Grand Rounds in Dermatology

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Baylor College of Medicine

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Disclosures

- I have no relevant disclosures
- Off label discussion of medications will be discussed

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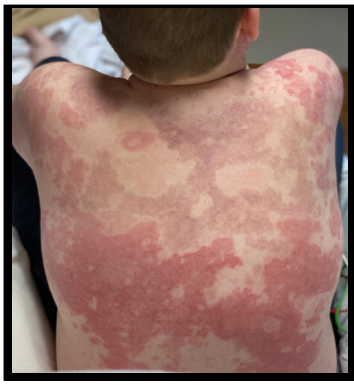
Case

3



- 11-year-old boy with no notable past medical history
- 6-week history of intermittent "prickling" rash
- ROS: Fevers, fatigue, anxiety, weight loss, photophobia, oral ulcers, chest pain, shortness of breath, nausea, vomiting, diarrhea, myalgias and arthralgias

Medications: none

Family medical history: no autoimmune disease

Social history: no pets

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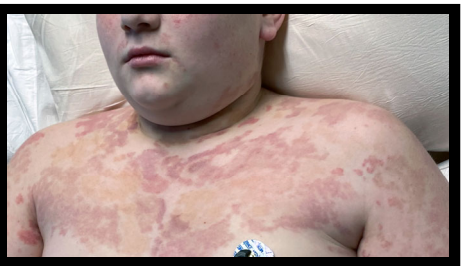
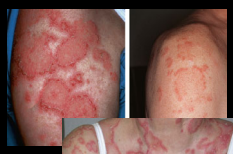
Physical Exam

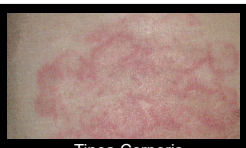


- Coalescing, annular, erythematous and dusky patches
- Bilateral conjunctival injection
- Tachypneic
- Anxious

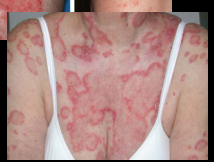
5

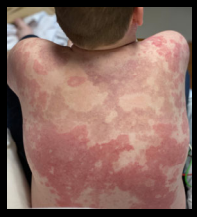
DDx





Tinea Corporis





Subacute Cutaneous Lupus Erythematosus

Dermatology, 3rd edition. Bolognia, Jorizzo, and Schaffer, 2012
V. Werth. Dermatology Advisor.

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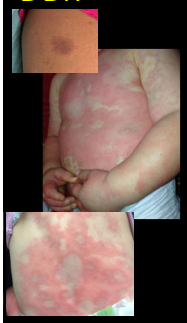
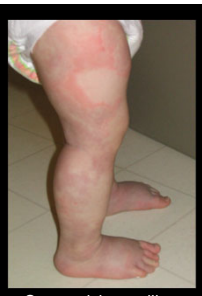
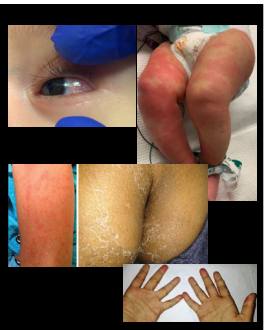
DDx





Serum sickness like reaction



Kawasaki disease

Urticaria Multiforme

Jones VG, et al. Hosp Pediatr. 2020
Gupta A, Singh S. Indian Dermatol Online J 2016;7:461-70

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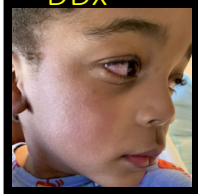
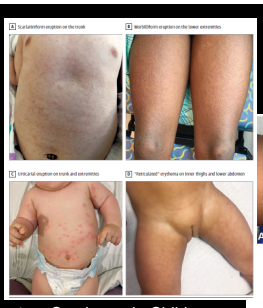
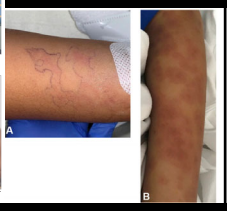
DDx







Multisystem Inflammatory Syndrome in Children

Rekhtmanet al. J Am Acad Dermatol 2021;84:408-14
Young TK et al. JAMA Dermatol. 2021 Feb 1;157(2):207-212.

