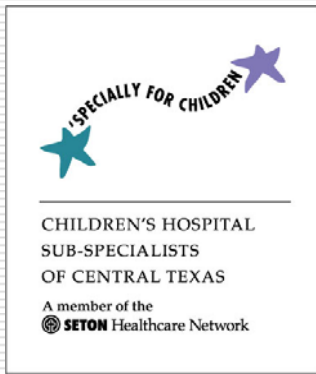


A Potpourri of Pediatric Dermatology – Is It Only Skin Deep?

Keeping Central Texas Children Well
May 17, 2008

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'Specially for Children
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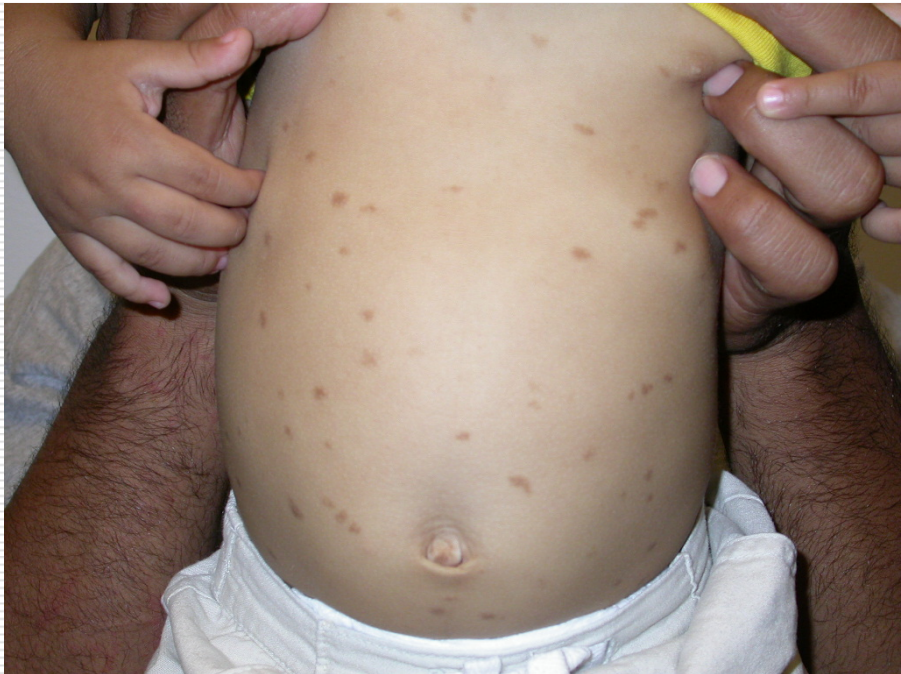


Potential Conflicts of Interest

- Investigator, Consultant, or Speaker for:
 - Astellas
 - Novartis
 - 3M
 - Amgen
 - GSK
 - Regenerx
 - None should apply for this presentation
-

Case 1

- ❑ A child presents in consultation regarding multiple presumed café au lait macules. These were first noted @ 6 months of age.



Mastocytosis/Urticaria Pigmentosa



Mastocytosis

- Urticaria pigmentosa
 - Diffuse cutaneous mastocytosis
 - Mastocytoma
 - Telangiectasia macularis eruptiva perstans (TMEP)
-

Mastocytosis

- ❑ Systemic complaints; pruritus, flushing, bronchospasm, gi, bone pain
- ❑ Diagnosis usually clinical (Darier's sign)



- ❑ Urinary, plasma histamine
 - ❑ **Serum tryptase levels**
 - ❑ ?Bone films, scans
 - ❑ Bone marrow
-

Mastocytosis/Management

- ... as indicated
 - Avoid precipitating causes
 - Antihistamines
 - Topical steroids (solitary lesions)
 - PUVA
 - EpiPen
-

Case 2



8 y/o girl seen in the EC for rash and fever.

Originally on clindamycin for osteo.

Switched to vancomycin due to c/o arthralgias.

Was on vancomycin 3-4 weeks before current complaints.

ATB continued, fluids given.

