GRAND ROUNDS PRESENTATION

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History and Examination

Historian: mother

HPI: 10 week old black female presented with reddish lesions on her face first noted at birth, and the lesions have been gaining “depth” over time. Patient’s mother also noted some new lesions recently in the forehead area. The right eye does not open as much as the left eye. The child is alert, active, and gaining weight appropriately. There is no significant gestational/birth history.

History and Examination

- PMH: none
- PSH: none
- POH: none
- Meds/All: none
- SH: none
- FH: none
- Birth/Development: normal

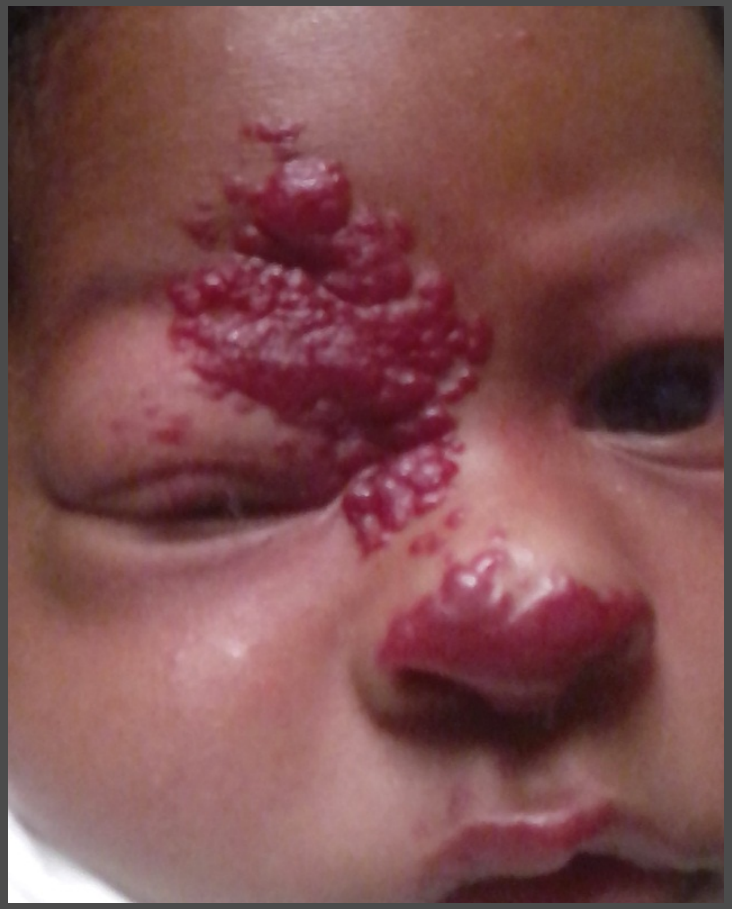
History and Examination

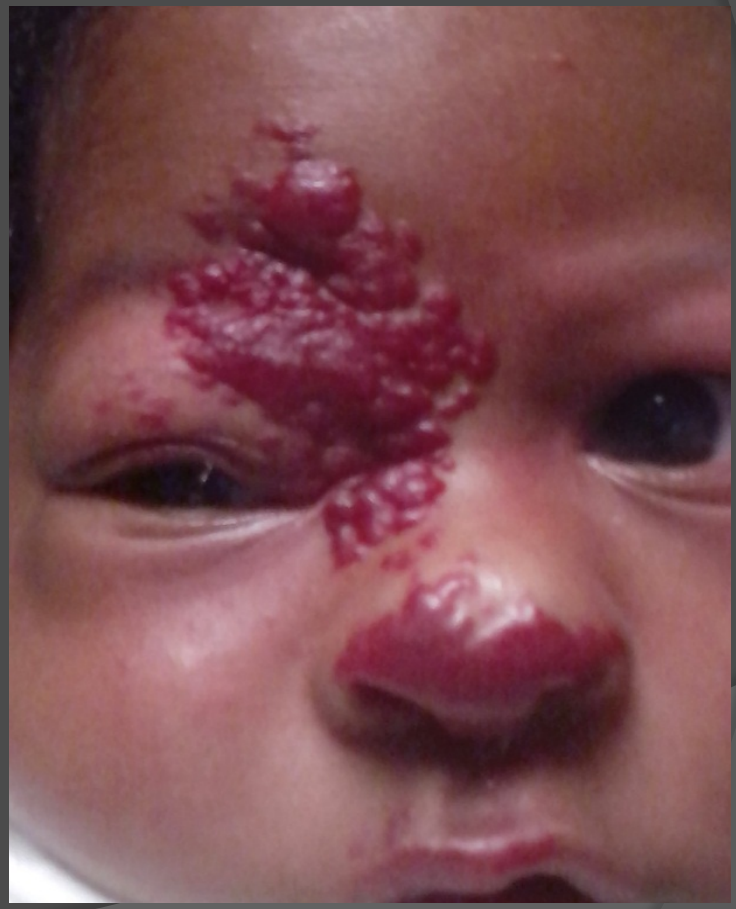
- PLE:
- LLA/HEENT:
  (see photo)
- C/S: W/Q OU
- AC: F/S OU
- I/P: R+R OU
- L: CI OU

- DFE:
- Vit: CI OU
- C/D: 0.2 s/p OU
- Mac: flat OU
- V/P: WNL

- CRx:
- OD: +5.00-2.00x90
- OS:+3.00

History and Examination





Patient Care

Your Differential Diagnosis?

