Pediatric Dermatology-
Pigmented Lesions

OPTI-West/Western University of Health Sciences- Silver Falls Dermatology
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Melanocyte Basic Science

• Neural crest origin
• Migrate to epidermis, dermis, leptomeninges, retina, choroid, iris, mucous membrane epithelium, inner ear, cochlea, vestibular system

• Embryology
  • First appearance at the end of the 1\textsuperscript{st} trimester
  • Able to synthesize melanin at the beginning of the 2\textsuperscript{nd} trimester
• Ratio of melanocytes to basal cells is 1:10 in skin and 1:4 in hair
• Equal numbers of melanocytes across different races
  • Type, number, size, dispersion, and degree of melanization of the melanosomes determines pigmentation
Nevus of Ota

- A.k.a. Nevus Fuscocoeeruleus Ophthalmomaxillaris
- Onset at birth (50-60%) or 2nd decade
- Larger than mongolian spot, does not typically regress spontaneously
- Often first 2 branches of trigeminal nerve
- Other involved sites include ipsilateral sclera (~66%), tympanum (55%), nasal mucosa (30%).
- ~50 cases of melanoma reported
  - Reported rates of malignant transformation, 0.5%-25% in Asian populations
- Ocular melanoma of choroid, orbit, chiasma, meninges have been observed in patients with clinical ocular hyperpigmentation.
- Acquired variation seen in primarily Chinese or Japanese adults is called Hori’s nevus
- Tx: Q-switched ruby, alexandrite, and Nd:Yag lasers
Congenital dermal melanocytosis

- AKA: Mongolian Spot
- Usually apparent at birth or within the first few weeks of life
- Regresses in >95% by age 18 years; more likely to persist in extensive or extra-sacral variants; most common in Asians and blacks
- Presents as a single or multiple, blue-gray patch(es) with indefinite borders; favors the lumbosacral area and buttocks > back
- Varies in size from a 2-20+ cm
- CALM and melanocytic nevi within Mongolian spots often have a ‘halo’ that lacks dermal melanocytes
- **DDx**: ecchymosis, child abuse, patch blue nevus, venous malformation
- Extensive lesions with phakomatosis pigmentovascularis (type 2, 4, or 5)
Nevus Fuscocaeruleus Acromiodeltoideus

• AKA: Nevus of Ito
• Bimodal age of onset:
  • 50–60% present at birth or before 1 year of age
  • 40–50% appear at or around puberty
  • All persist lifelong
• More common in Asians and African Americans; females > males
• Involves areas of skin innervated by the posterior supraclavicular and lateral brachiocutaneous nerves
• Typically unilateral
Café-au-Lait Macule (CALM)

- Light to dark brown macule or patch
- 10-20% of normal population can have a single lesion
- Generally 2-5 cm in diameter
- Conditions associated:
  - Neurofibromatosis
  - McCune-Albright syndrome (coast of Maine)
  - Legius syndrome
  - Noonan syndrome
  - LEOPARD syndrome
  - Fanconi anemia
  - Bloom syndrome
  - Ataxia telangiectasia
  - Tuberous sclerosis
  - MEN 1 and 2B
  - Piebaldism
  - More......
Ephelides

- Light brown macules in sun-exposed areas
- Onset typically within first 3 years of age
- If acquired after this, can be a marker for UV-induced damage
- Histo: NORMAL # of melanocytes, INCREASED pigment in keratinocytes
Lentigo Simplex and Oral Melanotic Macules

- Lentigo simplex
  - Common in younger patients
  - Increased numbers in childhood or puberty
  - Sometimes eruptive → lentiginosis
  - Not related to sun exposure

- Oral melanotic macules
  - Primarily in adults over 40

- Multiple lentigines seen in association with several genetic disorders:
  - LEOPARD syndrome
  - Carney complex
  - Tay syndrome
  - Pipkin syndrome
  - Cronkite-Canada syndrome
  - Bannayan-Riley Ruvalcaba syndrome
  - Cowden’s disease
  - Peutz-Jeghers syndrome
  - Laugier-Hunziker syndrome
  - More....
LEOPARD syndrome

