Differential Diagnosis from Hemangioma

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Introduction

The term "vascular anomalies" represents a diverse range of vascular lesions. In order to properly manage patients, it is essential to understand the difference between a hemangioma and other vascular anomalies, as the clinical course and potential complications are very different. To date, many individuals are diagnosed as having "hemangiomas" irrespective of the clinical progression, patient age, appearance, and behavior of the vascular lesion. In one study which reviewed "hemangioma" publications in PubMed, "terminological imprecision is prevalent among both medical and surgical fields. Inaccurate designation of the vascular anomaly is associated with an increased risk of erroneous management" [1]. These authors also found that nearly 50% of patients directed to their multidisciplinary vascular anomalies program were referred with an incorrect diagnosis of hemangioma.

This chapter will focus on approaches to distinguish hemangiomas from vascular malformations. Selected citations represent updated reviews, when possible. Reference to the updated ISSVA classification is recommended (ISSVA classification of vascular anomalies ©2014 available at "issva.org/classification") as well as the manuscript elucidating this classification [2]. (Refer to Table 8.1) illustrates the basic ISSVA classification, and (refer toTable 8.3) Table 13.1 further define diagnoses of importance and representative clinical features contributing to the accurate characterization of vascular lesions.

Differentiation Between Vascular Tumor and Vascular Malformation

Refer to Table 8.1 illustrates the introductory and basic compartmentalization of vascular anomalies into malformations vs. tumors, the latter group exhibiting proliferation during all or part of the life cycle of the lesion. The benign and locally aggressive vascular tumors (further described in refer to Table 8.3) predominantly occur in the pediatric population. The categories in Table 13.1 simplify this stratification by age group and delve further into features to distinguish vascular tumors/hemangiomas vs. vascular malformations by answering relevant queries. These tables validate the axiom "not every vascular anomaly is a hemangioma" and provide a rationale for judiciously acquiring a meaningful history (initial appearance and clinical evolution of the vascular lesion) and physical examination to suitably individualize the evaluation and management of the patient. Figures 13.1 and 13.2 illustrate visual differences among these diagnoses.

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Table 13.1 Features of vascular tumors/hemangiomas vs. vascular malformations

Query	Vascular tumor/hemangioma	Vascular malformation
What is the age of the patient – infant, older child, adult?	Infant child	Infant, child adult
Was the lesion diagnosed in utero?	Congenital hemangioma RICH – rapidly involuting NICH – non-involuting PICH – partially involuting Kaposiform hemangioendothelioma	May be diagnosed prenatally
Was it present at birth?	Precursor lesion of infantile hemangioma Congenital hemangioma Tufted angioma Kaposiform hemangioendothelioma	May be evident at birth or later
Has it remained stable, proliferated, or improved with time?	Minimally proliferative or abortive hemangioma [10, 11]	May remain stable unless subjected to trauma, infection, hormonal changes, aging, etc.
Is there more than one vascular lesion (and did they all appear at the same time or are more appearing over time)?	Does not distinguish diagnosis	Does not distinguish diagnosis
Location and quality – cervicofacial, trunk, intraoral, etc.; superficial, subcutaneous, or both; soft/firm; transilluminates, fills in dependent position; red/blue/purple/flesh colored; segmental distribution, smooth surface vs. cobblestoned, etc.	Location does not distinguish diagnosis however several features may point in the direction of a specific syndrome Segmental distribution cues PHACE[a] or LUMBAR[b] evaluation [12, 13]	Location does not distinguish diagnosis; however, several features may point in the direction of a specific syndrome or diagnosis, e.g.: VVM: fills in dependent position AVM: thrill, bruit LM transilluminates, serous/serosanguinous oozing, blebs
Are there any associated problems? (e.g., pain, bleeding – epistaxis/intraoral/other – oozing of clear or serosanguinous fluid, ophthalmologic issues, swelling, limb girth/length discrepancies?)	Location does not distinguish diagnosis; however, several features may point in the direction of a specific syndrome or diagnosis	Location does not distinguish diagnosis; however, several features may point in the direction of a specific syndrome or diagnosis, e.g., HHT: Recurrent epistaxis [14] Macrocephaly: PTEN or other vascular malformation syndrome [15–19]
Is there a family history of similar lesions, macrocephaly, cancers, other symptoms?	Rare in vascular tumors	Important to determine in many vascular malformations/vascular malformation syndromes [15, 20–24]

[a]*P*osterior fossa structural malformations, *h*emangiomas (segmental), *a*rterial anomalies, *c*ardiac defects, *e*ye anomalies, and sternal and other midline deformities

[b]*L*ower body hemangioma, *u*rogenital anomalies, *u*lceration, *m*yelopathy, *b*ony deformities, *a*norectal malformations, *a*rterial anomalies, and *r*enal anomalies