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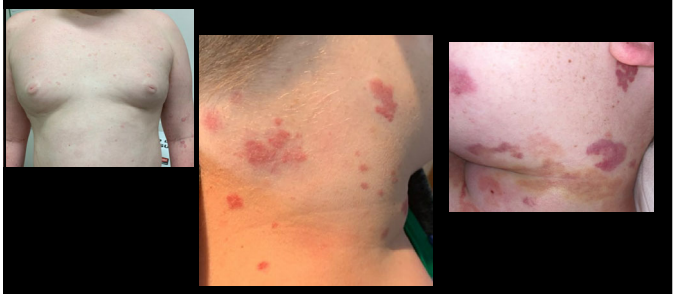
Evolution of skin lesions



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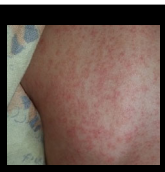
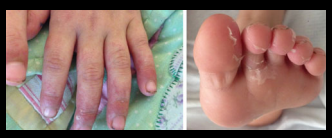
Additional History

- Accidental mercury exposure

DDx



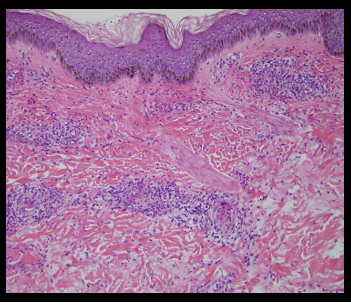


Mercury toxicity

Lai, et al. Dermatology Online Journal 22 (3): 7

10

Punch biopsy: perivascular neutrophilic infiltrate with vascular fibrin deposition consistent with leukocytoclastic vasculitis (LCV)



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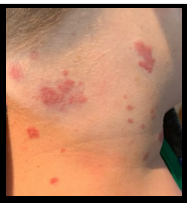

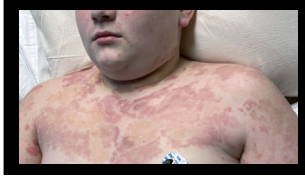

Laboratory Findings & Imaging

- Negative COVID PCR and antibody testing
- blood mercury (72 ug/L, normal <=10.0 ug/L)
- urine mercury (>80 ug/L, normal <=5.0 ug/L)
- ANA 1:1280
- Leukopenia
- Thrombocytopenia
- Transaminitis
- Coombs positive hemolytic anemia
- Anti-phospholipid antibodies
- Proteinuria
- Bilateral pleural effusions and pericardial effusion
- Low C3/C4
- Low C1q
- Biopsy: leukocytoclastic vasculitis

Hypocomplementemic Urticarial Vasculitis

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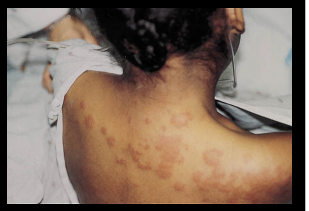
Hypocomplementemic Urticarial Vasculitis (HUV)

- Associated with renal, pulmonary, musculoskeletal, and GI involvement
- Uncommon diagnosis
- **Low C1q** is the most sensitive marker
- In a recent study of 54 children with HUV, all were diagnosed with Systemic Lupus Erythematousus (SLE) at presentation or developed SLE within a range of 1-24 months



DeAmicis T, et al. JAAD 2002;47(5):S273-S274.

Al Musalhi B, et al. J Am Acad Dermatol. 2020

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SLICC criteria for SLE (7 criteria and + ANA)

Requirements: ≥ 4 criteria (at least 1 clinical and 1 laboratory criteria)
OR biopsy-proven lupus nephritis with positive ANA or Anti-DNA

Clinical Criteria	Immunologic Criteria
1. Acute Cutaneous Lupus*	1. ANA
2. Chronic Cutaneous Lupus*	2. Anti-DNA
3. Oral or nasal ulcers *	3. Anti-Sm
4. Non-scarring alopecia	4. Antiphospholipid Ab *
5. Arthritis *	5. Low complement (C3, C4, CH50)
6. Serositis *	6. Direct Coombs' test (do not count in the presence of hemolytic anemia)
7. Renal *	
8. Neurologic *	
9. Hemolytic anemia	
10. Leukopenia *	
11. Thrombocytopenia (<100,000/mm³)	