LFTs peaked in 800s; Eosinophilia

Drug-Induced Hypersensitivity Syndrome (DIHS)/DRESS

- ❑ Systemic mono-like illness
- ❑ Fever, Exanthem, Lymphadenopathy
- ❑ Eosinophilia
- ❑ Leukocytosis
-Atypical lymphs
- ❑ Liver dysfxn
- ❑ ? Role of HHV-6 (BJD 2007;157:934, Arch Dermatol 2004;140:183 & 226)



DIHS/DRESS

- Carbamazepine
 - Phenytoin
 - PBS
 - Zonisamide
 - Allopurinol
 - Dapsone
 - Others (Vancomycin, present case)
-

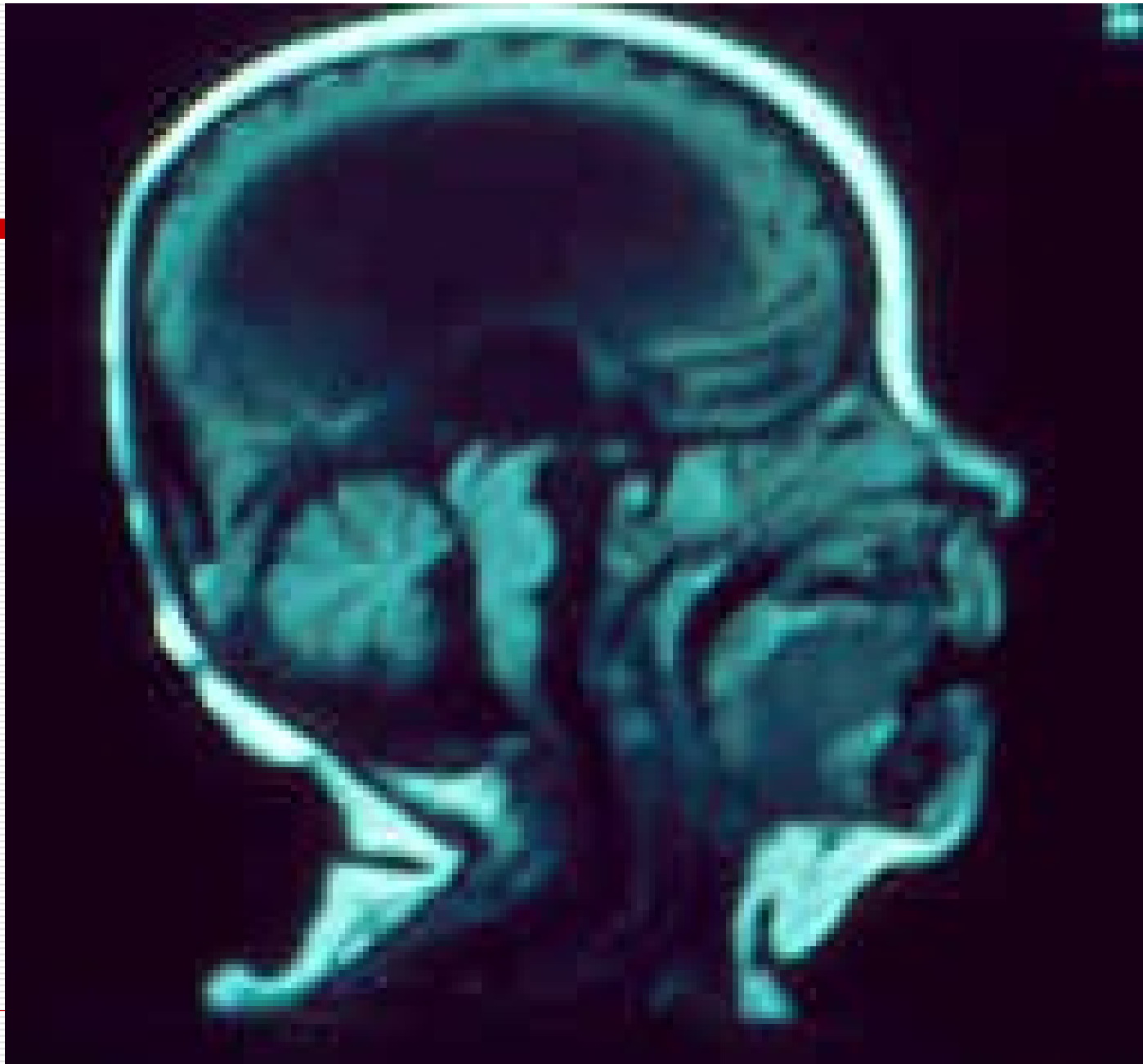
DIHS/DRESS Management

- ❑ Stop medication!!!
 - ❑ Monitor organ dysfunction
 - ❑ ?HHV titers, ? Other viral titers
 - ❑ Corticosteroids until LFTs improving
 - ❑ ? IVIG
 - ❑ Topical therapies, as indicated
-

Case 3

- You are evaluating a young girl with an extensive facial birthmark
- What evaluation should be pursued and what are you looking for?





Vascular Birthmarks

- “Older” classification; hemangioma as description for wide variety lesions w/differing etiologies, behaviors
 - Strawberry, capillary, juvenile
 - Port-wine stain

 - Doesn't allow for distinction in biological behavior between lesions
-



Vascular Birthmarks

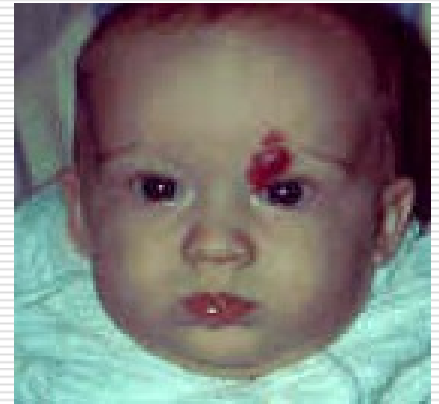
- “Newer” classification
 - Hemangioma**; rapid neonatal growth, slow involution
(hypercellular during growth; fibrosis/decreased cellularity during involution)
 - Malformation**; present @ birth, commensurate growth with child
(Normal rate endothelial cell turnover)
-



"Bummer of a birthmark, Hal."

Biological Classification of Vascular Birthmarks

□ Hemangiomas - vascular lesions marked by endothelial hyperplasia (i.e. enlarge by proliferation)



□ Malformations - lesions with normal endothelial turnover (i.e. true structural anomalies)



