Annotated Bibliography

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

This talk will review three challenging cases:

1) Ulceration in the setting of a large, segmental Infantile Hemangioma
2) Multifocal Infantile Hemangiomas
3) Infantile Hemangioma and PHACE Association

Learning Objectives

- Anticipate risk factors for ulceration in infantile hemangiomas
- Effectively manage infants with ulcerated hemangiomas
- Determine appropriate work up for multifocal infantile hemangiomas
- 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

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: Ulcerated Infantile Hemangioma

What are the risk factors for ulceration in infantile hemangiomas?
Mucosal or intertriginous sites, large size, segmental distribution, early white/gray discoloration.
What is the best management for ulcerated infantile hemangiomas?
In general, proper wound care and topical therapies including barrier oint (Vaseline or petrolatum/aquaphor). Pain control is necessary, topical lidocaine 5% oint in a small pea sized amount up to four times daily is helpful along with oral analgesic (Tylenol) when necessary. Topical timolol and oral propranolol are accepted as first-line treatments for ulcerated hemangiomas. For small uncomplicated ulcerations, topical timolol may be an initial measure. For larger, segmental or already ulcerated lesions, oral propranolol has become standard of care. Predicting/anticipating ulceration and preventing ulceration from occurring is ideal.


Case 2: Multifocal Infantile Hemangiomas
A prospective study in 2011 identified that 5 or more cutaneous IH are associated with hepatic involvement. Regular screening with abdominal ultrasonography can pick up hepatic involvement early. In the past, diffuse hepatic involvement carried significant mortality, however with early screening and swift treatment if needed, outcomes have improved. An additional complication of multifocal or diffuse hepatic hemangiomas includes hypothyroidism, as hemangioma tissue produces type 3 iodothyronine deiodinase which consumes thyroid hormone. Propranolol is effective in the treatment of diffuse hepatic hemangiomas.


Case 3: 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.