

Grand Rounds

8-19-09

Introduction: Marilyn Miller, MD (*Attending*)



This week's pediatric ophthalmology grand rounds presents several interesting cases encountered by our faculty. This week, we will focus on capillary hemangioma.

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Capillary Hemangioma: Elizabeth Grace, MD (*Resident*)



A 2 month-old Hispanic girl presented to the pediatric ophthalmology clinic with a 1-month history of right lower eyelid swelling and injection. There was no noted strabismus or nystagmus, and patient was otherwise healthy. On exam, swelling was noted of the right lower lid (Fig. 1) with inferior conjunctival injection (Fig. 2) and a 12-16 degree left hypotropia. The slit lamp exam and dilated fundus were otherwise normal.

The differential diagnosis included capillary hemangioma, lymphoma/leukemia, neuroblastoma, retinoblastoma, lymphangioma, and orbital cellulitis. The patient's work-up included a CT of the orbits which revealed a tissue mass with intraconal and extraconal extension. A MRI was read as an infiltrative process involving the intraconal and

extraconal spaces of the right orbit with extension to the lower lid, however without orbit erosion or optic nerve involvement (Fig. 3, 4).

The diagnosis was still unclear at this point, and further workup was done including a CT of the chest, abdomen, and pelvis which did not reveal any masses or lymph node enlargement. Labs including a CBC, basic chemistries, liver function tests, and urine VMA/HVA were all normal. The final diagnosis was confirmed by examination under anesthesia with a right anterior orbitotomy (Fig. 5). The mass had findings typical of a capillary hemangioma and no biopsy was necessary.



FIGURE 1
External photograph demonstrating swelling of the right lower lid.



FIGURE 2
Photograph demonstrating injection of the inferior bulbar conjunctiva.

BACKGROUND Capillary hemangiomas are the most common orbital tumor in children, with 'strawberry marks' seen on the skin in 2-4% of all children. There is an increased prevalence in Caucasians, premature infants, low birth weight or multiple gestation infants, and females (female:male ratio 3:2). Virtually all are evident by 6 months of age. The hemangioma is a benign mixture of clonal endothelial cells associated with pericytes, dendritic cells, and mast cells. Two phases occur in the lesion's natural history: proliferative and involutinal. The proliferative is marked by explosive growth of the tumor, lasts from 0-6 months of age, and has an preponderance of pro-angiogenic factors including bFGF and VEGF. During the involutinal stage the color dulls, tension decreases, and the mass slowly decreases in size. Histologically, capillary hemangiomas are unencapsulated aggregates of closely packed, thin-walled capillaries, filled with blood and lined by endothelium.

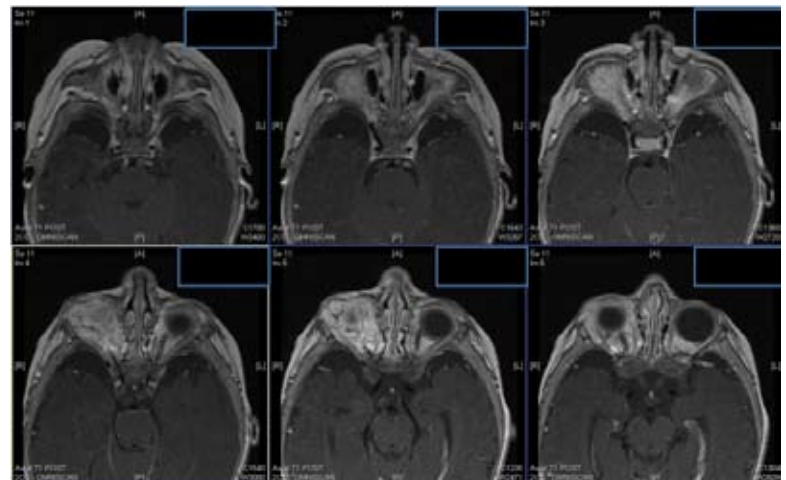


FIGURE 3
MRI T1 postcontrast image demonstrating enhancement of a mass located in the intraconal and extraconal spaces.

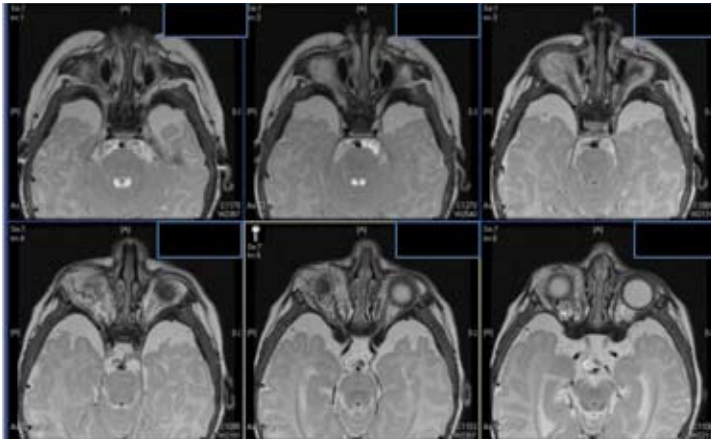


FIGURE 4
MRI T2 image demonstrating extension of the mass in the intraconal and inferior extraconal spaces, with involvement of the right lower eyelid.



FIGURE 5
Intraoperative photograph of vascular mass with findings typical of a capillary hemangioma.

Capillary hemangiomas and treatment: Sing Your Li, MD (Resident)



Capillary hemangiomas can be found in a variety of locations, including skin, mucous membranes, and internal organs, but have a predilection for the head and neck region. Periorbital hemangiomas can present as superficial strawberry nevi, dark blue or purple subcutaneous lesions, deep orbital tumors, or as a combination of these. They can be focal lesions or they can be segmental and appear to be distributed as a plaque over a certain geographic region.