ISSVA Classification

TABLE I. Classification of Vascular Birthmarks

Vascular tumors

Hemangioma of infancy

Kaposiform hemangioendothelioma

Tufted angioma

Pyogenic granuloma (lobular capillary hemangioma)

Hemangiopericytoma

Vascular malformations

Simple

Capillary (port-wine stain)

Venous

Lymphatic (including “lymphangioma” and “cystic hygroma”)

Arteriovenous (AVM)

Well-defined combined malformations

Capillary-lymphatic-venous (so-called CLVM—includes most cases of Klippel Trenaunay)

Capillary-venous (includes many milder cases of Klippel Trenaunay)

Capillary-venous with arteriovenous shunting and/or fistulae (Parkes-Weber syndrome)

Cutis marmorata telangiectatica congenita

Lymphatic-venous

Most vascular syndromes are associated with vascular malformations... ***not*** with hemangiomas

Syndromes & Vascular Anomalies

□ TUMOR

Hemang Infancy

Kaposiform HE

Tufted angioma

Spindle cell HE

□ CONDITION

Hemangiomas
Lumbosacral
"Beard" distribution

Kasabach Merritt

Kasabach Merritt

Maffucci Syndrome

Syndromes & Vascular Anomalies

□ SIMPLE MALFORMATION

Capillary

Venous

□ CONDITION

Cobb

Sturge Weber

Blue-rubber bleb
nevus (Bean)
Glomuvenous

Syndromes & Vascular Anomalies

□ COMBINED MALF

Cap-Venous

Cap-Lymph-Venous

Cap-Lymph-Ven-
Art

□ CONDITION

Keratotic cut cap
malf w/cerebral
cap malf

Klippel Trenaunay
Proteus

Parkes-Weber

Vascular Birthmarks

Associated Conditions

- ❑ Kasabach-Merritt Syndrome;
platelet sequestration with
Kaposiform
hemangioendothelioma
/tufted angioma
- ❑ Sturge-Weber Syndrome;
Capillary malformation in
V1 w/ipsilateral meningeal/
cortical malformation, seizures,
glaucoma