Differential Diagnosis

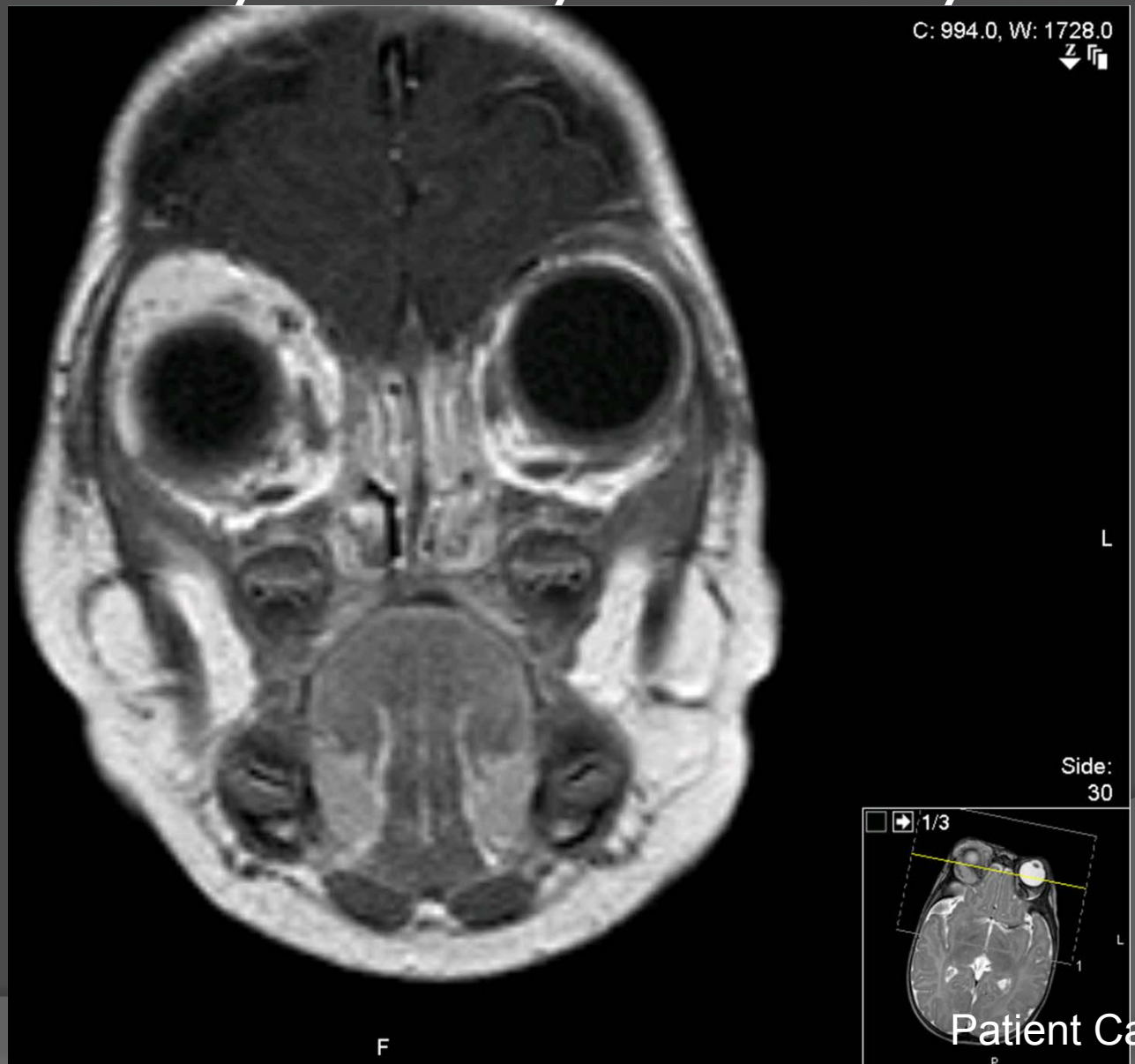
- PHACES syndrome
- Infantile Capillary hemangioma
- Diffuse neonatal hemangiomatosis
- Vascular malformation
- Kasabach-Merritt Syndrome
- Sturge-Weber Syndrome
- Von Hippel-Lindau Syndrome

Your Next Steps?

Labs/Imaging

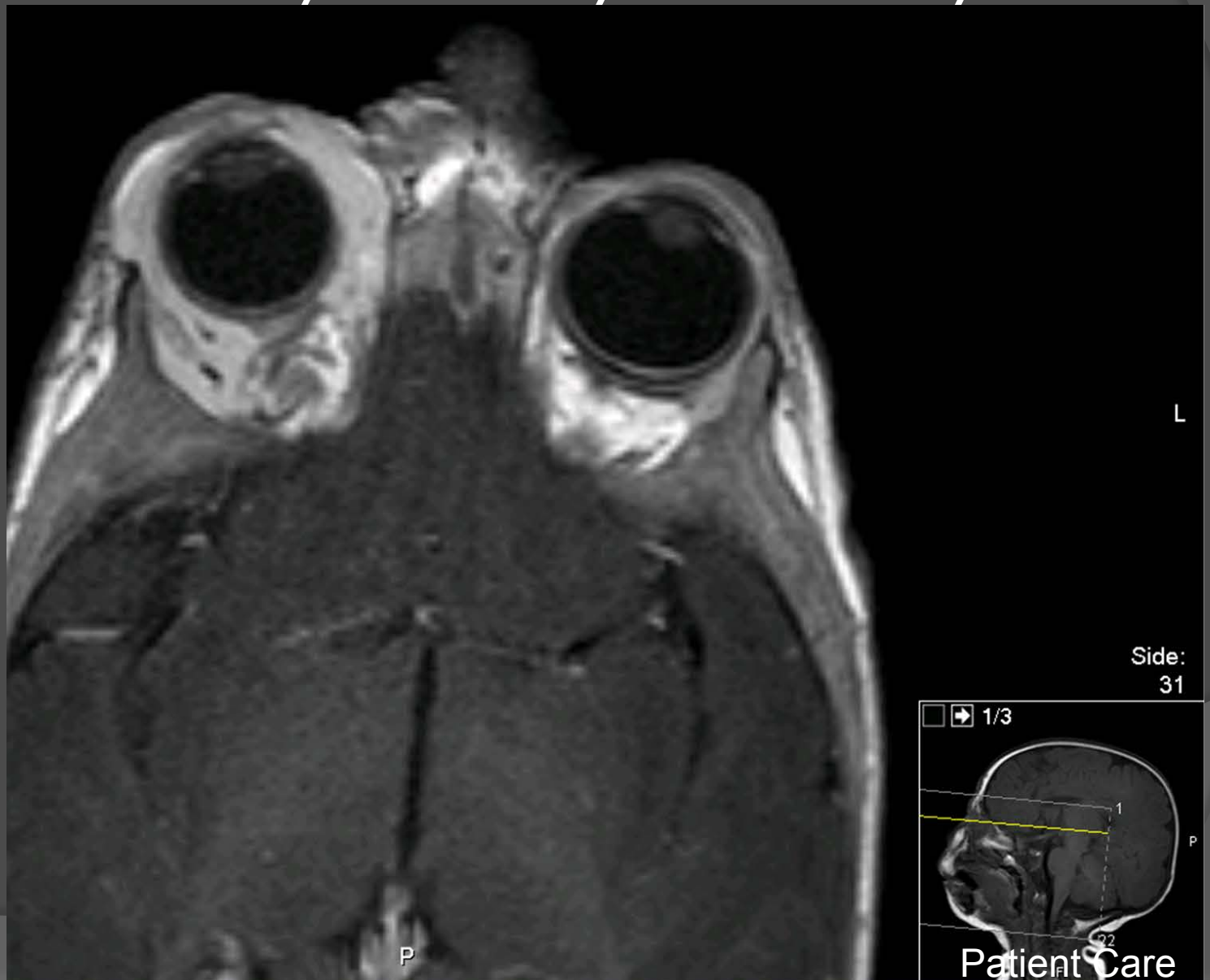
- CBC: 5.9>13.5/43.9<236
- MRI brain/orbits with contrast
- MRA brain/neck

