Approach to pediatric pigmented lesions

- Clinical features
- Dermatoscopic features
- Evidence based management
- Congenital melanocytic nevi
- Acquired nevi in childhood and adolescence
- Spitz nevi
- Pediatric melanoma
Approach to Dermoscopy: Pigmented lesions

- **Global features**
  - Symmetrical or Asymmetrical
  - Color uniformity or multi-colored

- **Pigmented Patterns**
  - Reticular
  - Globular
  - Homogenous
  - Starburst

- **Local concerning features**
  - Atypical network
  - Streaks
  - Atypical dots or globules
  - Irregular blood vessels
  - Regression
  - Blue-white veil
CONGENITAL MELANOCYTIC NEVI

Current definition, clinical and dermatoscopic features, melanoma risk, and neurocutaneous melanocytosis
Congenital melanocytic nevi (CMN)

- Present at birth
- 2-3% of neonates
  - Small and medium size – common
  - Large and Giant – 1/20,000-50,000 live births
CMN Classification

- Size (projected adult size)
  - Small (<1.5 cm)
  - Medium (1.5 – 20 cm)
  - Large (>20 cm)
  - Giant (>40 cm)

- Clinical characteristics
  - Location
  - Number of satellite nevi
  - Color heterogeneity
  - Surface rugosity
  - Dermal and subcutaneous nodularity
  - Hypertrichosis

CMN enlarge in proportion to child’s growth
Final diameter is predicted by estimate
- size increase from infancy to adulthood by a factor of: 1.7 on head 2.2 on legs and 2.8 in other sites
Dynamic evolution

- Morphologic change common
- Flat, evenly pigmented patch → thin plaque → polychromatic with mammillated, rugose, verrucous or ceribriform surface
- Superimposed papules and nodules may undergo rapid growth, ulceration, black or red color, and/or regression
- While changes warrant biopsy they do not necessarily herald malignancy in this subset of pigmented lesions
Benign proliferative nodules may arise within large CMN during infancy
- Histologic features may mimic melanoma or less often an undifferentiated spindle cell neoplasm

Melanomas more likely seen in ulcerated nodules

Comparative genomic hybridization
- Proliferating nodules: whole copy aberrations +/- partial aberrations
- Melanoma: partial chromosomal gain or loss
Dermoscopy

- Globular or “cobble stoned” pattern predominates
  - Lower extremities may have reticular pattern

- Additional associated features:
  - Perifollicular hypopigmentation
  - Milia-like cysts
  - Hypertrichosis
Figure 2. Large congenital nevus with a globular pattern.
Melanoma risk

Small and medium CMN
- Less than 1% risk
- After puberty
- Arise superficially with evidence seen at DEJ
  - Periphery of nevus MC site
  - Monitor with dermoscopy

Large and Giant CMN
- 2-5% risk
- Highest risk <5 yrs of age
- Arise from deep dermis or subcutis
  - Less dermatoscopic utility
- Sites: Trunk > Head and neck
- Satellite lesions --- low to no risk
Figure 3. Congenital melanocytic nevus (CMN) with melanoma. Dermoscopy allows the observer to visualize structures in the epidermis and just below the dermoeipidermal junction (DEJ). Because melanomas developing in small CMN tend to develop at the DEJ, dermoscopy can be useful in detecting these melanomas. (A) Clinical image of a small congenital nevus. (B) Dermoscopy of one area reveals cobblestone globules, comma vessels, and hypertrichosis, all features that are seen in CMN. (C) The other area reveals an irregular network and dots. This area is a melanoma arising from a CMN.
Neurocutaneous melanosis (NCM)

- Proliferation of melanocytes in CNS in addition to skin
  - *Pia matter of meninges*

- Satellite/Numerous CMN (any size) is strongest risk factor for NCM
- No increased risk for MM

- Symptomatic → worse prognosis
  - *Lethargy, seizures, hydrocephalus, irritability, photophobia, HA, N/V*
  - *melanocytic cells obstructing flow of CSF*

