Pediatric Epidermal and Appendageal Tumors: An Update

NSUCOM/Largo Medical Center Dermatology Residency Program

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Objectives

• Review *epidermal nevi* and their associations
• Examine the implications after the diagnosis of a *nevus sebaceous*
• Discuss various etiologies and appropriate management for *melanonychia striata* in the pediatric population
Which percentage of pediatric melanonychia striata in the dermatologic literature has been reported to result in invasive melanoma?

- A. 0%
- B. 1%
- C. 6%
- D. 14%
Epidermal Nevi
What is an epidermal nevus (EN)?

- Hamartoma characterized by *hyperplasia* of epidermal structures
- Usually present at *birth*
- Classified according to their predominant component:
  - Nevus verrucosus (*keratinocytes*)
  - Nevus sebaceous (*sebocytes*)
  - Nevus comedonicus (*hair follicles*)
  - Nevus syringocystadenosus papilliferus (*apocrine glands*)

1. Image credit: Nova Southeastern University
Etiology of epidermal nevi (EN)

- Activating fibroblast growth factor receptor 3 (FGFR3) mutations have been demonstrated in some non-epidermolytic EN²
- Acanthosis nigricans, EN, and seborrheic keratoses share many histopathological features
  - FGFR3 mutations have also been implicated in these tumors
  - Acanthosis nigricans and EN have been reported in the same tumor³
- Some patients with EN develop urothelial carcinoma at an unusually early age, in which a role of FGFR3 has again been associated⁴
- PIK3CA mutations are also implicated
Favored site: *extremities*

Distributed in a “*Blaschkoid*” pattern of alternating stripes of involved and uninvolved skin

– Mosaicism

Result of *migration of skin cells* during embryogenesis
Nevus unius lateris

• Describes *extensive unilateral* epidermal nevus
  – May involve an entire half of the body

• “*Systematized epidermal nevus*” describes extensive bilateral lesions with predominant truncal involvement\(^5\)
Epidermolytic hyperkeratosis

- Upon histologic evaluation of extensive epidermal nevi, look for **epidermolytic hyperkeratosis**
- This may imply a *mosaic* disorder of *keratin* genes
- When extensive, may *transmit* these mutations to offspring\(^6\)
  - Epidermolytic ichthyosis

*Clumping of keratin filaments*
Malignancy in EN

- **Squamous cell carcinoma, adnexal carcinoma**, and as well as **basal cell carcinoma** have been reported to develop within epidermal nevi.

- The youngest recorded patient in which a squamous cell carcinoma developed was **17 years of age**

- While **linear lesions** are more likely to be associated with **neurologic abnormalities**, **round lesions** are more **tumorprone** later in life.
Inflammatory linear verrucous epidermal nevus (ILVEN)
ILVEN

• First characterized by Altman in 1971
• Presents in a Blaschkoid distribution like other keratinocytic EN, but clinically is similar to psoriasis with more erythema and intense pruritus
• Far less common than non-inflammatory EN
• Usually present in infancy\(^9-10\)
Literature somewhat controversial

Clinically, intractable pruritus can be a characteristic of ILVEN when compared to psoriasis

Histologically, ILVEN appears similar with regular psoriasiform hyperplasia

Pathophysiologically, T-cell mediated dysregulation has been implicated in ILVEN

Some reports suggest ILVEN may resemble linear psoriasis and improvement with classic topical anti-psoriatic treatments and etanercept has been shown\textsuperscript{10-14}
ILVEN systemic implications

- Associated systemic abnormalities are rarely reported
  - *No* associated neurologic defects as could potentially be seen in other epidermal nevi
- Rarely *ipsilateral skeletal abnormalities* have been reported
Epidermal Nevus Syndrome
Epidermal nevus syndrome (ENS)

- Group of neurocutaneous disorders
- Characterized by *epidermal nevi* associated with *systemic defects*\(^\text{15}\)

**Neurologic**  
**Musculoskeletal**  
**Ocular**
Classification of ENS

- Originally, Happle et al classified ENS into these clinical subtypes:
  - *Nevus comedonicus syndrome*
  - *Pigmented hairy epidermal nevus syndrome*
  - *CHILD syndrome*
  - *Proteus syndrome*
  - *Schimmelpenning syndrome*\(^{16-17}\)
Nevus Sebaceous
Nevus sebaceous

- A congenital *organoid nevus* with epithelial and adnexal components
- Typically on the *head and neck* as a yellow hairless patch
  - Enlarges at puberty
- Associated with *secondary neoplasms*, most of which are benign
Secondary neoplasms in nevus sebaceous

TRICHOBLASTOMA

Basoloid cells without retraction space and fibroblastic stroma
As many as 40 different types of secondary neoplasms have been reported in nevus sebaceous.