MRI Face/Orbits/Brain w/Con

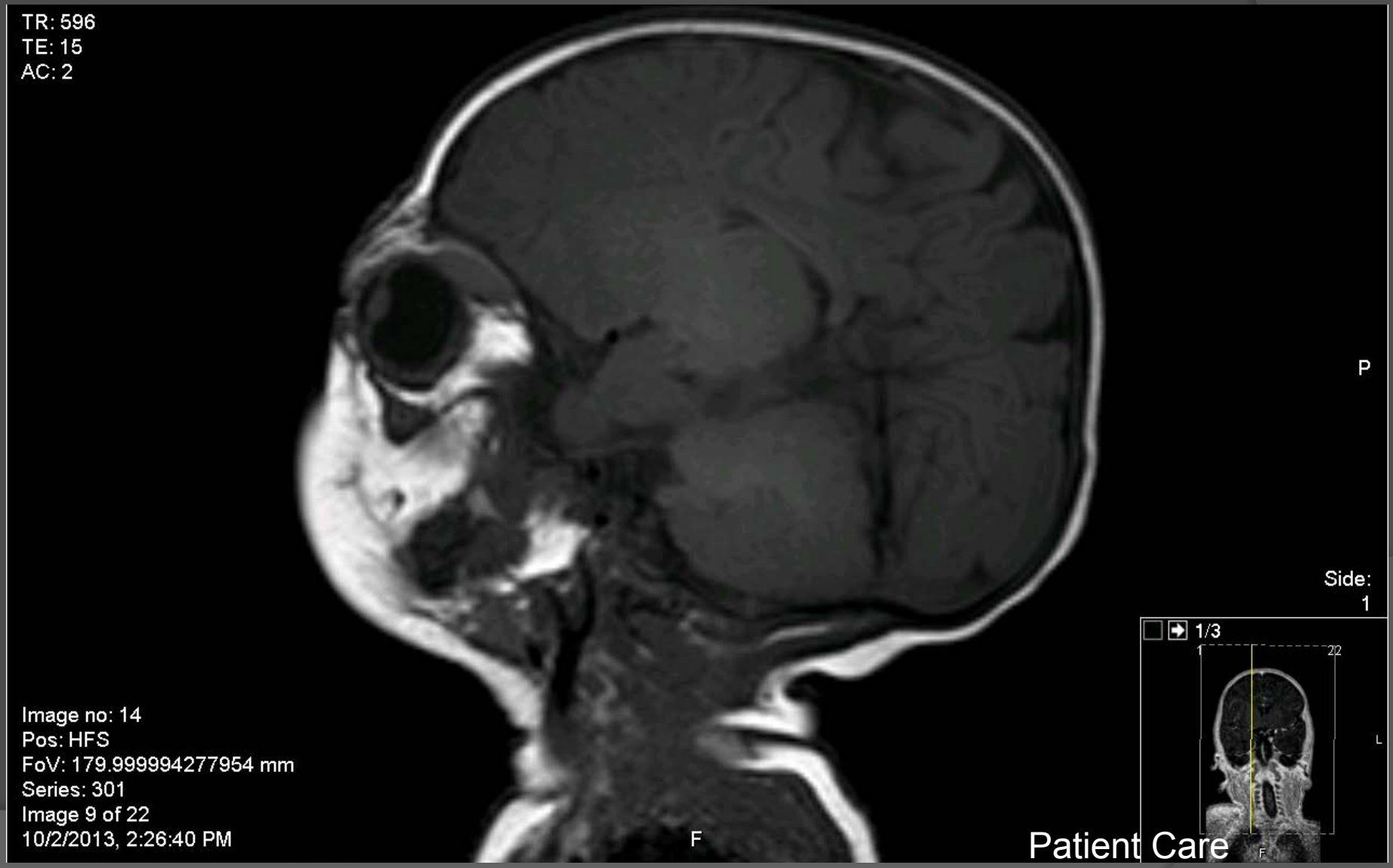


Patient Care

MRI Face/Orbits/Brain w/Con

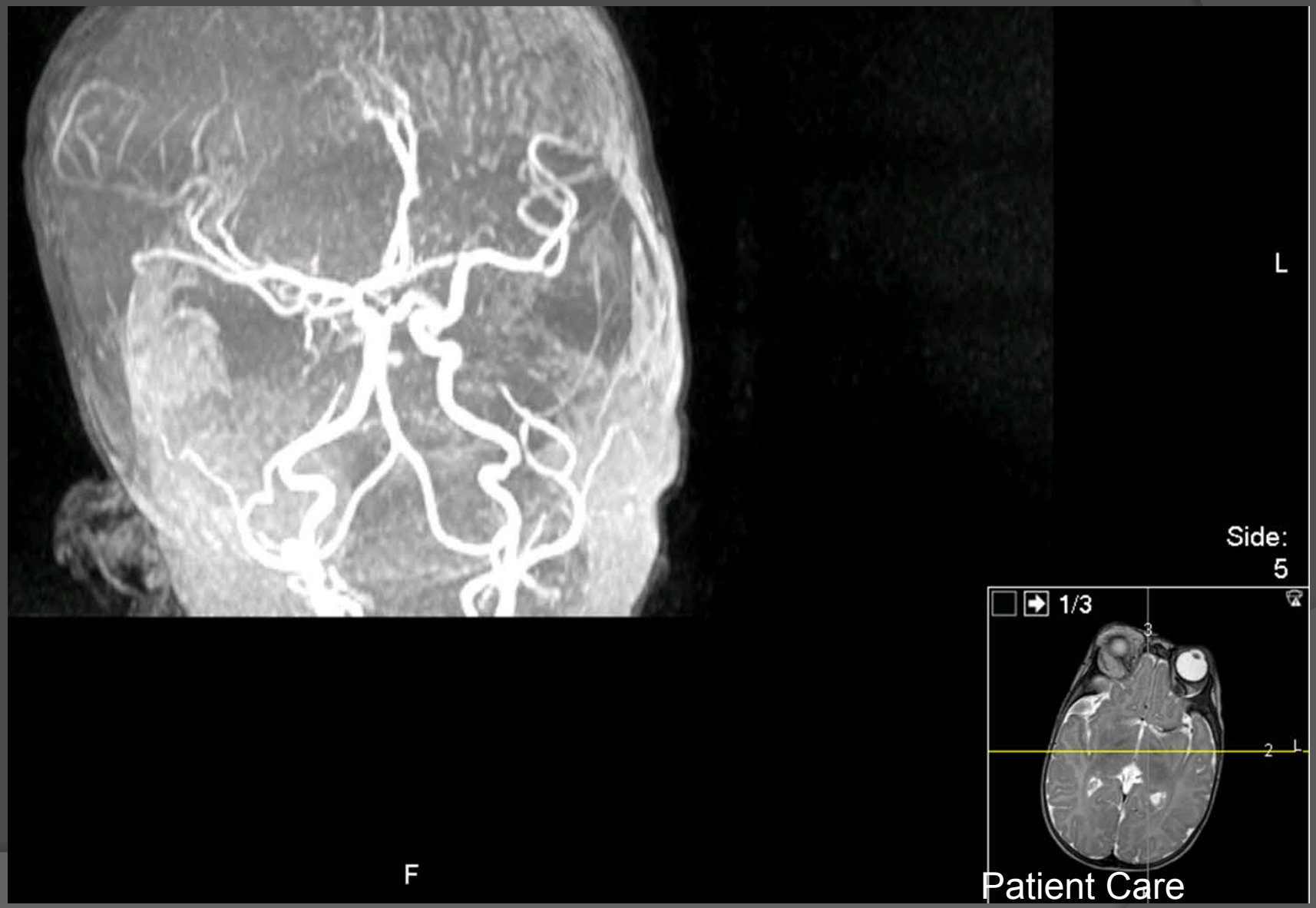


MRI Face/Orbits/Brain w/Con



Patient Care

MRA Head



PHACES Syndrome

- Posterior fossa malformations
- Hemangiomas
- Arterial anomalies
- Cardiac defects and coarctation of the aorta
- Eye abnormalities
- Sternal abnormalities or Ventricular Septal Defects

Ocular and Systemic Manifestations of PHACES (Posterior Fossa Malformations, Hemangiomas, Arterial Anomalies, Cardiac Defects and Coarctation of the Aorta, Eye Abnormalities, and Sternal Abnormalities or Ventral Developmental Defects) Syndrome

Alaina Kronenberg, MD,[a] Francine Blei, MD,[b,c] Emily Ceisler, MD,[d] Mark Steele, MD,[d] Louis Furlan, MD,[d] and Sylvia Kodsi, MD[a]