Features of Hemangiomas

Hemangiomas of infancy are considered the most common tumor of childhood. They exemplify benign growths of endothelial cells and have a unique natural history, distinguished by a rapid growth phase usually beginning during the first few weeks of life and continuing until 9–12 months of age. The typical growth curve of hemangiomas is noted in Fig. 13.1. Note that in addition to the more typical hemangiomas of infancy, congenital hemangiomas represent a distinct hemangioma subtype of that proliferates in utero and is thus present as an obvious mass at birth. Congenital hemangiomas may be diagnosed by prenatal ultrasound and may become symptomatic in utero due to arterial flow which can result in a high output state in the fetus. There

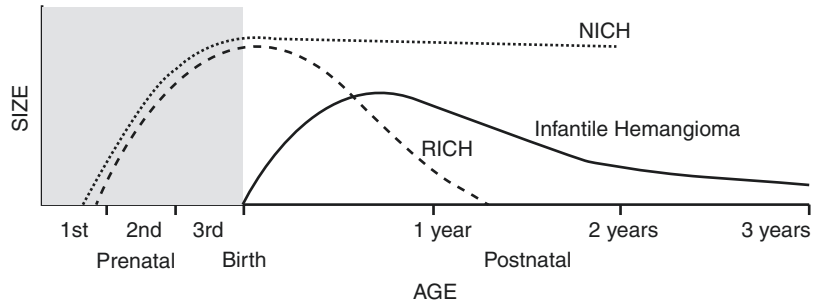

Fig. 13.1 Growth curves for infantile hemangioma, RICH and NICH (Mulliken and Enjolras [7]). *RICH* rapidly involuting congenital hemangioma, *NICH* non-involuting congenital hemangioma, *PICH* partially involuting congenital hemangioma

may be an associated transient, spontaneously resolved modest thrombocytopenia during the first week of life. Rapidly involuting congenital hemangiomas have a characteristic circumferential halo. Without treatment, most will undergo gradual involution. Often, the end result is a wrinkly and/or discolored area. Figure 13.2 depicts a representative RICH lesion, which was present at birth, had a circumferential halo, and improved without intervention. Partially involuting congenital hemangiomas (PICH) and non-involuting congenital hemangiomas will have the features of a RICH; however, the end result will differ based on the degree of improvement. In comparison, a hemangioma of infancy is minimally noted during the first week of life and proliferates postnatally. "Beard" distribution hemangiomas should alert the practitioner to possible airway involvement [3]. When hemangiomas are located in a segmental distribution, syndromes such as PHACE or LUMBAR should be considered [4]. Immunohistochemical differentiation between these lesions is represented by the absence of GLUT-1 staining in congenital hemangiomas and strong expression of GLUT-1 in hemangiomas of infancy. While they are histologically benign, hemangiomas may cause substantial psychosocial morbidity; thus, treatment during the initial growth phase aims to prevent further growth and associated morbidity, stimulate an earlier and more complete involution, and allow for an acceptable esthetic result. An updated, comprehensive guideline and executive summary published by the American Academy of Pediatrics provides a detailed review of hemangiomas, including clinical features, pathogenesis, and management [5, 6].

Kaposiform Hemangioendothelioma

Another relatively vascular lesion seen in the pediatric and neonatal age group is kaposiform hemangioendothelioma. This diagnosis and tufted angioma may be associated with Kasabach-Merritt phenomenon, with profound thrombocytopenia, hypofibrinogenemia, and elevation of D-dimers [8, 9]. Kaposiform hemangioendothelioma often appears boggy. The radiologic feature is stranding of the lesion into adjacent muscle tissue.

In contrast, *congenital vascular malformations* are present in utero and at birth (although not always detected until later in life) and do not undergo the proliferation and involution seen with hemangiomas of infancy. Observations and research in recent years have defined vascular malformations by the predominantly affected vessel type and potential associated symptoms and/or skeletal or other developmental anomalies. Depending on the location and extent of anatomic involvement and/or associated symptoms, patients may require early therapies. Those with significant cervicofacial and airway compromise may warrant heightened in utero monitoring and modified means of delivery[1]. However, some patients with

[1]e.g., EXIT procedure: *ex* utero *i*ntrapartum *t*reatment – cesarean section with partial delivery of the infant and establishment of a secure airway prior to detaching the infant from the umbilical cord.

