Vascular Anomalies

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There is a fundamental conceptual division between *hemangiomas* and *vascular malformations*—the former being proliferating tumors and the latter developmental errors.

62.1 Pathology

Infantile Hemangiomas

1. Mutation in a primitive stem cell is responsible for developing blood vessels.
2. Hemangioma is a model of pure, unopposed angiogenesis with a common expression of immunohistochemical markers including *glut-1, Fcy RII, and Lewis Y antigen*.
3. Possible derivation from or sharing a common precursor with placenta.
4. Angiogenic peptides.
   (a) Proliferating phase—expression of vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), and type IV collagenase.
   (b) Involution phase—tissue inhibitor of metalloproteinases (TIMP-I) and mast cell-secreted modulators.

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Vascular malformations are usually sporadic but can also be inherited in a family as an autosomal dominant trait. They are a manifestation of many different genetic syndromes that have a variety of inheritance patterns and chances for reoccurrence, depending on the specific syndrome.

62.2 Hemangioma Versus Vascular Malformation

Hemangiomas and vascular malformations may have nothing in common pathologically *except* a somewhat similar appearance. Vascular anomalies manifest with a very wide clinical spectrum of lesions ranging from small skin discoloration to very large life-threatening conditions.

Table 62.1 illustrates key clinical differences between these entities though in practice there can be difficulties in their separation (e.g., liver hemangiomas/vascular anomalies).

Table 62.1 Biological classification

Criteria	Hemangioma	Vascular malformations
Age, Sex	Only occurs in infants, F: M: 5:1	All ages, both sexes
Incidence	Most common benign tumor of infancy of proliferative endothelium with cellular hyperplasia	Localized defects of vascular morphogenesis of lymphatic, capillary, venous, arterial channels, or combined
Appearance	Variety raised, flat, smooth, bosselated, superficial, deep-blue subcutaneous	Thin and deep, diffuse, focal, or fruit-like appearance. Infiltrative and destructive
Timing	Not visible at birth, appear at 1–2 weeks	Usually visible and present at birth
Growth	Rapid for 0–9 months, stop growing between 6 and 18 months, GLUT-1 +ve	Most grow slowly after birth or sudden onset and slow/intermittent growth
Involution	Essentially all, slow may take up to 10 years, often with a cosmetic deformity	Essentially none, usually grow with an individual with growth spurts
Involuted stage	Permanent final residue	Permanent malformations
Locations	80% in Head and Neck, outside/inside body—e.g., brain, liver, intestine	Can be in the brain, liver, intestines, spine, stomach, or organs
Complications	Ulceration, infection, bleeding	Bleeding
Characteristics	Stay same when sick, feels spongy, warm, compressible, rapid refill, pulsatile, bruit	Lymphatic swell/shrink with respiratory illness. Venous fill when dependent, arterio-venous have a pulse when pressed. Transilluminate
Treatment	Straight forward and conservative	Complex, multidisciplinary modality
Referral	Problematic complicated ones	Most cases need early referral
Intervention timing	Early intervention is recommended but not always necessary	Early intervention is recommended to minimize the extent of surgery

Table 62.1 (continued)

Criteria	Hemangioma	Vascular malformations
Steroid therapy	Systemic/intralesional lead to faster regression in 1/3, stabilization in 1/3, and no response in 1/3	Responses, at best, are limited to occasional case reports
Propranolol	Rapid involution 2–3 mg/kg in 2–3 divided doses per day	No response, side effects of hypoglycemia, GORD, asthma, and bradycardia
Angiogenesis inhibitor therapy (Alpha interferon, VCR)	It induces involution in almost all. Reserved for lesions that pose a threat to life, vital functions, or tissue due to its serious potential toxicity in infants	Essentially none
Laser therapy	Some respond to laser	Some respond to laser
Sclerotherapy	Not indicated	Intralesional for venous/lymphatic lesions-ethanol, OK432, Bleomycin, Tetracycline
Embolization	In complicated large lesions, internal	For arterial malformations
Surgical therapy	For residual lesion, complications	Excision, contouring, or debulking
Prognosis	Generally good	Variable depends on the type

62.3 Specific Examples (Table 62.2)

62.3.1 Kasabach-Merritt Syndrome[1]

Characterized by the combination of a rapidly growing vascular tumor, thrombocytopenia, microangiopathic hemolytic anemia and consumptive coagulopathy. The blood clotting disorder results from platelets and other clotting factors from the blood being "used up" within the tumor. Seen in extremities and some viscera (e.g., liver). There is a high mortality rate in untreated cases. Treatment may be a combination of surgical excision, interferon, systemic corticosteroids.