J AAPOS 2005;9:169-173

TABLE 1. Ophthalmic abnormalities in PHACES

Patient no.	1	2	3	4	5	6
Side involved	OU	OS	OS	OD	OS	OD
Vision at last visit	20/25 OD LP OS	20/30 OU	OD prefer	Will not fix	CSM OU	CSM OU
Ptosis	No	Yes	Yes	Yes	Yes	Yes
Proptosis	Bilateral	No	No	No	Yes	No
Amblyopia	Right eye occlusion	No	Yes, occlusion and strabismic	Yes, occlusion	Yes, occlusion	Yes, occlusion
Strabismus	Sensory left hypertropia and exotropia	Early-onset esotropia	Early-onset esotropia	Sensory left exotropia	No	No
Anterior Segment anomalies	Anterior polar cataract OD	No	Loss of lashes, trichiasis	Trichiasis	Heterochromia OS darker	No
Posterior segment anomalies	Optic atrophy OS	No	No	No	No	No

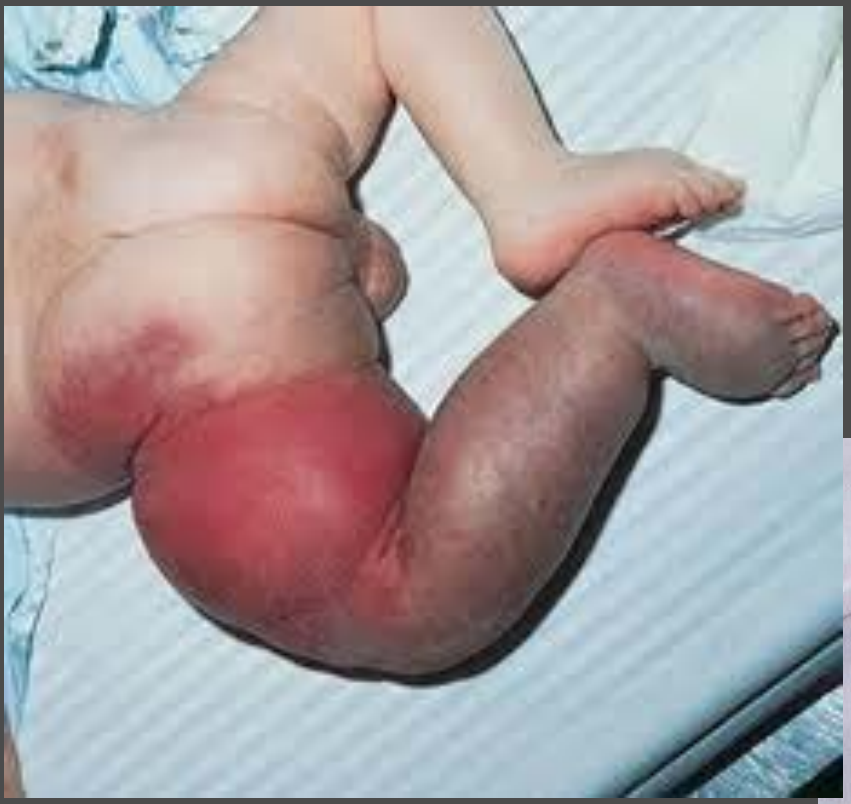
OD, right eye; *OS*, left eye; *OU*, both eyes; *CSM*, central, steady and maintained.

