# Neonatal Consultations: Vascular Lumps, Bumps, and Tumors in the Neonate

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Although most neonatal vascular lumps, bumps, and tumors are benign, proper diagnosis is important for prognosis and management. Therefore, knowledge of both common and rare conditions is important when evaluating a neonatal nodule. Differential diagnosis of neonatal vascular nodules must focus on important diagnostic clues that should prompt consideration and evaluation for less common and/or potentially threatening conditions. Infantile hemangioma (IH), congenital hemangioma (CH), venous malformation (VM), lymphatic malformation (LM), kaposiform hemangioendothelioma (KHE) and tufted angioma, and malignant tumors are reviewed here.

## Infantile Hemangioma

Infantile hemangioma, a benign proliferation of capillaries, is the most common tumor of infancy with reported incidence of up to 5% in neonates.[1] As such, suspicion for less common lesions is often predicated on identifying features that would be atypical for an IH. A superficial IH presents as a bright red papule, nodule, or plaque, while a deep IH presents as a flesh-colored to bluish nodule. Mixed IHs combine features of both superficial and deep lesions. The distribution may be focal or segmental, with segmental lesions encompassing a larger territory–like distribution and frequently displaying a thin, coarsely telangiectatic appearance.

Knowledge of the natural history of IH generally is crucial in differentiating it from other neonatal lesions. Infantile hemangiomas display a natural history that is distinct and predictable. They typically manifest within the first few weeks of life, though up to 30% present at birth with a premonitory mark, which may be a light red, pink, bluish, or vasoconstricted patch. Thus, mere presence of a lesion at birth is not the feature that distinguishes other congenital lesions from an IH. After initial appearance, IHs undergo a period of proliferation that occurs over 4 to 6 months in most patients. In some cases, areas of proliferation may be subtle, but nonetheless the presence of some areas of increased redness and/or volumetric growth generally is required to firmly establish the diagnosis of IH. Thereafter, IH will involute, a process that begins before 1 year of age in most cases and continues over years. Although IHs undergo involution, complete clearance may not occur, as nearly 70% will leave permanent residua such as fibrofatty masses or anetodermic skin.[2] Nevertheless, the presence of a proliferative phase followed by a slower period of involution is a hallmark feature of the IH.

Biopsy and imaging rarely are required for establishing diagnosis of an IH. Histopathology showing a proliferation of capillaries with positive glucose transporter 1 (GLUT-1) staining is characteristic. Imaging with ultrasound reveals a fast-flow lesion. Apart from exceptionally rare cases, a cutaneous IH typically does not cross muscle fascia, and thus alternative diagnoses should be considered for a cutaneous lesion that demonstrates infiltration into nerve, bone, joint, or other deeper tissues. Most IHs do not require treatment; however, a small subset may be associated with complications and thus require intervention. Complications of IH may include impairment of function (eg, vision, feeding, respiratory), ulceration, and risk for permanent disfigurement. When treatment is indicated, the most commonly employed options during the proliferative phase are the topical beta-blocker timolol and the oral beta-blocker propranolol. In addition, certain IHs may be associated with either syndromic presentations and/or visceral involvement, thus requiring further workup (Table).

## Congenital Hemangioma

A CH is an uncommon benign neonatal tumor that is distinct from an IH in behavior, biology, and treatment. Congenital hemangiomas may have a rapidly involuting course, referred to as RICH (rapidly involuting congenital hemangioma), or a noninvoluting course, referred to as NICH (noninvoluting congenital hemangioma). Partially involuting types also have been described.[3] A RICH typically presents as a highly vascular, red-violaceous or bluish plaque, nodule, or large mass at birth. An NICH