Vascular Birthmarks

Associated Conditions

- ❑ Klippel-Trenaunay Syndrome; ipsilateral hypertrophy in assoc. with capillary, venous malformations (Parkes-Weber; AV fistula + abn)
- ❑ PHACE(S) syndrome**;
Posterior fossa malformations,
Hemangioma, **A**rterial anomalies,
Cardiac anomalies,
Eye abnormalities, **S**ternal malformations





Hemangioma Classification

□ Hemangiomas

-Focal vs Segmental

-Segmental more often associated with internal manifestations (“beard” distribution and airway involvement)

Segmental Hemangioma

- ❑ Large
- ❑ Region or territory of skin
- ❑ Often plaque-like
- ❑ Higher risk complications & structural anomalies

Arch Dermatol 2002;138:1567

Arch Dermatol 2004;140:591



PHACE(S) Syndrome

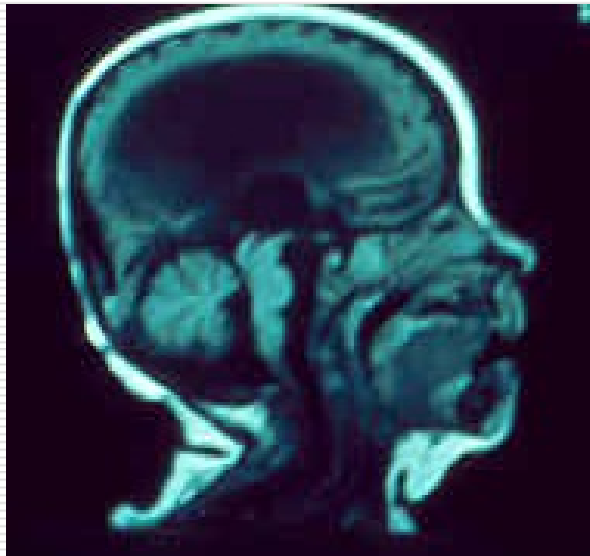


Table 2. PHACES Syndrome

Posterior fossa malformations, mostly commonly of the Dandy-Walker variant

Hemangiomas (especially large, plaque-like, facial lesions)

Arterial anomalies

Cardiac anomalies and coarctation of the aorta

Eye abnormalities

Sternal cleft and/or supraumbilical raphe

PHACE(S) Association/Stroke & Vasculopathy

TABLE 3 Neurologic Signs and Symptoms Reported With PHACES Association

Seizures

"Borderline mental development"/developmental delay

Contralateral hemiparesis

Opisthotonus

Head bobbing

Tremor

Hypotonia

Apnea

Migraine headache

PHACE(S) Association/Stroke & Vasculopathy

- ❑ Abnormal cervical/cerebral vasculature freq. in PHACE
- ❑ 4/8 with stroke reported by Burrows, et al -? Progressive vasculopathy
- ❑ 1/3 of 116 (review) and 57 % of 14 cases (single report) w/ cerebral vascular anomaly
- ❑ ? Use of antithrombotic therapy

Pediatrics 2006;117:959

PHACE(S) Association

- International PHACE registry
 - Denise Metry, M.D. (dmetry@bcm.edu)

<http://www.texaschildrenshospital.org/care-centers/Dermatology/Phace.aspx>

- PHACE genetic study
 - Dawn Siegel, M.D.
(siegeld@derm.ucsf.edu)

<http://www.texaschildrenshospital.org/care-centers/Dermatology/Phace-study.aspx>

Management of Hemangiomas

- ❑ Prevention/Reversal life- or fxn-threatening complications
 - ❑ Prevention disfigurement
 - ❑ Minimize psychological stress pt and family
 - ❑ Avoidance aggressive/potentially scarring procedures
 - ❑ Prevention/Adeq. Tx of ulceration (5-13%)
-