62.3.2 Klippel-Trenaunay Syndrome (KTS)[2]

Characterized by soft tissue hypertrophy and bony overgrowth of the extremity (usually single and lower limb) with PWS. Overgrowth is not present at birth and significant limb length discrepancy is possible later with prominent hypertrophy of

[1] Haig Kasabach (1898–1943) & Katherine Merritt (1886–1986)—American pediatricians described in 1940.

[2] Maurice Klippel (1858–1942), Paul Trénaunay (1875–?). Parisian physicians described case in 1900.

Table 62.2 Summary of clinical features

Hemangiomas	**Vascular malformations**
• Infantile hemangiomas • Congenital Hemangiomas – *Rapidly involuting CH-RICH* – *Non-involuting CH-NICH* • Tumors producing KMP • Tufted angiomas – Kaposiform hemangioendothelioma • Angiosarcoma	• *High-Flow Lesions* Arteriovenous malformations (AVM) Arteriovenous fistulas (AVF) • *Low-Flow Lesions* Lymphatic malformations (LM) Capillary malformations (Port-wine stain) Venous malformations Combined malformations (LVM)
Combined rare syndromes	**Combined rare syndromes**
Diffuse neonatal Hemangiomatosis Multiple, small, dome-shaped, cutaneous lesions. May be associated with visceral lesions in liver, gastrointestinal tract, and CNS High-output cardiac failure, hemorrhage, obstructive jaundice, and coagulopathy Involution of cutaneous and visceral lesions by age 2 years *Kasabach-Merritt Syndrome* (see text) *PHACE(S) syndrome* *P*osterior fossa CNS malformations (Dandy-Walker), *H*emangioma, *A*rterial anomalies, *C*ardiac anomalies, *E*ye anomalies, and (*S*ternal defects), lumbosacral lesions, spinal anomalies, genitourinary anomalies	*Klippel-Trenaunay Syndrome (KTS)* (see text) *Sturge-Weber syndrome (SWS)* Facial port-wine stain [V1 trigeminal sensory region must be involved] CNS involvement—seizures, mental retardation, "railroad track" calcifications on cortex—ophthalmologic, ipsilateral choroidal angiomatosis Glaucoma [can be seen with V2 lesions involving eyelid] *Parkes Weber Syndrome (PWS)* (see text) *Proteus Syndrome* PWS, partial gigantism, macrocephaly, epidermal nevi
Rare lesions	
Sinus Pericranii *Glomovenous malformation* *Banayan Riley Rubalcava Syndrome* *CMTC*—Cutis marmorata telangiectatica congenita: rare disorder identified by marbled (cutis marmorata) patches of skin caused by widened (dilated) surface blood vessels (livedo reticularis telangiectases) *Multifocal Lymphangioendotheliomatosis with Thrombocytopenia* *Hyperkeratotic cutaneous capillary-venous malformation*	*Maffucci Syndrome*: Venous malformations, enchondromas on distal extremities *Blue-Rubber Bleb Nevus Syndrome*: Venous malformations of skin and GI tract—compressible, painful lesions—GI hemorrhage are a common cause of death *Gorham's syndrome*: Venous and lymphatic malformations involving skin and skeleton—osteolytic bone disease *Bannayan-Zonana syndrome*: Subcutaneous/visceral venous malformation, lipomas, and macrocephaly *Cobb Syndrome*: Spinal cord vascular birthmarks or lesions—venous malformations of the spinal cord, truncal PWS *Wyburn-Mason syndrome*: Retinal and CNS AVMs, facial PWS *Riley-Smith syndrome*: Cutaneous venous malformation, macrocephaly

the foot and toes. No CNS or visceral anomalies, Treatment: premature epiphyseal closure of longer leg, Surgical debulking not usually feasible.

62.3.3 Parkes Weber Syndrome (PWS)[3]

Similar to KTS except that an arteriovenous malformation (AVM) occurs in association with a cutaneous capillary malformation and skeletal or soft tissue hypertrophy.

62.3.4 Sturge-Weber Syndrome (SWS)[4]

Facial port-wine stain in the region of the trigeminal cranial nerve. V1 lesions—may cause seizures, mental retardation. Look for "railroad track" calcifications and eye lesions (ipsilateral choroidal angiomatosis, glaucoma can be seen with V2 lesions involving eyelid).