†SLICC: Systemic Lupus International Collaborating Clinics

ACR/EULAR criteria for SLE: + ANA, serositis/pericarditis (6), low C3/C4 (4)=10

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Mercury Toxicity

- Home toxicology inspection revealed mercury contamination in the patient's bed
- Mercury exposure can induce or exacerbate systemic autoimmune disease or a lupus-like syndrome in genetically-susceptible strains of mice
- Mercury-exposed gold miners have a higher prevalence of ANA titers and increased autoinflammatory cytokines
- Potential elevated risk of SLE with self-reported occupational mercury exposure

Pollard KM, et al. Environ Health Perspect. 1999;107 Suppl 5:729-735
Gardner RM, et al. Environmental Research. 2010;110(4):345-354
Cooper GS, et al. J Rheumatol. 2004 Oct;31(10):1928-33
Crowe W, et al. Autoimmun Rev. 2017;16(1):72-80

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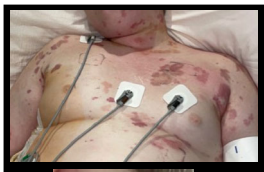

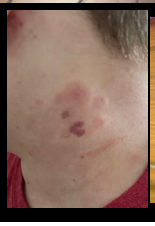

Conclusions

- HUV and SLE arising in the context of mercury poisoning in a pre-teen
- Although animal data and epidemiological studies support the possibility of mercury exposure triggering SLE/autoimmunity, no prior descriptions of this phenomenon in humans have been reported in the literature
- Stable with improving labs on hydroxychloroquine (s/p prednisone taper, IVIG x 3, mercury chelation therapy)

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Case

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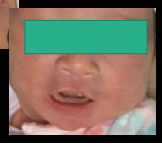
8-day-old baby



- Healthy FT infant
- Red lesion noted at birth
- Sometimes darker red sometimes lighter
- Erythematous vascular patch extending from forehead to cheek and chin, involving upper and lower eyelid

Biggest concerns on DDx?

Large facial capillary malformation
- Sturge Weber Syndrome

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Capillary malformations
GNAQ mosaic genetic mutation

- If occurs earlier in development:
  → syndromic (Sturge Weber syndrome)
- If occurs later in development:
  → Isolated facial port wine stain

Shirley MD, et al. NEJM 368: 1971-1979, 2013

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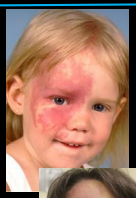
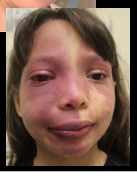
Sturge-Weber Syndrome

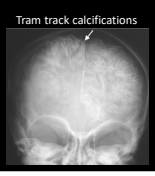
- Neuroectodermal syndrome
- Sporadic

Diagnostic criteria

- Capillary malformation on face
  - involving forehead and upper eyelid
  - If bilateral higher risk
- Glaucoma
  - Increased intraocular pressure
- Leptomeningeal vascular malformations (leptomeningeal angiomatosis)
  - May manifest as seizures







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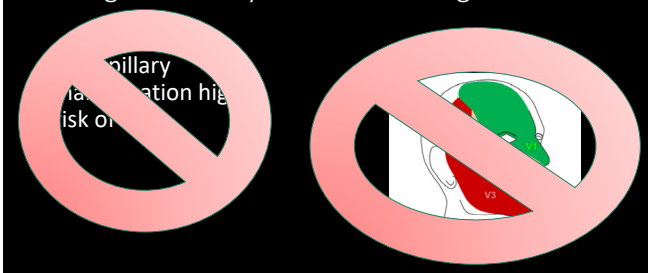
Sturge-Weber Syndrome: Old Dogma



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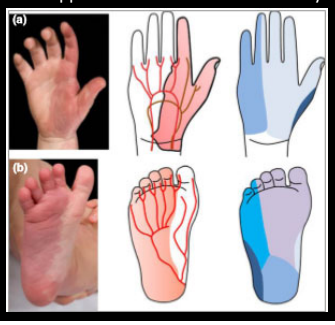
Observation:

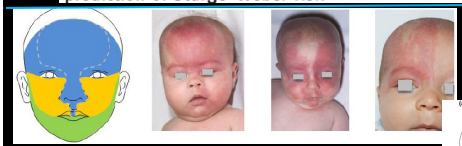
Capillary malformations on extremities appear to follow vascular anatomy and *not* nerve distributions