**Screening:** MRI of brain and spine for large CMN in first 6-8 mo of life, especially if overly spine, repeat at puberty

**Follow up:** serial neuro exam, head circumference, and developmental assessments

[Photo: Clinics in Dermatology (2015) 33, 368–386]
Management in high risk CMN

- Prophylactic early and complete surgical removal is ideal
  - Difficult, sometimes impossible (size, deep extension to fat, fascia, muscle)
  - Staged excision (down to fascia) with flap reconstruction and tissue expansion
- Common recurrence of pigment at and around scar
- Excision of nevus does not eliminate risk of malignancy
  - Melanoma developing under skin graft has been reported
  - Primary MM may arise in CNS or other extracutaneous sites
- Curettage, dermabrasion, ablative laser (CO2, erbium:YAG), or pigment specific laser may also have cosmetic benefit
  - Ablative laser: first 1-2 months of life a/w favorable risk/benefit ratio d/t active nevomelanocytes concentrated in upper dermis (decreased scarring)
Fig. 2. Serial excision for a large congenital melanocytic nevus of scalp. (Left) Before 1st stage age 3 months. (Second from left) Following 1st excision; (center) after 2nd resection; (second from right) 3rd excision; (right) complete removal after final stage at age 16 months.

Fig. 3. Serial excision of a large congenital melanocytic nevus of the cheek. (Left) Preoperative appearance at age 1 year. (Second from left) Following 1st excision; (second from right) 2nd resection; (right) after final 3rd stage. Periorbital component to be managed with skin grafts.

Fig. 4. Serial excision of large congenital melanocytic nevus of leg. (Left) Preoperative appearance at 5 months. (Second from left) Following 1st excision; (second from right) 2nd resection; (right) linear scar after final 3rd stage.
ACQUIRED NEVI IN CHILDHOOD AND ADOLESCENCE

Clinical and dermatoscopic features, Dynamic evolution over time
Evidence based management
Acquired nevi in childhood and adolescence

- Melanocytic nevi are an almost ubiquitous finding
- Nevus counts by the end of the 1\textsuperscript{st} decade of life\textsuperscript{1}
  - Caucasian children: 15-30 nevi
  - African, Asian, or Native American: 5-10 nevi
- Number of nevi peaks in 3\textsuperscript{rd} decade\textsuperscript{1}
Acquired nevi in childhood and adolescence

- **Solid brown**
- **Solid pink**
- **Fried egg-like**
- **Tan centrally with brown rim**
- **Eccentric focus of hyperpigmentation “Bologna sign”**
Bologna sign

- Described in 1994
- Nevus with eccentric peripheral hyperpigmentation
  - may have gray-black focus of hyperpigmentation in absence of other melanoma dermatoscopic features
- Common in children, benign

Dermoscopy

- Fitzpatrick I, II
  - **Globular pattern predominates**
  - **Head, neck, upper trunk**

- Fitzpatrick III, IV
  - **Smaller nevi with reticular pattern**

- Acquired in adulthood:
  - **Reticular pattern**
Nevus development

Environmental Factors

- Intense and intermittent sun exposure
  - Influence on number and location of nevi in childhood as well as later risk of melanoma
- Higher peak nevus # at earlier age seen in children living in tropical climate
  - Peak of ~50 nevi at age 15 vs temperate location ~25 at age 25

Genetic factors

- Genetic predisposition
  - Several genes linked to nevus development (#, pattern)
  - IRF4, TERT, CDKN1B, MTAP, and PARP1
- Pigmentary phenotype
  - Light skin – higher nevus counts
  - Dark skin – predisposition to nevi on palms and soles (unrelated to sun exposure)
Two pathways in evolution

1. Formation of soft, skin-colored papules (Intradermal nevi)
   - Link to nevi with **globular pattern**
   - Favor head/neck and dorsal trunk