62.4 Investigations

Most vascular birthmarks can be diagnosed clinically without imaging studies/biopsy.

- *Laboratory*—FBC, C-RP, coagulation parameters, genetic studies.
- *Imaging*
  - Ultrasonography and Doppler US examinations are the best initially.
- *MR scan*—usually needed in most symptomatic patients to confirm the suspected diagnosis and to evaluate the extent of the lesion (hemangioma, arteriovenous malformation or AVM, venous malformation, lymphatic malformation, cystic hygroma, etc.). In addition to making the diagnosis, MRI plays a major role in decision-making regarding how these lesions need to be treated surgery *versus* embolization/sclerotherapy.
- *Magnetic Resonance Angiography (MRA) and Magnetic Resonance Venography (MRV)* can supply additional information on vascularity.
- *CT scan and X-ray* (phleboliths, calcification) imaging have a limited role in vascular anomalies/birthmarks. On the other hand, new multi-detector CT scanners may be used.
- *CT angiography* in selected patients, particularly in patients with high flow vascular birthmarks (AVM, hemangioma, arteriovenous fistula).
- *Biopsy*: Rarely if malignancy cannot be excluded, e. g., infantile fibrosarcoma, teratoma, siloblastoma, and plexiform neurofibromatosis

[3] Frederick Parkes Weber (1863–1962). English physician, added to original description in 1907.

[4] William Allen Sturge (1850–1919). English physician.

62.5 Treatment

Treatment for hemangiomas depends upon their size, location, and severity.

- *Conservative treatment* is usually recommended for small, noninvasive hemangiomas, since they will become smaller (involute) on their own. However, hemangiomas that cause bleeding problems, feeding or breathing difficulties, growth disturbances, or impairment of vision may require multimodality treatment.

  Options include the following:

- *Medical Treatment*
  - *Steroid therapy*: Topical, intralesional triamcinolone, or systemic oral steroids. For example, prednisolone 3, 2.5, 1.2, 0.6, 0.3 mg/kg from week 1–5 and maybe repeated up to 6–12 months. Rebound is well known.
  - *Propranolol*: 2–3 mg/kg 2–3 times a day but has side effects of hypoglycemia, sleepiness, GORD worsening, irritable airways and bradycardia need monitoring.
  - *Antiangiogenic drugs and immunomodulation* in selected cases.
- *Laser therapy*
  - *CT/Fluoroscopy guided*—different lasers can be used for treatment.
  - *Nd:YAG laser photocoagulation*—particularly effective because of its deep penetration into tissue.
- *Interventional radiology*—embolization of the blood vessels in internal lesions.
- *Surgical removal*—large and/or life-threatening lesions after evaluation by a multidisciplinary team of specialists.

Treatment for vascular malformations depends upon the type of malformation. Each type of malformation is treated differently; the importance of obtaining a correct diagnosis is extremely important and often difficult. Most often, a combination of these various treatments is used for effective management of the lesion.

- *Laser surgery*
  - Usually effective for capillary malformations or port wine stains, which tend to be flat, violet, or red patches on the face.
- *Sclerotherapy*
  - Venous malformations are usually treated by direct injection of a sclerosing medication, which causes clotting of the channels. Sclerosing agents may include: ethanol (alcohol), Sodium Tetradecyl Sulfate (STD—Sotradesol™), doxycycline, and OK 432.
- *Embolization*
  - Arterial malformations-blood flow into malformation is blocked by injecting material near the lesion. Embolization is the procedure in which abnormal vessels that are doing more harm than good are closed off with various

substances (e.g., alcohol, glue, and coil). Various materials may be used, depending on whether vessel occlusion is to be temporary or permanent, or whether large or small vessels are being treated.

- *Surgical removal of the lesion*
  - For cosmetic/functional or complications.

62.6 Complications

Several complications have been described including alarming hemangioma involving vital/important structures: eye, larynx, ear, and distal extremities. DIC and coagulopathy with platelet trapping can occur. Cosmetically sensitive regions are nose, lip, eye, and ear might need early intervention. Usual complications include bleeding, infection, ulceration, calcification (microthrombi), thrombosis with rapidly growing lesions, hypopigmentation, and the residual lesions. Each modality of treatment has its own complications as well.

Further Reading

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