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## Vascular Lesions and Potential Syndromic Associations or Visceral Complications

| Clinical Feature | Syndrome/Disease Association | Workup |
|---|---|---|
| **Infantile Hemangioma** | | |
| Segmental IH of the head and neck >5 cm | PHACE syndrome[a] | MRI/MRA of brain and neck, echocardiogram, ophthalmology evaluation |
| ≥5 cutaneous IHs | Hepatic IH | Abdominal US with doppler |
| Segmental IH in beard distribution | Airway IH | ENT evaluation, endoscopy |
| Segmental IH of the lower body | LUMBAR syndrome[b] | MRI with and without contrast of lumbosacral spine, abdominal US with doppler |
| **Venous Malformation** | | |
| Multiple VMs | Familial mucocutaneous VM, blue rubber bleb nevus syndrome | Fecal occult blood test, CBC if anemia is suspected, referral for endoscopy if above are abnormal and/or if blue rubber bleb nevus syndrome is likely |
| Capillary lymphatic VMs | Klippel-Trenaunay syndrome | MRI with and without contrast to evaluate extent |

Abbreviations: IH, infantile hemangioma; MRI, magnetic resonance imaging; MRA, magnetic resonance angiography; US, ultrasound; ENT, ears, nose, and throat; VM, venous malformation; CBC, complete blood cell count.
[a]Posterior fossa defect, Hemangioma, cerebrovascular Arterial anomalies, Cardiac defects including Coarctation of the aorta, Eye anomalies.
[b]Lower body hemangioma, Urogenital anomalies and Ulceration, Myelopathy, Bony deformities, Arterial anomalies, Renal anomalies.

presents as a red-violaceous or bluish, coarsely telangiectatic patch, plaque, or nodule. A characteristic feature of the CH is the rim of vasoconstriction around the lesion, which is an important diagnostic clue (Figure 1). In contrast to IH, multifocal lesions are highly unlikely in CH, though it rarely has been reported.[4]

Regardless of subtype, CHs are fully developed at birth. Infantile hemangiomas, on the other hand, are either minimally present or not present at birth and thereafter proliferate. After birth, a RICH rapidly involutes over the first 9 to 12 months of life. This process generally is evident even in the first few weeks of life, which would not be expected of an IH and is therefore a major distinguishing factor. A NICH, on the other hand, is expected to be persistent, for the most part neither showing signs of proliferation nor involution.

Complications of CHs may include ulceration, functional impairment, or risk for permanent disfigurement depending on location. In addition, due to their fast-flow state and potential large size, some CHs may be complicated by high-output heart failure in the neonate. Distinguishing an IH from a CH is important not only for prognosis but also treatment. Beta-blocker therapy generally is not useful for CHs, and management usually is supportive in the neonatal period.

In the majority of cases, diagnosis can be achieved solely on clinical features. Biopsy with immunohistochemistry shows negative GLUT-1 staining, which will distinguish this lesion from an IH. At times, the highly vascular nature and/or striking size of a CH may lead some to consider the potential diagnosis of an arteriovenous malformation. However, soft-tissue arteriovenous malformations involving the skin are almost never fully developed in the neonatal period and generally take years to evolve from a quiescent state to a destructive lesion.

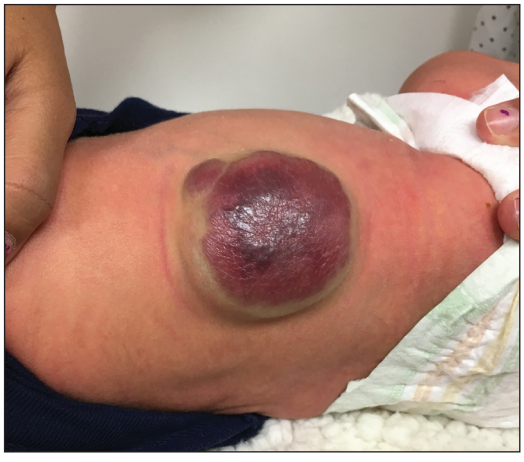

**FIGURE 1.** A rapidly involuting congenital hemangioma with a rim of pallor that is a characteristic feature.

### Venous Malformation

Venous malformations are congenital malformations of veins that may be apparent at birth or later. They appear as

bluish to flesh-colored, compressible nodules or plaques. They tend to increase in size when the affected body part is in a dependent position, and this maneuver can be a helpful distinguishing clue. Although the majority of patients have a single lesion, multifocal involvement may occur uncommonly (Table). The diagnosis of VM usually is clinical, though at times, a VM may be difficult to distinguish from a purely deep IH. However, a VM will persist over time, growing in proportion to the patient. In addition, a VM displays low flow on ultrasound, a distinguishing feature from the fast-flow IH. Magnetic resonance imaging with and without contrast is the imaging study of choice. At times, cutaneous VMs will demonstrate infiltration into other tissue planes such as muscle and joint. Pain may occur secondary to thrombus formation within the malformation. In extensive lesions, intravascular coagulation may be notable, as reflected in elevated D-dimer and decreased fibrinogen levels. Treatment with sclerotherapy or surgery may be considered in select cases during infancy; however, in general, an asymptomatic VM may be observed early on in life.

