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

Keeping Central Texas Children Well
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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
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

<table>
<thead>
<tr>
<th>TUMOR</th>
<th>CONDITION</th>
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<tbody>
<tr>
<td>Hemang Infancy</td>
<td>Hemangiomatosis</td>
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<tr>
<td></td>
<td>Lumbosacral “Beard” distribution</td>
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<tr>
<td>Kaposiform HE</td>
<td>Kasabach Merritt</td>
</tr>
<tr>
<td>Tufted angioma</td>
<td>Kasabach Merritt</td>
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<tr>
<td>Spindle cell HE</td>
<td>Maffucci Syndrome</td>
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</tbody>
</table>
Syndromes & Vascular Anomalies

- SIMPLE MALFORMATION
  - Capillary
  - Venous

- CONDITION
  - Cobb
  - Sturge Weber
  - Blue-rubber bleb nevus (Bean)
  - Glomuvenous
## Syndromes & Vascular Anomalies

<table>
<thead>
<tr>
<th>COMBINED MALF</th>
<th>CONDITION</th>
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<tbody>
<tr>
<td>Cap-Venous</td>
<td>Keratotic cut cap malf w/cerebral cap malf</td>
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<tr>
<td>Cap-Lymph-Venous</td>
<td>Klippel Trenaunay Proteus</td>
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<tr>
<td>Cap-Lymph-Ven-Art</td>
<td>Parkes-Weber</td>
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</tbody>
</table>
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 + abo

- PHACE(S) syndrome**: Posterior fossa malformations, Hemangioma, Arterial anomalies, Cardiac anomalies, Eye abnormalities, Sternal malformations
Hemangioma Classification

- 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
<table>
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<tr>
<th>TABLE 3</th>
<th>Neurologic Signs and Symptoms Reported With PHACES Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizures</td>
<td><em>“Borderline mental development”/developmental delay</em></td>
</tr>
<tr>
<td>Contralateral hemiparesis</td>
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<tr>
<td>Opisthotonus</td>
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<td>Head bobbing</td>
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<td>Tremor</td>
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<td>Hypotonia</td>
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<tr>
<td>Apnea</td>
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<td>Migraine headache</td>
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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/carecenters/Dermatology/Phace.aspx

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

- Risk of dissemination or transfer
- Patient’s vs parental desire
- AAP (Removal advisable “when possible” to prevent autoinnoculation or spread)
Molluscum Contagiosum

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

Or not to treat...
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 ≥ 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