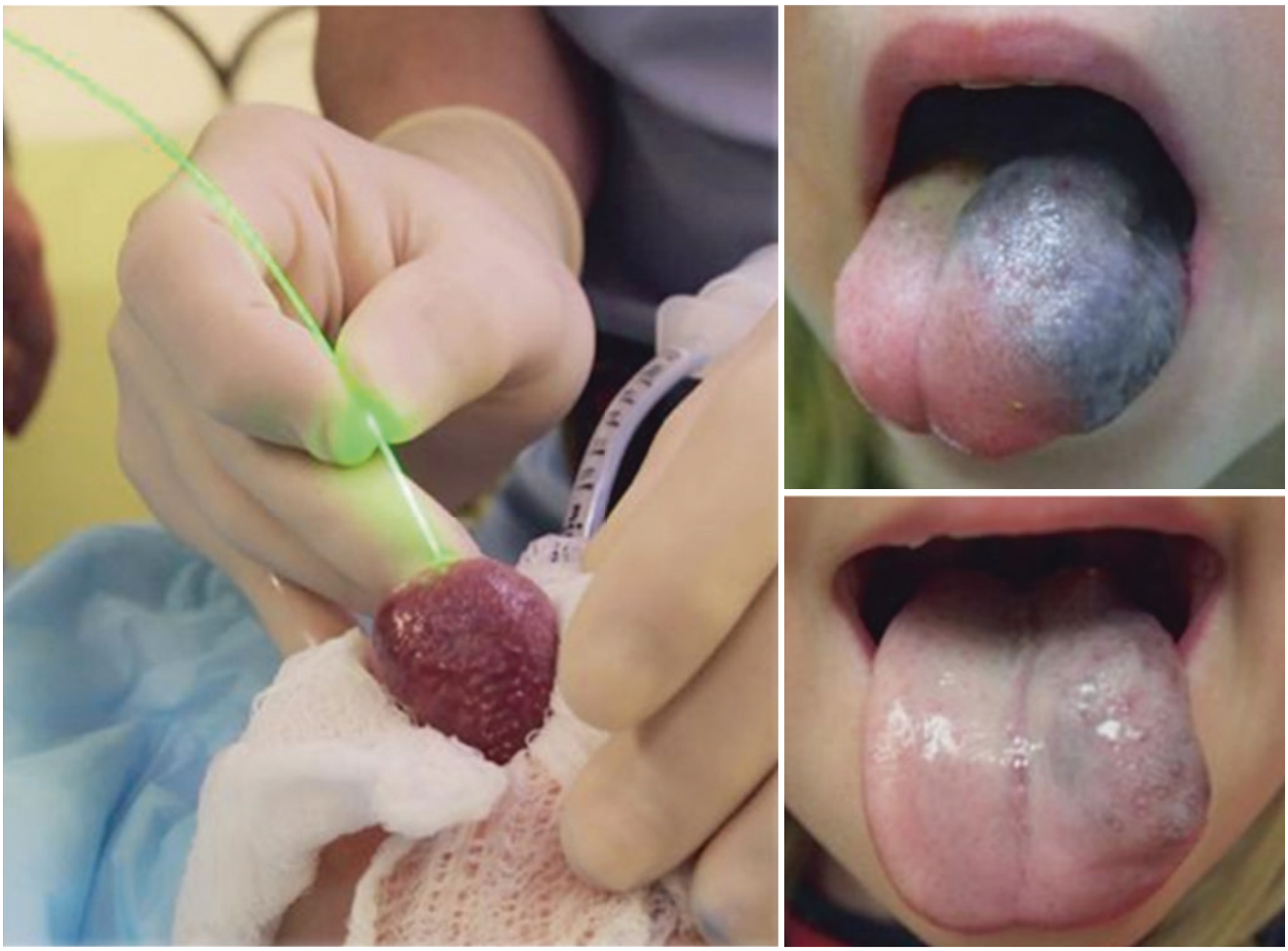


Fig. 33.18 KTP bare laser fiber coagulation of a tongue venous malformation. The tip of the fiber is passed directly into the tissue (left), and the laser operator must use careful clinical judgment to judge the depth and duration of energy delivery. Preop (top right) and postop appearance (bottom right)