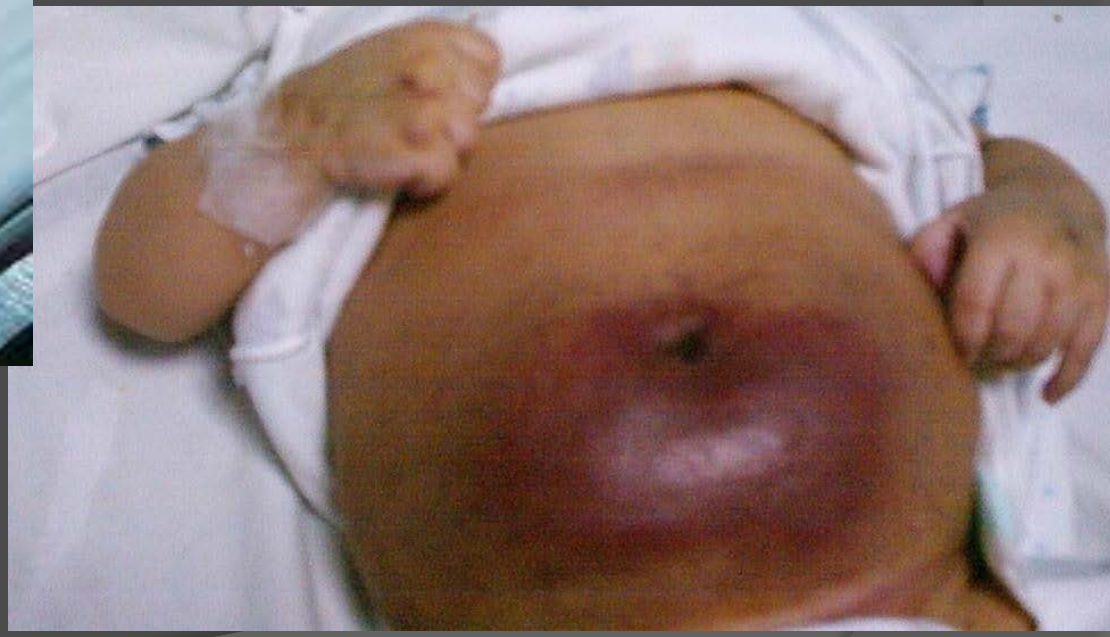
Practice-Based Learning and Improvement

Kasabach-Merritt Syndrome

- Hemangioma with thrombocytopenia
- Vascular tumor present at birth
- Can trap platelets when growing rapidly; also uses up clotting factors → bleeding/DIC
- Usual location is trunk, upper and lower extremities, retroperitoneum, cervical/facial areas
- Treated with surgery, embolization, external compression bandages, corticosteroids, alpha interferon

Kasabach-Merritt Syndrome

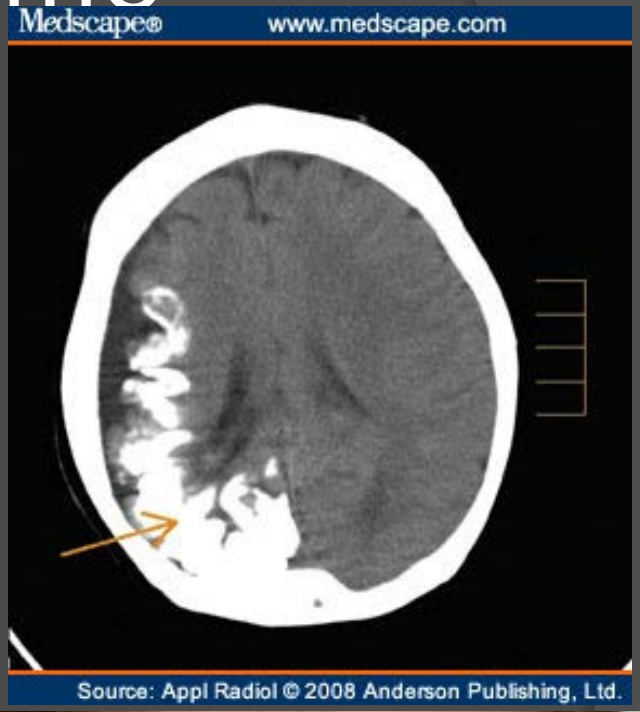


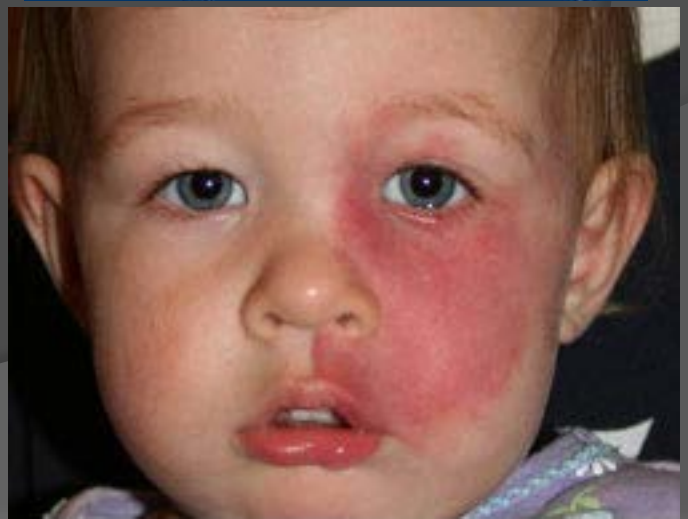


http://trombositopenia.pbworks.com/w/page/22488618/Kasabach-Merritt%20Syndrome

Sturge-Weber Syndrome

- Occurs sporadically; mutation in GNAQ gene
- Port-Wine stain
- Glaucoma
- Seizures
- Mental retardation
- Ipsilateral leptomeningeal angioma





http://www.aapos.org

Infantile Hemangiomas: Epidemiology

- 2-3x more common in females
- Most common in Non-Hispanic whites
- Increased in preterm infants
- Multiple gestation pregnancies associated with multiple hemangiomas
- Older maternal age, placenta previa, pre-eclampsia are other risk factors

Hemangiomas: Pathophysiology

- Composed of plump, proliferating endothelial cells
- Clonal proliferations of endothelial cells resulting from vasculogenesis, not angiogenesis
- Increased FGF, VEGF R expression, PCNA, MMPs
- Rapid proliferation in first year of life, then gradual replacement by fibrofatty tissue
- GLUT1 highly expressed in endothelial cells of hemangiomas during proliferative and involutional phases