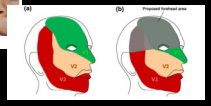


Waelchli R, et al. Br J Dermatol. 2014 Oct;171(4):861-7

22

New vascular classification of port-wine stains: improving prediction of Sturge–Weber risk





	Forehead involved	Forehead not involved	Fisher's exact P-value
Seizures	36/111	0/33	< 0·001
Abnormal neurodevelopment	42/93	0/30	< 0·001
Glaucoma	45/92	0/15	< 0·001
Abnormal magnetic resonance imaging scan	69/94	0/4	0·002

Patterns correspond to vascular development patterns and *not* to trigeminal nerve distribution

Waelchli R, et al. Br J Dermatol. 2014 Oct;171(4):861-7

Dutkiewicz AS , et al. J Am Acad Dermatol. 2015 Mar;72(3):473-80

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- Refer to pediatric neurology
- Refer to pediatric ophthalmology

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Consensus Statement for the Management and Treatment of Sturge-Weber Syndrome: Neurology, Neuroimaging, and Ophthalmology Recommendations

Sara Sabeti, BS [a], Karen L. Ball, MS [b], Sanjoy K. Bhattacharya, MTech, PhD [c], Elena Bitrian, MD [c], Lauren S. Blieden, MD [d], James D. Brandt, MD [e], Craig Burkhart, MS, MPH, MD [f], Harry T. Chugani, MD [g], Stephen J. Falchek, MD [h], Badal G. Jain, MD [i], Csaba Juhasz, MD, PhD [j], Jeffrey A. Loeb, MD, PhD [k], Aimee Luat, MD [l,k], Anna Pinto, MD, PhD [l], Eric Segal, MD [m], Jonathan Salvin, MD [n], Kristen M. Kelly, MD [a,*]

[a] Department of Dermatology, University of California, Irvine School of Medicine, Irvine, California

- Expert consensus (2021)
- Patients with high-risk facial port-wine birthmarks
  - Refer to pediatric neurologist
  - Refer to pediatric ophthalmologist (glaucoma monitoring and treatment)
- For newborns with no history of seizure or neurological symptoms, routine imaging for brain involvement is *not* recommended
- Routine follow-up neuroimaging is *not* recommended in children with stable neurocognitive symptoms

Sabeti S, et al. Pediatr Neurol. 2021 Aug;121:59-66

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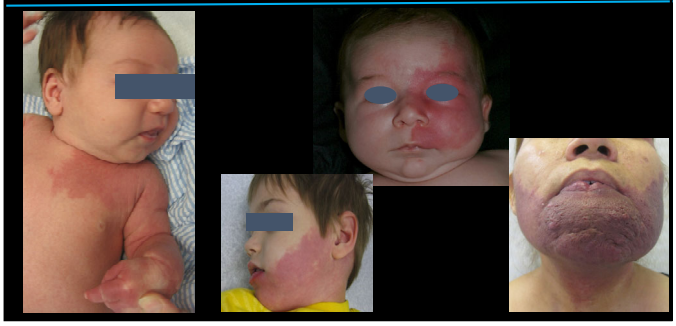
Capillary malformation : ~3/1000 newborns (port wine stain, nevus flammeus)



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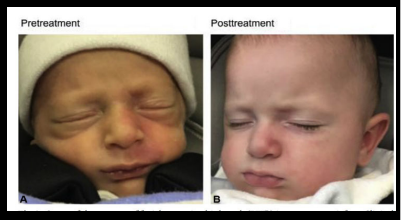
CASE REPORT

Successful treatment of facial port-wine birthmark in a premature infant

Chelsea Fidai, MD,* and Roy G. Geronemus, MD*,†
New York, New York

JAAD Case Rep. 2021 May 4;13:33-35

- Started pulsed dye laser at 2 weeks of life
- Treatment every 2 weeks x 14 treatments
- No anesthesia
- Stainless steel corneal shield used



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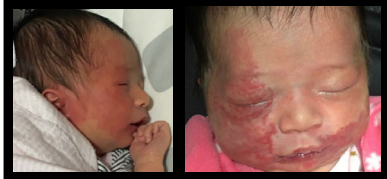
At age 13 days, baby presents at ED with difficulty breathing



Day 8 Day 13

- No fever
- Congestion x 2 days
- Respiratory distress
- Stridor

New diagnostic concern?