The treatment of *venous malformations* might include laser therapy, sclerotherapy, surgical excision, medical suppression, or combinations of all four. Venous malformations of the head and neck are often best approached by sclerotherapy, as the malformation is usually transmural, visible just beneath the epidermis and through the oral mucosa. In such situations, surgical debulking may be accompanied by excessive bleeding that is difficult to control, inability to adequately resect the involved area or excessive scarring and post-surgical deformity. A series of sclerotherapy sessions using alcohol or sodium tetradecyl sulfate under fluoroscopic or ultrasound guidance is often the best treatment option. The laser or milder sclerosing agents such as bleomycin or polidocanol can be used for superficial dermal components. Although considered old technology, the potassium-titanyl-phosphate or KTP laser, a 532-nanometer green light laser, delivers a continuous beam of laser energy rather than pulses of light and is useful for intraoral coagulation. The laser light travels down a fiberoptic cable which can be inserted directly into the malformation for intralesional photocoagulation (Fig. 33.18). However, the technique is highly operator-dependent, the amount of laser energy delivered is difficult to judge, and the thermal effects can be difficult to limit, making it less precise than sclerotherapy.

Venous malformations of the tongue can be directly excised or significantly debulked with very limited blood loss by clamping the base of the tongue with cushioned vascular clamps. The incised edge can be oversewn prior to the release of the clamps. Because of the anticipated postoperative tongue edema, patients will require in-hospital observation for airway monitoring or overnight intubation.

Lower extremity venous malformations can be treated only if the malformation does not serve as the main vascular runoff for the involved leg. Sclerosis of a major venous malformation or varicosity using ultrasound guidance is commonly performed by interventional radiologists. To prevent the passage of sclerosant or clot into the circulation, the radi-

ologist may occlude the draining vein with coils or glue, and it is occasionally necessary to ligate vessels that communicate with a major normal draining vein prior to an attempt at sclerotherapy. Large caliber varicosities such as those seen commonly along the lateral leg in patients with Klippel-Trenaunay syndrome (lateral vein of Servelle) may also be amenable to endovenous laser therapy, usually done by interventional radiologists with ultrasound guidance. As many of these conditions are now associated with PIK3CA genetic mutations, Rapamycin (sirolimus) has become an important treatment option for patients who are not candidates for surgery or sclerotherapy.

Lymphatic malformations are among the most frustrating of the vascular malformations to treat surgically. Hours of painstaking dissection often result in minimal benefit, facial nerve injuries, or postoperative edema that takes a very long time to subside. The best results are with macrocystic lymphatic malformations that are amenable to repeated sclerotherapy, often obviating direct surgical debulking. Sclerosing agents have included alcohol, doxycycline, and bleomycin. Microcystic lymphatic malformations do not always respond to sclerotherapy and direct surgical debulking carries a high complication rate, especially for cervicofacial malformations. Sometimes a combination of surgical debulking and postoperative compression in the extremities will help to maintain a reasonable decrease in size. The carbon dioxide laser can be used to vaporize cutaneous lymphatic vesicles, offering limited palliative improvement for draining dermal lymphatics. Topical sirolimus may be useful in controlling cutaneous lymphatic lesions such as angiokeratomas. Oral sirolimus and future targeted medical therapy may ultimately become the most effective treatment strategy. In cases of chronic pleural effusions or ascites due to obstructed lymphatic flow due to abnormalities of the thoracic ductal system, lymphatic imaging and intervention by highly specialized teams may provide relief.

Arteriovenous malformations can either be followed conservatively with periodic palliative selective embolization or excised in their entirety. Simple ligation of the major feeding vessels without removal of the malformation is contraindicated, as the AVM will readily recruit flow from other regional arteries making future management even more difficult. Preoperative embolization a day prior to surgery might significantly decrease intraoperative blood loss and also provide the surgeon with a vascular roadmap. Ideally, the malformation should be completely excised to remove all vascular shunting (Fig. 33.12). The subsequent defect sometimes requires sophisticated flap reconstruction to optimize the postoperative outcome.

Overgrowth syndromes such as CLOVES may benefit from multidisciplinary therapy. Currently, sirolimus, an mTOR (mammalian target of Rapamycin) inhibitor, and in the future targeted PIK3CA inhibitors may prove to be more effective than sclerotherapy and direct surgical debulking. Significant intraoperative bleeding can be associated with aggressive surgical debulking (Fig. 33.15), and it may be safer to try to shrink as much of the malformation as possible with initial medical suppression and sclerotherapy prior to surgery.

