“I almost missed that melanoma”

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Hidden Melanomas

- Acral lentiginous MIS
- Curetted/Amelanotic MM
- Verrucous MM
- Blue nevus-like metastasis
- MM with lichenoid inflammation
Acral Lentiginous Melanoma
Acral Lentiginous Melanoma

- 2-3% of all melanomas, but higher proportion of melanomas in darker-skinned patients
- Weight-bearing areas of foot
- Subungual MM: great toe and thumb more common
- C-KIT mutation (up to 37%)
  - Other mutations detected *BRAF, NRAS, NF1, GNAQ*
    - *Journal of Investigative Dermatology* (2018) 138, 933e945
- In situ component can be difficult to diagnose
Acral Lentiginous Melanoma
Compare to keratinocyte nuclei
hind·sight /ˈhɪn(d)ˌsɪt/ =
woulda + shoulda + coulda
Case 1: 60 y.o. woman
lateral nail fold of thumb
Signed out as junctional dysplastic nevus, re-excision recommended
Re-excision: “scar, no tumor”
1 year later, r/o atypia
Signout: verrucoid keratosis
A closer look
No further treatment
One Year Later
Invasive vertical growth phase 1.2mm
Problems

- Early acral MIS
- Margin assessment of acral MIS
- Overdiagnosis and Underdiagnosis of acral melanocytic lesions
Evaluating acral melanocytic lesions

- Dermoscopy
  - Parallel ridge pattern $\rightarrow$ MM
  - Parallel furrow (sulcus) $\rightarrow$ nevus
Acral nevus: pigment in sulcus
Acral nevus: pigment in furrow (sulcus)
Problem

- Requires grossing the wedges of tissue perpendicular to the ridges
- Difficult if you have busy laboratory
Acral nevus
Acral nevus, MART1 stain
Histopathological diagnosis of acral lentiginous melanoma in early stages

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Evaluating acral melanocytic lesions

• Architectural features
  ❖ Nesting
    ▪ Nesting → nevus
    ▪ Single cells → both nevus and MM
  ❖ Poor cohesion and confluence → MM
  ❖ Pagetoid growth → both nevus and MM
Evaluating acral melanocytic lesions

- Cytological features: melanocytes
  - Nuclear size < keratinocyte nucleus $\Rightarrow$ benign
  - Nuclear size > 2x keratinocyte nucleus $\Rightarrow$ MM
Case 2

• 40 year old woman
• Forearm
• Rule out actinic keratosis or BCC
Actinic Keratosis?
MART-1
MART-1
MART-1, melanoma in situ
Amelanotic melanoma in situ
Case 3

• 60 year old, cheek
• Actinic keratosis vs basal cell carcinoma
In contrast

• Squamous cell carcinoma in situ
Helpful clues

- Pigment
- Intercellular bridges
- Sparing of basal layer ("eyeliner" sign)
Amelanotic MIS

- Limited data
- Most reported amelanotic MM are nodular or desmoplastic
- Data on amelanotic invasive MM suggests higher death rate because more advanced at presentation
Amelanotic MIS

- Not clinically suspected
- Most reported on sun damaged skin
- Clinically erythematous plaque
  - Actinic keratosis
  - Basal cell carcinoma
  - Dermatitis
Amelanotic

MIS

MM 0.3mm
Invisible melanoma in situ

FIGURE 17. “Invisible” melanoma (epithelioid melanoma in situ). A, Punch biopsy showing minimal pigmentation and (B) the presence of epithelioid, atypical cells within the lower part of the epidermis surmounted by parakeratosis, mimicking the picture of an actinic keratosis; and (C) staining for Melan-A shows that most cells in the lower part of the epidermis are melanocytes with prominent dendrites.
Use of immunochemistry in melanocytic lesions

- Overutilization
- Underutilization

- Insurance companies will assess our efficiency (turnaround time) and cost effectiveness

- Find happy medium
  - Don’t order 4 melanocytic markers when one will suffice
  - If unsure: order the MART (or SOX10, etc)
Case 4

A 62 year old woman presents for a scaly plaque on the nose
Pathology Report

• Shave biopsy: Squamous cell carcinoma
Next step

- Send the patient for Mohs surgery
Mohs frozen sections
Mohs Surgeon

• “This doesn’t look right to me”
• No pathologist in office
• Send Mohs tissue to dermatopathology
Pathology Report (phone call)

• Right nose: Malignant Melanoma
What happened ⎯?!!