Hemangiomas vs Vascular Malformations

- Hemangiomas

-appear in first few weeks of life

-spontaneously regress

- Vascular malformations

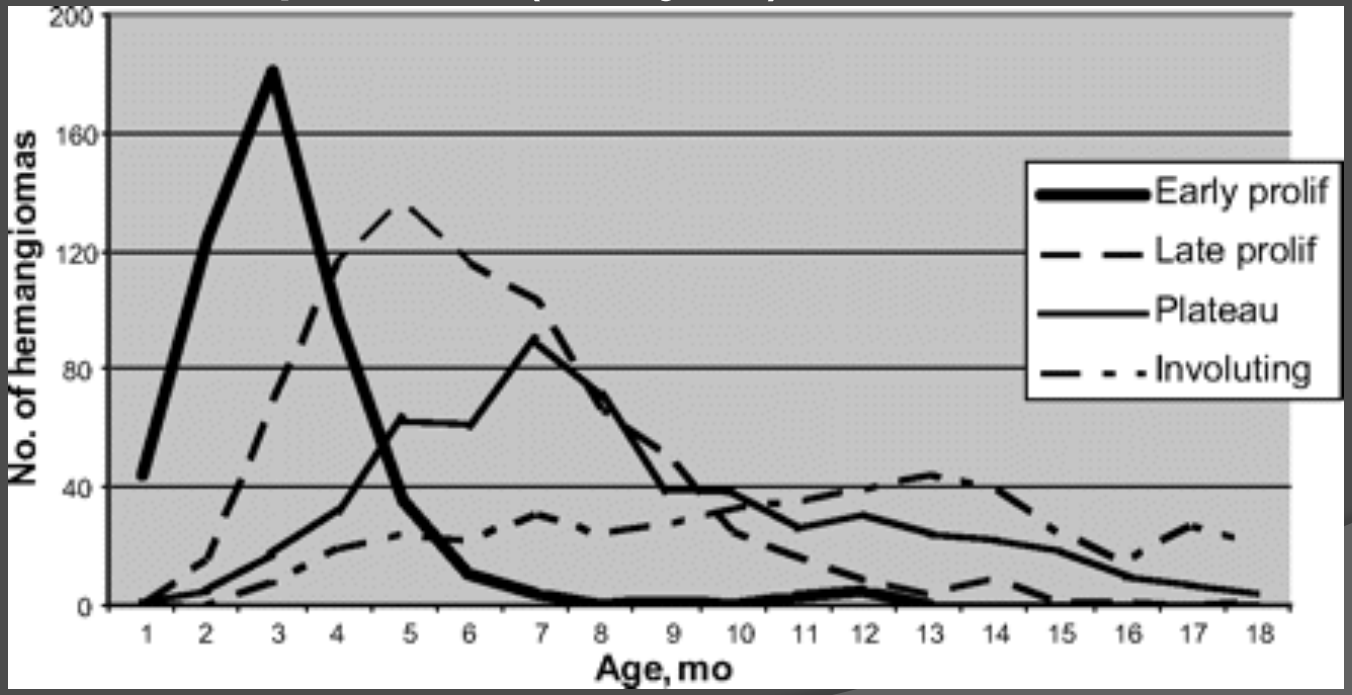
-always present at birth

-persist unchanged through adolescence and adulthood

Stage	Morphologic Subtype	Description
Nascent		
Early proliferative	Localized	Superficial
Late proliferative	Segmental	Deep
Plateau	Indeterminate	Mixed
Involuting		
Abortive		

Natural History of Hemangiomas

- Proliferation Phase (0-1 yrs)
- Involuting Phase (1-5 yrs)
- Involuted phase (>5 yrs)

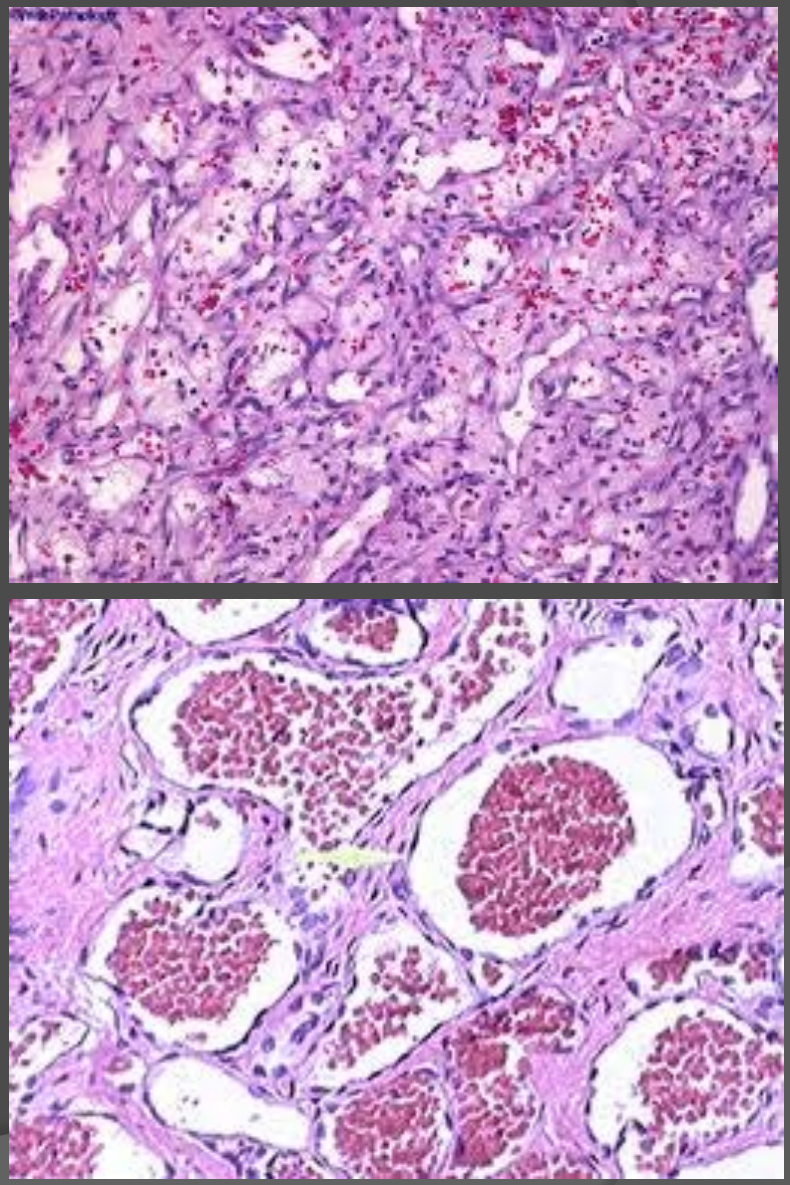


Growth characteristics of infantile hemangiomas: implications for management. Pediatrics. 2008 August; 122(2): 360–367

Medical Knowledge

Histopathology

- Aggregates of closely-packed, thin-walled capillaries with endothelial lining
- Blood-filled vessels separated by scant connective tissue
- Glut1: a marker highly specific for hemangiomas



Indications for Treatment

- Life-threatening conditions (heart failure, respiratory distress)
- Functional risks (amblyopia, swallowing disorders)
- Painful, ulcerated hemangiomas
- Aesthetic considerations

Growth Characteristics of Infantile Hemangiomas: Implications for Management

Chang et al. Pediatrics 2008 122:2, Table 1

Anatomic Location/Morphology	Associated Risk
Facial, large segmental	PHACES syndrome (posterior fossa malformations, hemangiomas, arterial anomalies, cardiac defects, eye abnormalities, sternal clefting)
Nasal tip, ear, large facial (especially with prominent dermal component)	Permanent scarring, disfigurement
Periorbital and retrobulbar	Ocular axis occlusion, astigmatism, amblyopia, tear-duct occlusion
Segmental "beard area," central neck	Airway hemangioma
Perioral	Ulceration, disfigurement, feeding difficulties
Segmental overlying lumbosacral spine	Tethered spinal cord, genitourinary anomalies
Perineal, axilla, neck, perioral	Ulceration
Multiple hemangiomas	Visceral involvement (especially liver, gastrointestinal tract)