## Lymphatic Malformation

A lymphatic malformation (LM) is a congenital malformation of lymphatic vessels and may be further differentiated into microcystic, macrocystic, or mixed types depending on the size of the channels. An LM may present at birth or later and persists over time. Superficial microcystic LMs, synonymous with the term *lymphangioma circumscriptum*, characteristically appear as a group of clear and violaceous hemorrhagic vesicles on the skin. Deeper LMs appear as a tense or spongy, flesh-colored nodule or mass. Involvement of the head and neck is common. Complications frequently occur in LMs. Cutaneous LMs may ooze or bleed. Infection and hemorrhage into cysts may occur, which will cause acute pain, redness, swelling, and induration. Cervicofacial lesions may result in respiratory distress. Thus, the majority of LMs require treatment, though asymptomatic lesions may be observed in the neonate. An ultrasound will demonstrate a low-flow lesion, and magnetic resonance imaging is the diagnostic modality of choice for diagnosis and definition of extent.

## KHE and Tufted Angioma

Kaposiform hemangioendothelioma is a rare, locally aggressive, vascular tumor that is frequently associated with a potentially life-threatening coagulopathy, Kasabach-Merritt phenomenon. Tufted angiomas are now understood to belong on a spectrum with KHEs, which usually present in the neonatal period or infancy as firm, red-violaceous plaques, nodules, or large tumors. Infiltration into nerve, muscle, and bone may occur. The firm/hard nature and deep violaceous appearance generally are initial clues that it is not an IH. Kasabach-Merritt phenomenon manifests as thrombocytopenia as well as low fibrinogen and elevated D-dimer levels. Thrombocytopenia is generally profound in Kasabach-Merritt phenomenon and results from platelet trapping within the vascular tumor. Given these potential complications, KHEs generally require immediate medical attention, and various treatment protocols including prednisone, vincristine, and sirolimus are utilized for complicated cases.[5] The diagnosis may require biopsy to distinguish it from malignant tumors, particularly sarcomas.

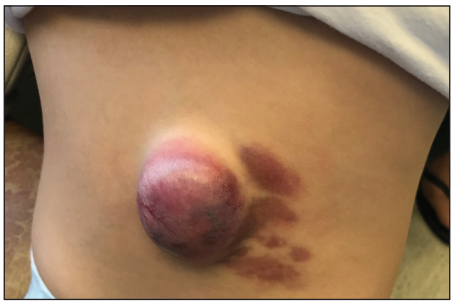

**FIGURE 2.** A vascular-appearing nodule with infiltrative edges in an infant. Biopsy showed a spindle cell sarcoma.

## Malignant Tumors

Various malignancies, including congenital leukemia, neuroblastoma, Langerhans cell histiocytosis, infantile fibrosarcoma, and rhabdomyosarcoma, rarely may present as cutaneous nodules or masses in a neonate mimicking hemangiomas or other vascular lesions (Figure 2). Neonates may present with multiple bluish papules and nodules resembling a blueberry muffin baby; multiple violaceous-red nodules; or a single red-violaceous, highly vascular–appearing mass mimicking hemangiomas. Malignant tumors may display vascularity on imaging, and thus the presence of vascular flow on ultrasound should not dissuade one from the possibility of a malignancy if other clinical features are atypical or unusual for a hemangioma. When a neonatal malignancy is suspected, a large punch biopsy or incisional biopsy is required for workup.

## Final Thoughts

Although IHs are the most common vascular nodules in neonates and young infants, other conditions such as VMs, LMs, CHs, KHEs, and malignancy may occur less commonly. Identifying features that would be considered atypical for IH is crucial to recognize these less common possibilities.

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