A. First path report was wrong
B. Second path report was wrong
C. Collision tumor
D. Mohs tissue was affected by freeze artifact
Original Shave Biopsy
Permanent sections from Mohs tissue
MART-1 stain
Diagnosis

• Verrucous melanoma
• Melanoma with pseudoepitheliomatous hyperplasia
• Hyperkeratotic melanoma
Verrucous Melanoma

- Melanomas with a thickened and hyperkeratotic surface
- Clinically confused with SCC, SK, benign nevi
- Acral verrucous MM can be confused with warts and callouses

http://dx.doi.org/10.1016/j.jaad.2014.09.044
Hyperkeratotic Acral Melanoma Mimicking a Common Wart

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Carlotta Scarpa, MD, PhD
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Summary: Acral melanoma is a great pretender; anything but infrequently, it adopts clinical faces, simulating skin conditions that make the healthcare provider diagnose it as a benign disease of the palms, soles, and ungual regions. We present a case of a hyperkeratotic acral melanoma that has been misdiagnosed and that has led to an amputation of the thumb. (Plast Reconstr Surg Glob Open 2015;3:e377; doi: 10.1097/GOX.0000000000000336; Published online 17 April 2015.)

Case report

Verrucous nevoid melanoma with satellite lesions on the scalp of a young man

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International Journal of Dermatology 2015, 54, 1291–1293
Melanoma with Pseudoepithematous Hyperplasia

- Epidermal, follicular or eccrine epithelial hyperplasia
- EGFR (epidermal growth factor receptor), or other cytokines and growth factors secreted by MM
- Mimics SCC or SK
Pseudoepitheliomatous Hyperplasia

- Deep infections
- Chronic ulcer
- Lymphedema
- Halogenoderma
- Granular cell tumor
- Hypertrophic lupus and lichen planus
- *Malignant Melanoma*
DERMOGRAPHY CASE OF THE MONTH

Not all lesions with a verrucous surface are seborrheic keratoses

Caterina Longo, MD, PhD, Elvira Moscarella, MD, Simonetta Piana, MD, Aimilios Lallas, MD, Cristina Carrera, MD, Giovanni Pellacani, MD, Iris Zalaudek, MD, and Giuseppe Argenziano, MD
Reggio Emilia, Italy; Barcelona, Spain; and Graz, Austria

J Am Acad Dermatol 2014;70:e121-3

Seborrheic keratosis-like melanoma

Gabriel Salerni, MD, PhD, Carlos Alonso, MD, Mario Gorosito, MD, and Ramón Fernández-Bussy, MD
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Take home messages

• Be aware that some melanomas have verrucous surface

• “Easy” cases may really be “difficult” cases
Case 5

- 70 year old woman followed in Pigmented Lesion Clinic
- Excision of Malignant Melanoma of distal lower leg, anterior aspect
  - Level IV, SSM, 1.08mm
  - MR=1/mm²
  - No ulceration
  - TILs: non brisk
  - Negative sentinel lymph node bx (0/2)
Clinical History

• 14 mo after MM surgery, patient noted pigmentation of posterior aspect of the same leg
• Biopsy done by her local dermatologist
Special Stains

- Fontana Positive
- Prussian Blue negative
- Biopsy interpreted as blue nevus
Clinical History

• Patient seen for follow up examination in the Pigmented Lesion Clinic in 4 months later
Melanoma Scar
anterior leg
Additional Clinical History

- The patient denied any local symptoms
- She was confident that the lesions were new
- She denied use of medications that cause pigmentation (eg, minocycline)
- Felt well, Review of Systems negative
Additional Clinical History/Exam

• Approximated 10 blue macules were noted, all on the same leg (posterior)
• No lesions around the MM scar
• No other distant lesions noted
• No lymphadenopathy
• No hepatosplenomegaly
• Additional biopsies were performed
Biopsy from calf
Diagnosis?