Patient Management

- Decision to initiate propranolol and titrate to maximum tolerated dose (goal 2 mg/kg/day)
- Initial Pediatric cardiology consult for EKG/Echo
- Follow-up with dermatology and pediatrics
- Educated mother regarding condition and its effects on the eye

Patient Care, Interpersonal and Communication Skills, Professionalism, Systems-Based Practice

Steroid Therapy

- May function by direct inhibition of production of angiogenic factors (VEGF-A, IL-6, MMP)
- Usual systemic dose: 3-6 mg/kg/day for 1-2 months, depending on lesion size
- Most common complication: cushingoid facies; however other complications of steroid use possible

Steroid Therapy

- No longer first line for infantile hemangiomas
- Local intralesional steroids for small localized lesions: triamcinolone 3mg/kg (overall 85% response rate in a retrospective review
- Topical corticosteroids: clobetasol cream- best for small superficial hemangiomas at risk for ulceration

Interferon Therapy

- Inhibits angiogenesis; used for aggressive hemangiomas not responsive to steroids
- Dose: 3 million U/m2/day for weeks-months
- AE: fever, irritability, neutropenia, LFT abnormalities; severe neurotoxicity including spastic diplegia (3.6% of 441 patients in one study)

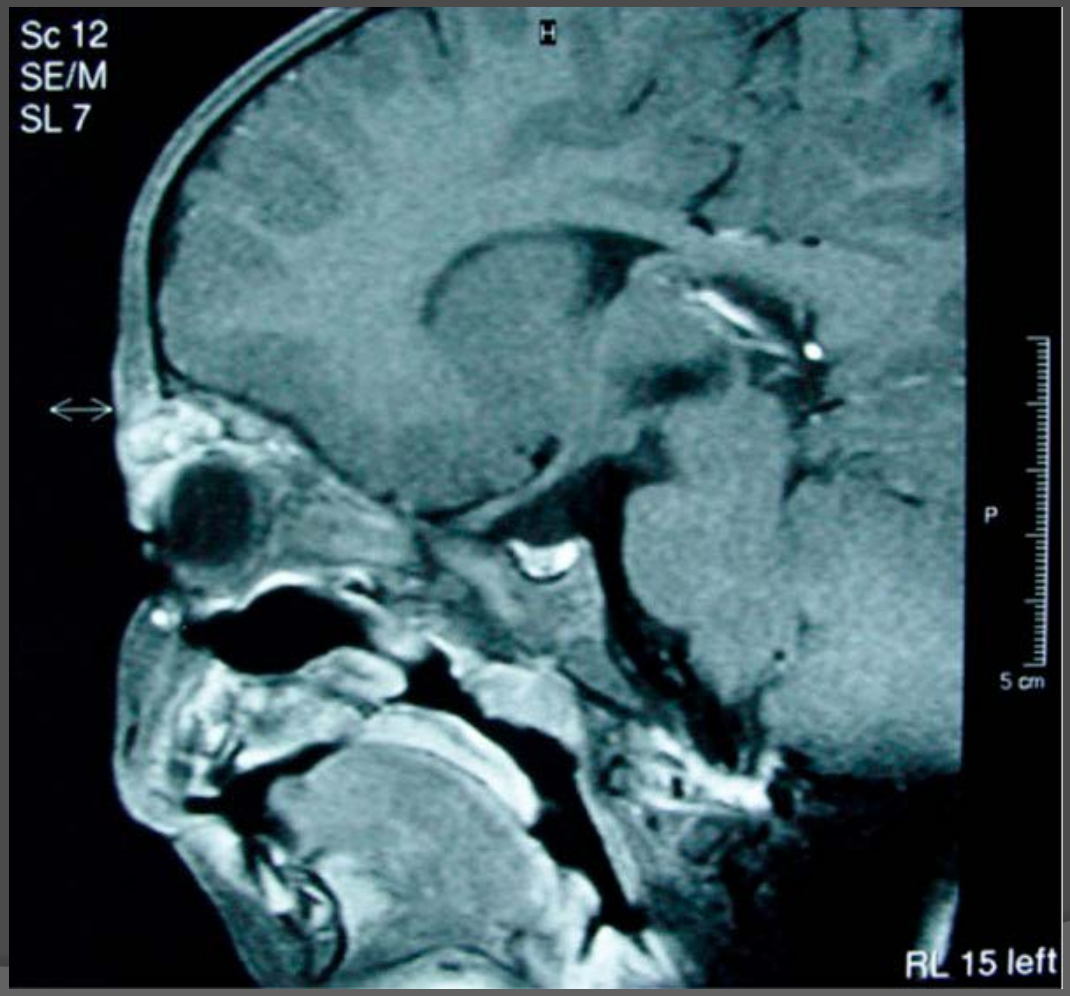
QUESTION

- An 2 ½ yr old female with a history of confirmed orbital cavernous hemangioma via neuroimaging presents to your practice with sudden and severe LUL swelling, intense pain and exophthalmos OS. The left pupil has an afferent pupillary defect and imaging suggests intraorbital hemorrhage. What is/are your next step(s)?

Orbital cavernous hemangioma in an infant with intracranial lesions: a case report

Eleni Evagelidou[1], Elena Tsanou[2]*, Ioannis Asproudis[3], Spiridon Gorezis[4], Miltiadis Aspiotis[1], Dimitrios Peschos[2] and Antigoni Siamopoulou[1]

Cases Journal 2009, **2**:6912



- Removal of cavernous hemangioma via anterior orbitotomy
- Second procedure required due to persistence of growth
- End result: Atrophy of left optic nerve