Warts



- ❑ Usually benign infection of skin/mucous membranes; found in 16th century mummy
- ❑ Caused by HPV; > 100 serotypes
- ❑ Some site specificity
- ❑ dsDNA virus; high rate of subclinical disease
- ❑ Virus replicates in epithelial cells

Warts

- ❑ Infection is not associated with inflammatory response
 - ❑ **Host “ignorant” of virus; leads to chronic course of disease**
 - ❑ Various theories re: absence of adequate immune response; one sugg. HPV-specific lymphs weak effectors cytokine response & recruiting additional effectors
 - ❑ Dense mononuclear response around regressing lesions predominately of Th-1 type
-

Wart Treatments

- Observation
- Tape Occlusion
- ***Destructive/Surgical***
 - Cryotherapy
 - Curettage/Desiccation
 - Laser
 - Excision
 - PDT
- ***Destructive/Chemical***
 - /Cytotoxic***
 - Salicylic acid
 - Cantharidin
 - TCA
 - Podophyllin/-toxin
 - Retinoids
 - Formalin
 - Bleomycin, 5-FU
 - Cidofovir
- ***Immunotherapies***
 - Cimetidine
 - Contactants
 - IFN
 - Imiquimod

BMJ 2002;325:1

Warts – *Home* Therapy

- ❑ After inflammation subsides from office tx (e.g. cryo, cantharidin, TCA)
 - ❑ Imiquimod to wart(s)
 - ❑ Cover with 40% salicylic acid patch
 - ❑ Apply occlusive tape (duct or similar)
 - ❑ Repeat every 3 days
 - ❑ If severe irritation/discomfort, wait 1 wk and repeat
 - ❑ Continue for one month; if persistent return for nurse visit
-

Molluscum Contagiosum

- ❑ Poxvirus (Molluscipox virus); proliferates w/in follicular epithelium and replicates w/in cytoplasm
 - ❑ Avoids host defense mechanisms
 - ❑ MCV 1-4; MCV-1 in 75%-90%
 - ❑ Humans; 2%-8% worldwide
286 cases as 1°, 2° dx in our office FY '03
 - ❑ Few reports in chickens, sparrows, pigeons, chimpanzees, kangaroos, dog, horse
-

Molluscum Contagiosum

- ❑ Incubation period 2-7 weeks; up to 6 months;
Spontaneous involution 6 months-5 years
 - ❑ No racial, gender differences
 - ❑ In children (one study cited in Pediatric News)
found age of presentation roughly equal <3 yrs
- >8 yrs
 - ❑ Most cases in immunocompetent patients
-

Molluscum Contagiosum

- ❑ Majority (63%) with < 15 lesions
- ❑ 30% with 15-30 lesions
- ❑ Most with truncal involvement (72%); almost 25% with scalp, face
- ❑ Axillae, antecubital/ popliteal fossae, crural folds



Molluscum Contagiosum

□ *To treat...*

- Risk of dissemination or transfer
 - Patient's vs parental desire
 - AAP (Removal advisable "when possible"
to prevent autoinnoculation or spread)
-

Molluscum Contagiosum

□ *Or not to treat...*

- Normal evolution
 - Treatments may be painful
 - Some treatments may scar
-

Molluscum Contagiosum

Treatments

- Observation
 - Cantharidin (shorter contact)
 - Imiquimod
 - Cimetidine
 - Tretinoin
 - TCA
 - Cidofovir
 - Curettage
 - ? Laser
 - ? KOH
-

Molluscum – *Home* Therapy

- ❑ After inflammation subsides from office tx (e.g. cryo <rare>, cantharidin)
 - ❑ Imiquimod to remaining lesions at bedtime
 - ❑ Continue until inflammation appears and stop
 - ❑ Return for nurse visit if still present in 4 weeks
-

Imiquimod PK/Safety

- Open label; 2-12 yrs
-22/30 enrolled
- MC \geq 10% BSA
- Imiquimod applied 3x/wk
- Serum levels after 2, 4, 8 hrs and final

Imiquimod PK/Safety

- Application site reactions; 10/22 (45%)
 - Higher levels in 2-5 y/o vs 6-12 y/o
 - ≤ 1 ng/ml
 - highest level seen below that seen after 100 mg PO (adults) w/o IFN- α
-