PHACE(s) syndrome

Airway hemangioma

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PHACE(s) syndrome

P	Posterior fossa malformations	Dandy–Walker malformation; cerebellar atrophy; hypoplasia or agenesis of various CNS structures
H	Hemangioma	Extensive facial; plaque-like; segmental; occasional airway involvement
A	Arterial anomalies	Mainly head and neck; aneurysms, anomalous branches, aberrancy, hypoplasia, stenosis, tortuosity; increased risk of AIS
C	Cardiac anomalies and aortic coarctation	Coarctation, PDA, VSD, ASD, PS, others
E	Eye abnormalities	Horner syndrome, increased retinal vascularity, microphthalmia, optic atrophy, cataracts, coloboma, others
(S)	Sternal clefting and supraumbilical abdominal raphe	Ventral midline developmental defects

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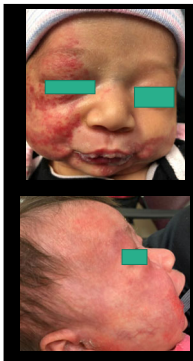
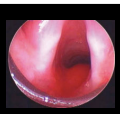


- Laryngoscopy



- MRI/A
  - Dandy Walker malformation
  - Hypoplastic right vertebral artery
  - Aberrant right subclavian artery
- Echocardiogram
  - Within normal limits
- Ophthalmologic exam
  - Within normal limits
- Treatment: escalation of oral propranolol to 2 mg/kg/day–to up to 3 mg/kg/day (if not responding well)

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Evaluating the Safety of Oral Propranolol Therapy in Patients With PHACE Syndrome

Gerilyn M. Olsen, BA[1]; Leanna M. Hansen, BS[1]; Nicole S. Stefanko, MD[1]; et al
Author Affiliations | Article Information

JAMA Dermatol. 2020;156(2):186-190. doi:10.1001/jamadermatol.2019.3839

- multicenter retrospective, n= 76
- No reports of serious adverse events (ie, stroke, transient ischemic attack, or cardiovascular events) during treatment with oral propranolol
- 38 % nonserious adverse events:
  - sleep disturbance
  - minor gastrointestinal tract symptoms
  - minor respiratory tract symptoms
- Lowest possible dose recommended; TID dosing

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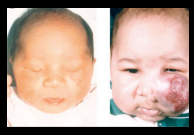
Hemangiomas at birth

Most infantile hemangiomas are NOT present at birth, sometimes a precursor lesion is present

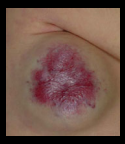
Most appear ~2 weeks of life

Proliferation is expected



Congenital hemangiomas are "fully formed" at birth

May involute or may not



Leung AKC, Lam JM, Leong KF, Hon KL. Infantile Hemangioma: An Updated Review. Curr Pediatr Rev. 2021;17(1):55-69

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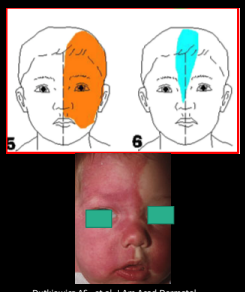
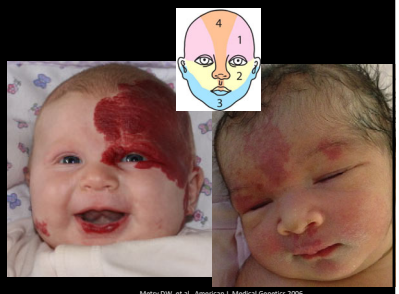
Conclusion: Sturge Weber Syndrome capillary malformation facial patterning is reminiscent of segmental patterning of hemangiomas in PHACE syndrome





Dutkiewicz AS , et al. J Am Acad Dermatol. 2015 Mar;72(3):473-80

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Conclusions: PHACE syndrome

- In the first 2 weeks of life, a segmental infantile hemangioma may mimic facial capillary malformation
- Propranolol appears to be safe in PHACE syndrome
  - Caution advised
    - Use lowest dose necessary
    - Start with dose divided three times daily

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THANK YOU

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