Practice-Based Learning and Improvement

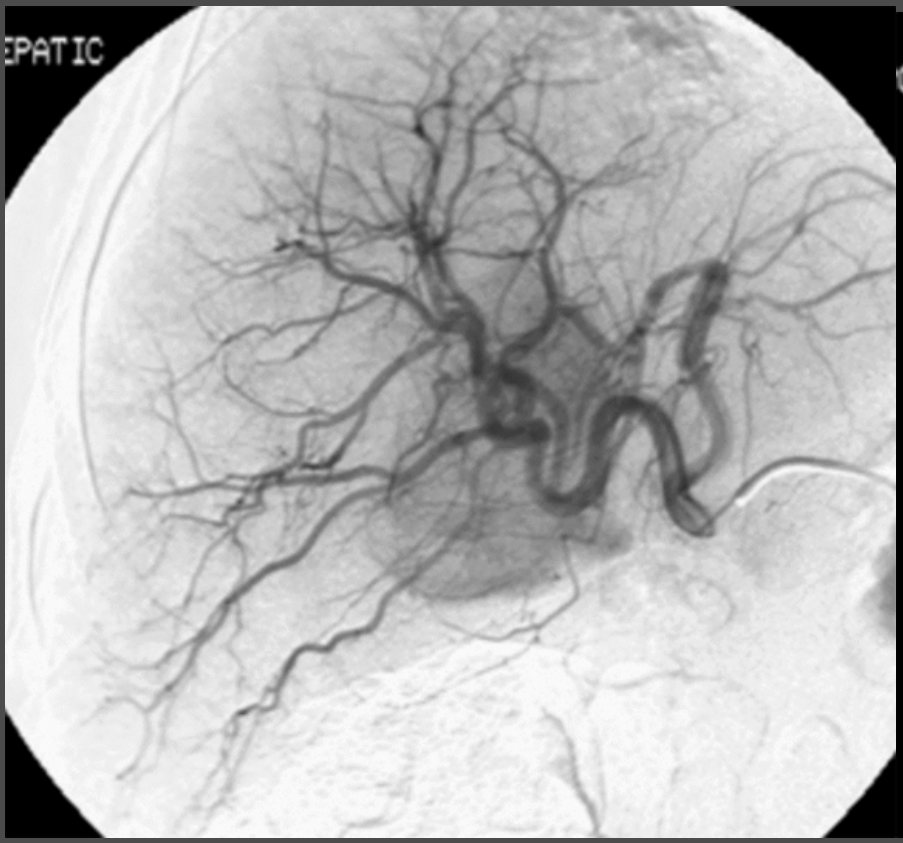
Surgical Therapy

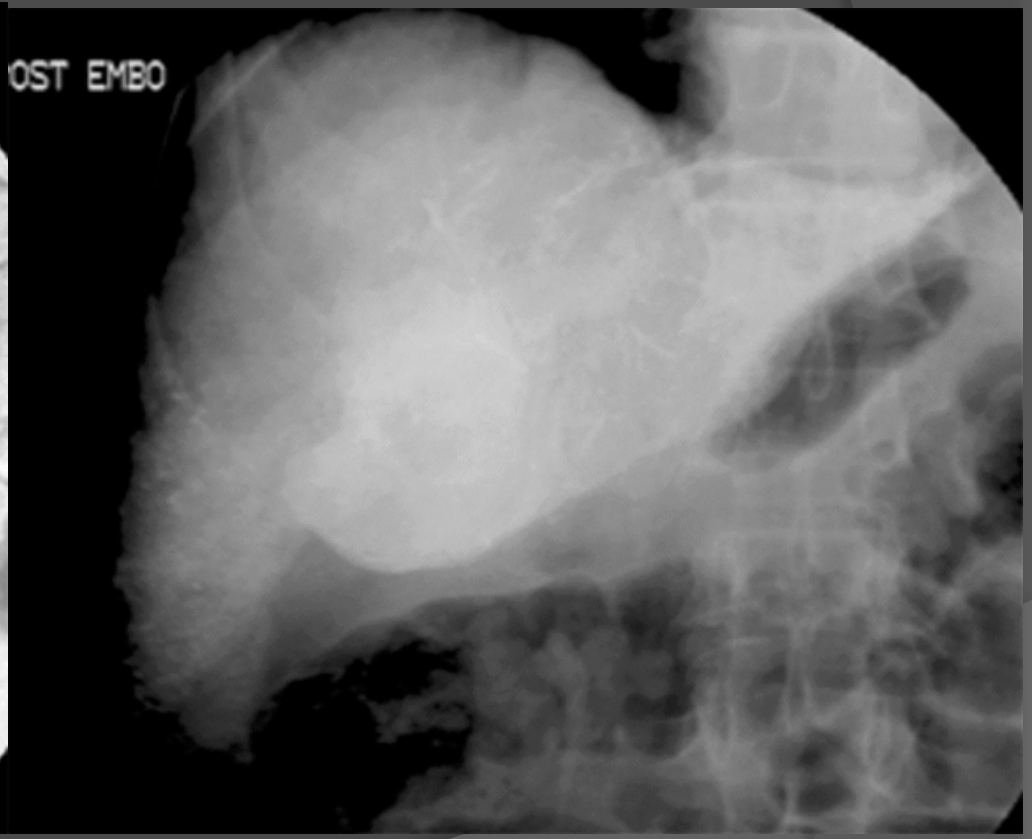
- Indications: involuted lesions with residual scars or loose skin, small localized periorbital hemangiomas, slowly involuting lesions of cosmetic significance; when risks of medical therapy>surgical therapy

Embolotherapy

- Indicated when risk of spontaneous hemorrhage is high or causing functional anomaly due to size
- Also useful prior to surgical resection
- Goal is to block a large percentage of tumor vessels.
- Embolic materials: Polyvinyl alcohol particles or microspheres

Embolotherapy





Practice-Based Learning and Improvement

Propranolol Therapy

- First-line treatment for rapidly advancing, high-risk infantile hemangiomas
- Titrate to a target dose of 2 mg/kg/day
- Mechanism(s): vasoconstriction, modulation of pro-survival signal transduction pathways, endothelial cell apoptosis
- Topical beta blockers for small superficial hemangiomas- long term data missing
- Contraindications include bradycardia, hypoglycemia, bronchial asthma

Topical Beta blocker Therapy

- For superficial hemangiomas of minor cosmetic concern
- Timolol 0.5% topical gel
- May help prevent rebound growth in children being tapered off oral propranolol

Key Points

- Periorbital hemangiomas have the potential to cause amblyopia and significant ocular morbidity
- A multidisciplinary workup for systemic syndromes should be initiated for large facial hemangiomas
- Treatment for hemangiomas should be based on age, size of the lesion, functional risk and damage to nearby structures, and cosmetic considerations

Patient Update

- Patient continues treatment with propranolol; followed by ophthalmology, dermatology, and pediatrics

Reflective Practice

- This case allowed me to care for a pediatric patient with a potentially sight-threatening variation of fairly common condition. I learned about the variety of patient presentations and treatment options available to manage this condition.

Core Competencies

Patient Care: The case involved thorough patient care and careful attention to the patient's past medical history. The patient received timely and appropriate medical management and follow up care in the eye clinic in addition to dermatology and pediatric medicine.

Medical Knowledge: This presentation allowed me to review the presentation, differential diagnosis, proper evaluation/work up and treatment options for infantile hemangiomas.

Practice-Based Learning and Improvement: This presentation included a literature search of current treatment modalities for infantile hemangiomas.

Interpersonal and Communication Skills: The patient and family were treated with respect and every effort was made to communicate with the family in a logical, understandable manner.

Professionalism: The patient's workup and treatment was initiated in a timely manner. She was informed of her diagnosis and explained the reasoning behind our workup.

Systems-Based Practice: The patient was managed by the oculoplastics and pediatric ophthalmology services, in addition to dermatology and pediatrics.

Selected References

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Thank You

- Patient and mother
- Dr. Elmalem