Periocular capillary hemangiomas can cause several ocular complications. They can cause proptosis or displacement of the globe. Orbital tumors may also cause exposure keratopathy and compressive optic neuropathy. Amblyopia can occur in 43-60% of patients¹ as a result of

induced anisometropia, deprivation, or strabismus. Strabismus may be a result of tumor infiltration into an extraocular muscle, inhibition of mobility, or may be secondary to amblyopia. Skin breakdown may cause bleeding, ulceration, and infection.

Systemic associations are rare for periocular hemangiomas. Kasaback-Merritt syndrome is a coagulopathy caused by consumption of platelets and clotting factors within the vasculature of the tumor. Periocular hemangiomas can be associated with visceral hemangiomas, which carry a wide array of systemic complications, including gastrointestinal hemorrhage. They can also be associated with tumors of the upper respiratory tract that may cause airway compromise. PHACES syndrome is the association of large facial hemangiomas with posterior fossa abnormalities, arterial, cardiac, and eye anomalies, and sternal cleft or supraumbilical raphe.²

Therapies for capillary hemangiomas include systemic corticosteroids, which is a mainstay of treatment. Use of steroids, whether oral or pulse IV followed by oral taper, is limited by well known side effects, including behavioral changes, growth delay, hypertension, and gastrointestinal upset. Intralesional steroids have been shown to be efficacious, but there have been report of retinal embolization of steroid particles, eyelid necrosis, retrobulbar hemorrhage, and there is a risk of ocular injury and need for general anesthesia in children. Interferon-alpha is efficacious, but the most disturbing of its systemic side effects is perhaps its neurotoxicity, including spastic diplegia. For this reason, vincristine has replaced interferon alpha as second line therapy for lesions resistant to systemic steroids. Cyclophosphamide, well known as toxic agent, may have potential, as limited evidence demonstrates safety at low doses and short durations needed for treatment of hemangiomas.

Surgical intervention is reserved for lesions resistant to medical therapies and includes: surgical ligation or embolization of feeding vessels, cryotherapy, diathermy, and excision. Radiation may have a role, but there is a large concern for inducing malignancy. Laser treatment may also have a role, but is limited in large part by its superficial penetration.

- REFERENCES:**
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 2. Metry DW, Dowd CF, Barkovich AJ, Frieden IJ. The many faces of PHACE syndrome. *Pediatr.* 2001 Jul;139(1):117-23.
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Propranolol in treatment of Capillary Hemangiomas: Genie Bang, MD (Resident)



The use of propranolol for capillary hemangiomas was first described serendipitously in France after physicians noted regression of capillary hemangiomas while the patients were on non-selective beta blockers for cardiac conditions. After this observation, the physicians tried propranolol treatment for severe infantile capillary hemangiomas in 9 additional patients, with excellent results. The precise mechanism in which propranolol causes involution of capillary hemangiomas is unknown, but 3 mechanisms are proposed: 1) vasoconstriction, 2) downregulation of VEGF, and 3) apoptosis of endothelial cells. The side

effects of propranolol include hypotension, bradycardia, bronchospasm, and blunting of clinical signs of hypoglycemia, thus requiring careful monitoring of treated infants.

We present a patient successfully treated by the UIC pediatric and pediatric hematology/oncology team. This child first presented at birth with a slight discoloration noted to the right side of her face. At age 2 weeks old, the discoloration became much more noticeable, and appeared to be a large segmental hemangioma involving the right periorbit, right face and pinna, and extending towards the right jaw and chin (Fig 6).

She was initially started on oral prednisone, with no progression of the hemangiomas. She did have some involution of the hemangioma in the region of the right pinna, but then developed a yeast infection of her neck due to the steroid. 3 months after initiation of prednisone, she began to have stridor and imaging revealed extensive hemangiomas involving the neck and anterior chest causing airway narrowing. She was then started on propranolol 2mg/kg/day PO.

The patient was followed, with subsequent involution and improvement in the appearance of the capillary hemangioma (Fig. 7, 8, 9).



FIGURE 6
External photograph at 2 weeks of age demonstrating large capillary hemangioma.



FIGURE 7
External photograph taken 1 month after initiation of propranolol.



FIGURE 8
External photograph taken 3 months after initiation of propranolol with mild improvement.



FIGURE 9
External photograph taken at 8 months after initiation of propranolol with further improvement.

Discussion:

Capillary hemangiomas, as noted above, comprise the most common type of orbital tumor in children. Most should be carefully observed, unless there is a risk of ocular complications—most commonly, amblyopia. Although propranolol may have a possible effect and role in decreasing the size of capillary hemangiomas, it must be noted that it too can have some potentially serious side effects. Furthermore, because the natural history of capillary hemangiomas is to undergo a period of growth followed by involution, we cannot draw any conclusions as to whether the involution noted in our patient was due to the propranolol. However, in a case such as the one presented, where the patient did not respond well to steroids and was at risk of serious complications due to the hemangiomas, propranolol may be a worthwhile option.

UPCOMING CME COURSES

March 13-19, 2010	Illinois Eye Review
April 4, 2010	Retina Symposium
April 16, 2010	Uveitis Symposium
May 21, 2010	Oculoplastics Symposium
June 25, 2010	34 th Annual Alumni Day
September 25, 2010	Pediatric Ophthalmology/Adult Strabismus

Upcoming Grand Rounds

Illinois Eye and Ear Infirmary Ophthalmology Grand Rounds are held Wednesdays at 5:00 pm on the UIC campus at 909 S. Wolcott in the College of Medicine Research Building. For a complete schedule go to www.uic.edu/com/eye and click on Grand Rounds under the Education drop down menu. Or, call 312-996-6590.