Gene: PTPN11, AD

- Lentigines
- ECG abnormalities
- Ocular hypertelorism
- Pulmonary Stenosis
- Abnormal genitalia
- Retardation of growth
- Deafness
- *** LEOPARD Syndrome has no mucosal involvement
LEOPARD syndrome
Noonan Syndrome

AD, PTPN11

- Wide set ears
- Ulerythema ophryogenes (keratosis pilaris rubra atrophicans faciei)
- Webbed neck
- Undescended testes
- Low posterior neck hairline
- Pulmonary stenosis
- Lymphedema
- Keloid formation
- CALMs
## CARNEY Complex

### NAME
- Nevi
- Atrial myxoma
- Myxomas (myxoid tumors)
- Ephelides & Endocrine
  - Sertoli tumors
  - Psammomatous melanotic schwannomas
  - Pigmented pituitary adenomas
  - Cushingoid features

### LAMB
- Lentigines
  - Most common on lips, face, sclera and vulva.
- Atrial myxomas
  - Tumors of heart tissue, often originate in atria
  - May obstruct blood flow through the heart → fainting, shortness of breath, chest pain
- Mucocutaneous myxomas
  - Papules or nodules
  - Various anatomic sites: breasts, shoulders, oral mucosa and tongue.
- Blue nevi – can be found anywhere on body
CARNEY complex

AD inheritance

• PRKAR1A gene
• Encodes the type 1A regulatory subunit of protein kinase A
  • Cell cycle regulation, growth, and/or proliferation.
• Referral to cardiology and endocrinology
Peutz-Jeghers

AD, STK11/LKB1 gene mutation
(Encodes serine-threonine kinase tumor suppressor)

• Mucocutaneous melanotic macules
  • Onset before age 5, often fades after puberty
  • Mouth
  • Lips
  • Buccal mucosa
  • Gingiva
  • Tongue
  • Eyes
  • Palmoplantar
  • Anogenital
Peutz-Jeghers

- Hamartomatous polyps
  - Bleeding
  - Intussusception (50%)
- Increased incidence of malignancy
  - 47% mortality rate from cancer by 57 yrs of age
  - GI adenocarcinoma
    - Colorectal- 39%, Stomach- 29%
    - Colonoscopy, upper endoscopy q2-3 yrs beginning in late teens
- Breast cancer
  - Female incidence 45-50%
  - Mammogram and breast MRI yearly starting at age 25
- Pancreatic cancer
  - MRCP q1-2 years starting at age 25 to 30
- Ovarian, uterine, cervical, testicular cancer
Laugier-Hunziker Syndrome

Sporadic inheritance

• Mucocutaneous melanotic macules
  • Oral: Buccal, lip, tongue, gingiva
  • Melanonychia
    • Longitudinal
    • Half
    • Complete
  • Genital melanosis
  • Neck
  • Trunk
  • Palmplantar

• Cutaneous pigmentation may fade over time, oral pigmentation often permanent

• No increased risk of cancer

• Dx of exclusion
  • R/o Peutz-Jeghers, Addison’s disease, SLE
Bannayan-Riley Ruvalcaba

AD, PTEN mutation

• Allelic to Cowden’s syndrome
• Genital Lentigines (penile > vulvar)
• Macrocephaly
• Intestinal polyposis
• Lipomas
• Hemangiomas
• Scoliosis
• Mental retardation
Spitz Nevus

• 2 mm to >2 cm well-circumscribed, dome-shaped, red or pigmented papule or nodule
• Comprises ~1% of excised melanocytic lesions
• Typically children or young adults (<40 yrs)
• Majority are acquired, up to 7% congenital
• M/c on the head or neck
• Histologically can mimic melanoma
  • Differentiate with S100A6, Ki-67, P16
Spitz Nevus