Complications

Surgical excision of a vascular lesion always carries a risk of bleeding; therefore, the surgeon must decide which cases require a type and crossmatch for packed red blood cells or preoperative embolization. If the risk of bleeding is significant, most parents will prefer a directed donor unit in spite of evidence that banked blood statistically is safer. Particularly with hemangiomas, the surgeon should be confident that the surgical scar will be better than the deformity left by natural involution. Hemangiomas that are debulked prior to complete involution can have greater intra-operative bleeding, increased risk of nerve damage due to poor visualization and distorted anatomy, and poor healing with dehiscence of the incision since sutures are often placed into skin edges compromised by vascular tissue. When the breast is involved in girls, early debulking is contraindicated as injury to the breast bud may affect normal breast development.

A further note regarding the use of lasers, the use of any laser can cause scars, ocular injury, and operating room fires. The pulsed dye laser for port-wine stains can cause a flash burn if it causes upper lip and nasal hairs to singe in an oxygenated environment.

Surgeons must keep current on alternative treatment options, especially as targeted medical therapy becomes increasingly available with the identification of new drugs that suppress and shrink vascular anomalies. In many patients, it may be safer for surgical excision to follow medical suppression and sclerotherapy or embolization. As debulking surgery becomes less frequent, surgeons will still have an important role in acquiring tissue for genetic analysis.

Editor's Comments

No lesion that causes a child or their parents shame, anxiety or embarrassment, regardless of how small, seemingly minor or easy to conceal, should ever be dismissed as merely a cosmetic concern. Vascular birthmarks have the added problem of occasionally being associated with trenchant albeit irrational feelings of shame and stigma within a family. They also tend to generate a certain amount of "doctor shopping"

which although well-intentioned sometimes leads to an ill-advised and overly aggressive surgical approach. Regardless, parents' concerns should always be treated with patience and compassion.

The care of children with vascular malformations has greatly improved in recent years with more effective medications being developed, the increasing skill and experience of interventional radiologists with techniques such as embolization and sclerotherapy and, perhaps most importantly, the emergence of multidisciplinary vascular malformation clinics that make available the expertise of devoted specialists and evidence-based modern therapies.

Obvious dermal lesions pose a challenge because the aesthetic results of surgical therapy are often no better than if the lesion were left untreated. These patients are best treated by an experienced pediatric plastic surgeon or vascular malformation team. Subcutaneous lesions may be more subtle but often cause a great deal of anxiety due to concerns about the potential for malignancy. Unless imaging studies are able to reliably confirm that the mass represents a hemangioma and is therefore safe to observe, most of these patients should probably be offered excision or at least a biopsy. If there is any possibility of involvement of deeper structures, an ultrasound or MRI may help avoid intraoperative surprises.

Surgical excision is not always straightforward and requires detailed planning and contingencies for avoiding blood loss such as preoperative embolization, clipping feeding vessels, or the use of a pressurized tourniquet. It is unnecessary in most cases to leave a drain, even when large tissue flaps are created. Postoperative seromas are usually safe to observe, unless symptomatic or infected, in which case it can be drained painlessly with a needle placed directly in the incision, which is insensate. Recurrence of a vascular malformation that is completely excised is uncommon, but notable exceptions include lymphatic malformations and intramuscular venous malformations, for which sclerotherapy or embolization should be considered. Large facial hemangiomas, especially those that threaten the airway or compromise vision, pose a significant dilemma as waiting for them to involute can cause serious complications. Even hemangiomas that resolve spontaneously can leave a fibrofatty residual mass that is disfiguring and requires surgical excision.

Propranolol has replaced corticosteroids as the primary medical therapy for hemangiomas. Patients should be carefully monitored for serious adverse effects, which thankfully are rare. The drug should be administered by experienced clinicians as part of a carefully designed protocol that includes periodic follow-up visits. Intralesional corticosteroid injection is a useful adjunct in some cases (hemangiomas of the airway) but requires skill and experience to avoid a devastating complication.

It is important to involve the parents completely in the decision-making process and to manage their expectations. In the event of a suboptimal cosmetic outcome, they will question whether a different course of action might have achieved a better result. When in doubt, one should consult with a multidisciplinary clinic that specializes in vascular malformations.

Further Reading

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