Is it only Skin Deep: A Conceptual and Checklist Approach

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DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

DISCLOSURES

Venthera/Biobridge: Consultant – Consulting Fees
Pfizer Chair Data Safety monitoring board – Fees
Goals of this Session

- Clinical approaches to important birthmarks/neonatal conditions
- Practical take-aways
- What would “the experts” do?
Overview: Topic Areas

- Pits and Protuberances
- Newborn Rashes
- Vascular Birthmarks
- Pigmented birthmarks
- Hamartomas

Caveat: Selected not comprehensive
The overall mental checklist

- What is the correct diagnosis
- What is the likely natural history of the condition
- Is there a risk of extra-cutaneous disease
  - If so, best approach
- Is timing important in decision-making
Tips: Birthmarks in Newborns

- Perinatal trauma (e.g. bruising, desquamation) or things called “trauma” might not be

- Hemoglobin concentration = 15g/dl versus 9g/dl age 3 mos

- Vasomotor instability (e.g. cutis marmorata, blotchiness)

- Pigment differences
  - Fairer skin at birth overall
  - Melanocytic nevi often darker at birth
Tips: It may take some time…

- Certain birthmarks need time to fully declare themselves
- Tardive onset “birthmarks”
  - Epidermal nevi (versus sebaceous)
  - Beckers/Smooth muscle hamartomas
  - Nevvoid pigmentation
For Many Birthmarks: Mosiacism Common Denominator

- **In Utero Timing:** younger $\rightarrow$ more extensive
- **Tissues affected** e.g. ectoderm, mesenchyme
- **Location of mutation:** upper body, lower body, unilateral,…
- **Specific gene functional effects:** How deleterious, which tissues are impacted
- **Genetic background of patient**
From Campbell et al. Trends in Genetics 2015; 31:382-92
Real-life examples

- Small nevus sebaceous on scalp has very low risk of CNS anomalies vs. more widespread NS
- Proteus not heritable: causative genes only can survive in mosaic state
- Large port-wine stain arm – same mutation but can’t cause Sturge-Weber syndrome
Birthmark-Cancer Genomics Connection

- Many of these are due to activating mutations in oncogenes
- Most of these are in Ras-Map-Kinase or M-Tor pathway
- These genes control growth and development
  - In developing fetus: aberrant growth and development typically not malignant transformation
  - Some have risk of malignancy
Should we be doing more gene-testing?

- 57 subjects with tissue samples using next-gen sequencing affected patients
- Using highly sensitive panel found likely pathogenic (LP) variants in 10 genes – most in m-TOR and Ras pathways
  - 86% of paraffin-embedded specimens and 72% of fresh specimens

Gene-testing Birthmarks: It depends

- Specific clinical circumstances
  - Usually not covered by insurance unless “actionable”

- Yield depends on location, specimen, gene of interest

- Options include overgrowth panels available at several laboratories, whole exome sequencing

- Cost range 2018 ~$1000 to 3000