2. Gradual fading away via atrophy or fibrosis (regression)
   - Linked to nevi with **reticular pattern**
   - Favor extremities
Enlargement is often characterized by a **peripheral rim of brown globules**

- Up to 50% of nevi in children enlarge over 1 year period, and this is not a/w histologic atypia
  - *Changing nevi are nearly 2x as likely to have histologic evidence of atypia in adults (63%) than in children and adolescence (35%)*
Figure 4. Actively growing nevus. A peripheral globular pattern is evident. (A) Baseline and (B) 2, (C) 4, and (D) 10 month after baseline.
Management

- Change in nevus should not be used as sole criterion for excision in pediatric patient
- Nevus phenotype manifests during first decade of life
  - *Signature mole to find the “ugly duckling”*
- Atypical nevi tend to appear around puberty and continue to develop during adulthood
  - *Majority with benign behavior*
- Biopsy: avoid sampling unless lesion is large or in cosmetically sensitive area
- >50 acquired nevi and presence of clinically atypical nevi → risk for melanoma
  - *FBSE beginning at puberty*
- Lifetime risk of any particular nevi turning into melanoma 1/10,000\(^1\)
  - *More than 50% of melanomas arise de novo*
PEDIATRIC SPITZ NEVI

Clinical features, Power of dermoscopy, When to be concerned, Evidence based Management
Spitz Nevi

- Benign melanocytic neoplasm
  - *Spindled and epitheloid cells*
- <20 years of age
- Solitary pink, red, or brown papule
  - *Face or lower extremity*
- Rapid growth
- Smooth or verrucous surface
  - *Ddx: wart, pyogenic granuloma, DF, JXG, mastocytoma*
- Clinical and histopathologic overlap with melanoma

Solitary pediatric papule Ddx:
- Spitz Nevi
- JXG
- Mastocytoma

*Photo: Clinics in Dermatology (2015) 33, 368–386*
Figure 9. Spitz nevi. (A) Dermoscopic image of the starburst pattern. (B) Spitz nevus with a negative network pattern. (C) Spitz nevus with a globular pattern. (D) Pink Spitz nevus with dotted vessels.
Pigmented Spitz Reed nevi

- Starburst pattern
- Central dark, homogenous pigment surrounded by peripheral streaks (radial streaming with pseudopods)
- Multiple studies examining dermatoscopic progression:
  - *Reticular or homogenous pattern* → regress over months/years

Non-pigmented Spitz Nevi

- Dotted vessels and negative (white) network
Dynamic evolution of Spitz Nevi

Natural evolution of Spitz Nevi. Argenziano et al, Dermatology 2011;222:256-260

- Large study of non-pigmented and pigmented Spitz nevi in children and young adults (mean age 10 yrs) found that 80% (51/64) underwent involution over a mean of 25 months.
Management

- Controversial due to histopathologic overlap with melanoma
- Several groups endorse **longitudinal follow-up** with classic clinical and dermatoscopic features in children less than 12 years\(^1\)
  - Monitor q 3-6 months until stabilize
- **Postpubertal** new spitz nevi, or those with atypical features → biopsy\(^1\)
Management of Atypical spitzoid neoplasms

- Borderline histologic features indistinguishable from melanoma
- Uncertain malignant potential
- Excisional biopsy with normal margin preferred over shave biopsy for diagnostic accuracy and tx\textsuperscript{2}
  - *Careful follow up recommended*
- Positive SLNB is NOT a/w prognostic significance in any age group or for melanomas in children
- Systematic review of 303 SLNB with atypical spitzoid neoplasms
  - 119/303 (39\%) were positive, only one died at mean follow-up of 5 years
- No evidence that further lymph node dissections or adjuvant systemic therapy are efficacious for pts with positive SLNB and atypical spitzoid neoplasm
  - *Risk long term complications and lymphedema*
Additional diagnostic tools: Spitz nevus vs Melanoma