While basal cell carcinoma appears to be the most common malignant neoplasm associated, the most common benign neoplasm remains controversial.
Secondary neoplasms associated with nevus sebaceous of Jadassohn: A study of 707 cases

Munir H. Idriss, MD, and Dirk M. Elston, MD
New York, New York

- 707 cases
- 21.4% with secondary neoplasms
- Benign: 18.9%
- Malignant: 2.5%
- BCC
- SPAP
- Trichoblastoma

Most common

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NSU
Nevus sebaceus: a clinicopathological study of 168 cases and review of the literature

Kambiz Kamyab-Hesari¹, MD, Hassan Seirafi², MD, Shahin Jahan², MD, Nessa Aghazadeh², MD, Pardis Hejazi², MD, Arghavan Azizpour², MD, and Azadeh Goodarzi², MD
Secondary neoplasms arising from nevus sebaceus: A retrospective study of 450 cases in Taiwan

Ming-Chun HSU,¹ Jau-Yu LIAU,² Jin-Liern HONG,³ Yin CHENG,⁴ Yi-Hua LIAO,⁴ Jau-Shiuh CHEN,⁴ Yi-Shuan SHEEN,⁴ Jin-Bon HONG⁴
Management of nevus sebaceous

• Prophylactic excision is *controversial*
  – In *children*, may elect to observe clinically due to general anesthesia risks
  – As most secondary tumors arise *after puberty*, this may be an appropriate age to first consider elective excision

• Since *BCC* is the most common malignant neoplasm, new nodules presenting in a nevus sebaceous *should be biopsied* at any age
Melanonychia striata
Melanonychia striata

- Melanocytic proliferations of the *nail matrix or bed*
  - Can be congenital or acquired
- Very rare in Caucasians
  - 2.5% of black infants
  - 23% of Asian infants\(^{21}\)
- **Hutchinson’s sign** is suggestive, but not pathognomonic of melanoma
  - May be noted in benign nevi of the nails in children
Multiple pigment bands of the nails

- Addison’s or Cushing’s disease
- Peutz-Jeghers syndrome
- Pernicious anemia
- Laugier-Hunziker syndrome (only reported in adults)
- Adults with AIDS
- HIV-positive patients on zidovudine (AZT)

Single pigmented band of the nail

- Congenital or acquired melanocytic nevus
- Lentigo
- Bacterial pigment from Gram-negative organisms
- Mycotic pigment (Aspergillus, Exophiala, Alternaria)
- Subungual hematoma
- Atypical melanocytic hyperplasia
- Melanoma
Nail unit pediatric melanoma

• While 6% of adult melanomas present as melanonychia striata, only a few cases have been reported in childhood

• All childhood cases reported to date have been melanoma in situ

• These cases may not have the same biological activity as melanoma in situ in an adult$^{21}$
Worrisome features of melanonychia striata in the child

- Pigment bands broader than 3 mm
- Changing pigmentation or shape
- Associated nail dystrophy
- Hutchinson’s sign
- Non-homogenous color bands
- Blurred lateral borders
- Irregular lines that are not parallel on dermoscopy
- Rapid evolution
Majority of cases of melanonychia striata in those under 18 years of age can be managed conservatively with clinical follow-up alone.

Biopsy reserved for those cases with concerning features (e.g.: Hutchinson’s sign).

Aggressive surgery, with excision of nail matrix, reserved for cases in which melanoma cannot be excluded after expert review of clinical and histologic findings.
Take home points

• Activating fibroblast growth factor receptor 3 (FGFR3) mutations have been demonstrated in some epidermal nevi as well as acanthosis nigricans and seborrheic keratoses

• Children with extensive epidermal nevi should be monitored for neurologic and musculoskeletal defects

• Secondary neoplasms may develop around puberty in nevus sebaceous, with basal cell carcinoma being the most common malignant neoplasm

• In current literature, no cases of melanonychia striata have been reported to result in invasive melanoma in pediatric patients
Which percentage of pediatric melanonychia striata in the dermatologic literature has been reported to result in invasive melanoma?

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References

Thank you!