Treatment of Complicated Vascular Tumors in Children
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Annotated Bibliography

Disclosures:
- I have no conflicts of interest
- Several of the therapies I discuss are off-label

This talk will review three challenging cases:

1) Infantile Hemangioma and PHACE Association
2) Congenital Hemangiomas
3) The clinical spectrum of Tufted Angioma

Learning Objectives

- Broaden your differential diagnosis for a variety of vascular lesions in children
- Identify well established and several newly reported risk factors for PHACE syndrome and direct appropriate work up
- Describe emerging associations with PHACE syndrome including hearing loss, endocrine dysfunction, neurodevelopmental anomalies and dental enamel concerns
- Distinguish between the subtypes of congenital hemangiomas and describe their post-natal course
- Recognize the clinical features of tufted angioma and discuss potential treatment options
- Determine appropriate work up and coordinate care for infants with high risk vascular lesions

The following references were helpful in creating an evidenced-based discussion surrounding each case.

Introduction:
The classification for vascular anomalies was recently updated by the International Society for the Study of Vascular Anomalies (ISSVA). This classification is based on the original Mulliken and Glowacki binary classification for vascular tumors and malformations introduced in 1982. The field has grown rapidly over the last several years and so too has our knowledge of vascular anomalies in many ways: Histopathology, genetic basis and much more. A recent summary and recommendations of the new updated ISSVA classification was published in Pediatrics in 2015.


Case 1: Infantile Hemangioma and PHACE association

*What is the most well-established risk factor for PHACE syndrome?*
A large facial infantile hemangioma, involving in particular the S1 segment is high risk for underlying PHACE association. In one prospective study, 85% of patients with PHACE had facial hemangiomas in the S1 distribution. A thorough work up to evaluate for underlying PHACE association includes MRI/MRA of the head and neck, eye examination, echocardiogram and consideration for thyroid function tests.


Hemangiomas occurring in several other locations in addition to the face have been reported to confer a risk for underlying PHACE association. These include segmental scalp distribution, retro-orbital involvement and large, segmental hemangiomas on the upper extremity or torso.


**What are newly emerging associations with PHACE syndrome?**

We continue to learn more about PHACE over time. New publications in the last several years identify additional areas of concern in patients with PHACE. These include neurodevelopmental concerns, endocrine abnormalities, hearing loss and dental enamel concerns. The following reference is an excellent up to date summary of PHACE association.


### Case 2 Congenital Hemangiomas

**Distinguish between subtypes of congenital hemangiomas and describe their post-natal course.**

Congenital hemangiomas (CH) are rare and distinct from infantile hemangiomas both clinically and histologically. They are present fully formed at birth and follow a distinct post-natal course depending on subtype. Congenital hemangiomas have recently been found to share a unique genetic basis and most likely exist within a spectrum – they both arise due to mutations in GNAQ or GNA11. Clinically CH share similar features in that they present as blue to violaceous plaques or nodules with overlying telangiectasia and a surrounding pale halo. They demonstrate elevated blood flow on Doppler evaluation.

Clinical subtypes of CH include the following: rapidly involuting congenital hemangioma (RICH), non-involuting congenital hemangioma (NICH) and partially involuting congenital hemangioma (PICH). These are aptly named and follow a distinct post-natal course, with RICH involuting quickly in the first 6 months of life, while NICH persist over time.

Tufted angioma (TA) is a rare vascular tumor which shares clinical, histopathologic features and lineage with kaposiform hemangioendothelioma (KHE). Tufted angiomas are heterogeneous in their clinical presentation, but have a predilection for the head and neck and extremities. They often present as ill-defined pink to violaceous plaques or nodules, hypertrichosis and hyperhidrosis are often observed. Tufted angioma are generally more superficial and less invasive than KHE. The most concerning possible complication is Kasabach Merritt Phenomenon, a consumptive coagulopathy resulting in extreme thrombocytopenia. Treatment options depend on size, location and symptoms but may include excision, systemic chemotherapeutic agents such as vincristine and oral steroids. Sirolimus is also emerging as an effective treatment modality for both TA/KHE.