- Spitz nevi, atypical spitzoid neoplasms and spitzoid melanoma exist on a spectrum
- Comparative Genomic Hybridization
  - *Detects chromosome copy number and changes within genome*
- Fluorescent in situ hybridization
  - *Detects chromosome copy number and changes in loci*
- Both promising to distinguish between -- Spitz, atypical spitz and melanoma
  - *Limited accessibility, high cost, ?inconsistent results*

S100-A6 histologic stain for distinguishing atypical spitz vs melanoma
PEDIATRIC MELANOMA

clinical features, modified ABCDEs, dermoscopy tips, management
Pediatric Melanoma

- Melanoma extremely rare in childhood
  - ~4% arise in patients less than 20 years of age\(^2\)
  - < 0.5% of melanomas occur in patients younger than 10 years of age\(^1,2\)
- **Appear amelanotic and nodular** – presenting like a rapidly growing “bump” may mimic pyogenic granuloma, keloid or wart rather than a changing nevus\(^1\)
- Main risk factor in pediatrics: **large congenital nevus**
  - Other: *atypical spitzoid neoplasms, immune suppression, genetic syndromes* (ie. XP)
- **Atypical nevi arise after puberty** → regular follow-up esp in children with Fhx of melanoma, fair skin, and hx of sunburns
Fig 3. Amelanotic melanoma arising in a large congenital melanocytic nevus in a 17-year-old boy.
Modified ABCDEs for pediatric melanoma
Cordoro et al. JAAD 2003

- Amelanotic
- Bleeding, bump
- Color uniformity
- De novo (any diameter)
- Evolution
Pediatric vs Adult melanoma


- Higher breslow thickness at presentation
- Higher incidence of lymph node involvement
- Overall better prognosis
- Family history melanoma – important risk factor in all ages
- Genetic influence in younger children (0-9 cohort)
- Environmental exposure (sunburn >3) and greater # nevi in older children
Dermoscopy

- Atypical pigment network
- Streaks
- Negative pigment network
- Crystalline structures
- Atypical dots and globules
- Off center blotch
- Blue-white areas over raised areas
- White-scar like (regression) structures
- Atypical vascular (Milky red, dotted or twisted vessels)
- Peripheral brown structureless areas
Fig. 10. (A) Melanoma in situ arising within a congenital nevus in a 17-year-old girl. The patient had a fair skin phototype and multiple nevi. (B) Dermoscopy shows a diffuse cobblestone pattern with a focal area of blue-white structures (the latter corresponding to in situ melanoma).
Pediatric melanoma

- Treatment mainstay: EARLY DETECTION
- Suspicious lesion – Excisional biopsy with narrow margin
  - Spitz nevi after puberty or changing spitz nevi (large, ulcerated, rapid growth, nodular)
  - Solitary amelanotic or bleeding bump
- Histopathology from reliable dermatopathologist
- If confirmed → excision with wide margins
- Regular dermoscopic follow up
- Skin exams starting in puberty (high risk)
- ?Role of SLNB
- ?Role of adjuvant therapies
Take home points:

- Dermoscopy is a powerful diagnostic tool for pediatric pigmented lesions.
- All large and giant congenital melanocytic nevi should be monitored appropriately for risk of melanoma and neurocutaneous melanosis.
- All nevi have the capacity for subtle change over time, such as growth in proportion to the patient, appearing lighter or darker in color, regressing, or slowly becoming thicker in depth, over the course of years.
- Identify the patient’s “signature nevus” pattern, and use “ugly duckling sign” for lesions needing close evaluation and consideration for biopsy.
- “Classic Spitz nevus” appears in childhood, with typical history and clinical features, can be managed conservatively by clinical monitoring.
- Atypical spitz nevi (at any age) and classic spitz nevi developing during or after puberty should be excisionally biopsied.
- Pediatric-specific ABCDE melanoma criteria: amelanosis, bleeding bump, color uniformity, denovo development (diameter variability), evolution.
References

1. Schaffer J. Update on melanocytic nevi in children. Clinics in Dermatology. 2015 (33); 368-386
Thank you!