• Pathogenesis
  • No particular etiologic factors have been identified to correspond with Spitz nevi
  • Widespread eruptive Spitz nevi have been associated with many of the same triggers as for common nevi:
    • HIV infection
    • Addison’s disease
    • Chemotherapy
    • Pregnancy
    • Puberty
    • Trauma
  • Spitz nevi with pregnancy and puberty
    • Possible hormonally-activated dormant nevi

• Atypical spitz nevus risk factors for metastasis: Ulceration, ↑ Breslow depth, atypical mitoses, H-RAS mutation

• Treatment: Full-thickness excision
Nevus Spilus (Speckled lentiginous nevus)

• Tan patch containing brown macules that develop over time
• Can contain atypical nevi and small and medium-sized congenital nevi
  • Typically larger nevus spilus
• No gender predilection
• Small risk of cutaneous melanoma
Clinical Features and Associations

- More common on the trunk and extremities
- Tan patch persists, central nevi increase over time
- Cutaneous melanoma arising within a nevus spilus has been reported
- Associated syndromes involving nevus spilus include
  - Phakomatosis pigmentovascularis types III and IV
  - Phakomatosis pigmentokeratotica
- “Speckled lentiginous nevus syndrome”
  - Ipsilateral dysesthesia, muscular weakness or hyperhidrosis in patients with nevus spilus
Halo Nevus (Sutton’s)

• Nevus with peripheral white halo

• Epidemiology
  • Most common in teenagers with multiple nevi
    • Mean age is 15 years
    • Typically appears on the back
  • No Gender predilection

• Pathogenesis
  • Development thought to involve either:
    1. An immune response against dysplastic nevus cells with tumor progression
      • This theory is not supported by histologic evaluations
    2. An autoimmune (cell-mediated and/or humoral) reaction against non-specifically altered nevomelanocytes, such as in vitiligo.
      • The now favored hypothesis
Halo Nevus (Sutton’s)

• May have underlying vitiligo (~20%)
• Can occur in the setting of melanoma (local or elsewhere)
  • More common in adults
• Can develop in association with sunburn
• Histopathology
  • Residual melanocytes with heavy infiltration of lymphocytes and histiocytes
• Management
  • Full skin examination to r/o melanoma and vitiligo
Melanoma

- Malignant tumor that arises from melanocytes
- Leading cause of skin cancer death
- Incidence rates of melanoma have increased over the past four decades by three- to five-fold
- Mortality rates began to stabilize in the early 1990s
- Rare in pediatric population
  - However, 3% of all pediatric cancers are melanoma
  - The annual transformation rate of a single mole into melanoma is estimated at $\leq 0.0005\%$ for individuals younger than 40 years.
- Misdiagnosed in pediatric population 40% of the time
- Prepubescent patients tend to have thicker lesions, can be difficult to distinguish from atypical Spitz nevi histologically
- Favorable prognosis compared to adults
  - Age is a more important prognostic factor for pediatric patients than sentinel lymph node positivity
Becker’s Nevus

- Acquired, unilateral hyperpigmentation +/- underlying smooth muscle
  - Usually involving the upper trunk of adolescent males
  - Occasionally may present earlier in life on extremities
- Etiology is unknown, but the lesion is associated with a localized increase in androgen receptors
- No malignant transformation
- Becker’s Nevus Syndrome
  - Becker’s nevus with unilateral breast and areolar hypoplasia, focal acne, pectus carinatum, limb asymmetry, and spina bifida, scoliosis
  - Evaluate for musculoskeletal dysfunction with referral as needed
- Histopathology
  - Epidermal thickening, elongation of the rete ridges, and hyperpigmentation of the basal layer with increased melanocytes
Blue Nevus

• Blue to blue–black firm papule, nodule or plaques, often with an onset during childhood or adolescence

• Aggregates of dermal, dendritic, heavily pigmented melanocytes

• Approximately 50% are found on the dorsal aspect of the hands and feet, with the face and scalp being other common sites

• Somatic activating mutations in \textit{GNA11} and \textit{GNAQ} (primarily the latter) have been detected in 65–75% of blue nevi
References


References


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