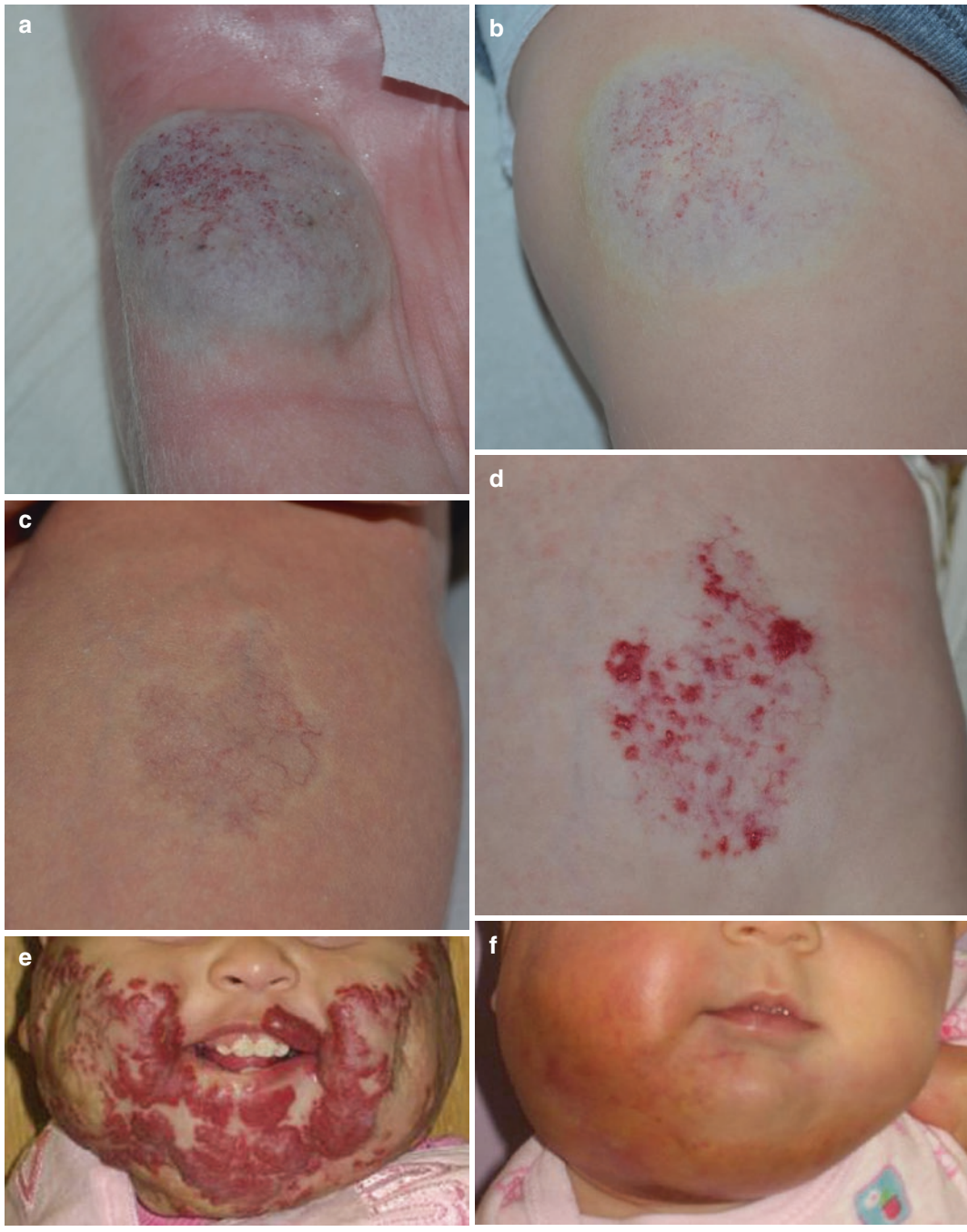

Fig. 13.2 (**a**) Vascular mass (RICH) of a 9-day-old infant. Lesion was present at birth. Note circumferential halo. (**b**) Vascular mass of same patient at 9 months of age, with spontaneous improvement. (**c**) Vascular lesion at 6 days of age. (**d**) Vascular lesion in C at 2 months of age. (**e**) Segmental vascular lesion with postnatal proliferation and stridor. Bronchoscopy revealed subglottic hemangioma. Imaging demonstrated arteriopathy compatible with PHACE syndrome. (**f**) Kaposiform hemangioendothelioma, with boggy fullness. Patient had profound thrombocytopenia, hypofibrinogenemia, and elevation of D-dimers (Kasabach-Merritt phenomenon)

less acute areas of involvement can be monitored over time, with treatments timed to associated or impending symptoms. Identification of the correct diagnosis is essential to guide the appropriate monitoring. This information is included in Table 13.1. It is now recognized that some vascular malformations are syndromic and an expanding list of causal germline and somatic mutations has been identified as reviewed in Chap. 4.

Conclusion

Differentiation of vascular malformations from hemangiomas is important in order to provide appropriate care and inform patients and families of realistic expectations. Fortunately, there is a mounting interest in vascular anomalies in the medical community, which ideally will translate into a heightened awareness of the differences among these diagnoses and improved clinical care.

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