• Eruptive blue nevi?
• Agminated blue nevi?
• Dermal melanocytosis?
• Metastatic melanoma?
• Drug pigmentation?
Help!

- Pull Primary Melanoma Slide
Melanoma anterior leg
VGP showed pigmented melanoma cells, but NOT many dendritic tumor cells
Clinical Course

• Work up for metastatic disease was negative (PET CT)
• No treatment recommended
• Follow every 3 months
16 months from presentation of first blue macule
Impression/Plan

• Stable examination
• Follow every 3 months
18 months from presentation of first blue macule
Ki-67 (MIB1) Stain
Clinical course

- This site was re-excised
- An additional site was excised and interpreted as metastatic melanoma with melanoma cells in lymphatic channels
- Since then she has developed more leg lesions and treated with limb perfusion
Blue nevus-like metastatic melanoma
Weselthier JA, White WL. Cutaneous metastasis of ocular malignant melanoma. An unusual presentation simulating blue nevi.

*Am J Dermatopathol* 1996;18:289-95

- 59 year old woman with ocular melanoma
- Blue gray macule nose
- Biopsy was reported as blue nevus
- Similar lesions develop on forehead, arm, and scalp
Weselthier JA, White WL. Cutaneous metastasis of ocular malignant melanoma. An unusual presentation simulating blue nevi.

*Am J Dermatopathol* 1996;18:289-95

- Work up for metastatic disease was negative
- 6 months later patient developed metastatic melanoma of liver and lung; subsequently died of metastatic melanoma
Weselthier JA, White WL. Cutaneous metastasis of ocular malignant melanoma. An unusual presentation simulating blue nevi.

- Compared the histological features with 20 blue nevi (included both cellular and common)

- No histologic feature was reliable in distinguishing the benign lesions from the metastases
Metastatic Melanoma to the Skin Simulating Blue Nevus


• 10 Biopsies from 3 patients
• All lesions occurs in same anatomic region as the primary tumor or near scar of a positive node dissection
• All patients had either lymph node metastases or in transit metastases
Metastatic Melanoma to the Skin Simulating Blue Nevus


• 10 blue nevus-like mets were compared with 20 common blue nevi

• Features seen in mets, not blue nevi
  ❖ Mitoses
  ❖ Dense lymphocytic infiltrate
  ❖ Epithelioid atypia
Metastatic Melanoma to the Skin Simulating Blue Nevus


• Some, but not all mets had atypical features (atypical nuclei, mitoses or a lymphocytic infiltrate)
• Some of the lesions were interpreted as blue nevi by pathologists
• Key is clinical-path correlation
Distinguishing Epithelioid Blue Nevus From Blue Nevus-like Cutaneous Melanoma Metastasis Using Fluorescence In Situ Hybridization


- 10 epithelioid blue nevi
- 10 blue nevus-like melanoma metastases
- Fluorescence in situ hybridization (FISH)
  - Probes targeting 6p25, 6q23, 11q13, Cep6
- Evaluated blindly
• 9/10 blue nevus like mets showed significant aberrations, meeting criteria for melanoma

• 0/10 epithelioid blue nevi met criteria for melanoma
Blue Nevus–Like Metastasis of a Cutaneous Melanoma Identified by Fluorescence In Situ Hybridization

Molly Campa, MD,* Mahir Patel, MD,* Pamela Aubert, MD,† Gregory Hosler, MD, PhD,‡ and Daniel Witheiler, MD§

(Am J Dermatopathol 2016;38:695–697)
Lentigo Maligna Melanoma With Local and Distant Blue Nevus-like Metastases
David S. Baird, MD,* Michael D. Ioffreda, MD,†† Klaus Helm, MD,*† Catherine G. Chung, MD,*† and Sara Ferguson, MD*
Blue Nevus-Like Melanoma Metastases

- Rare reports of melanoma metastases clinically and histologically resembling blue nevi.
- Most reported cases were initially diagnosed histologically as blue nevi

- Clinically occur in the same anatomic region as the primary tumor or near dissected lymph node metastasis
Case 6

- 65 year old man
- Upper chest
- Rule out BCC
Diagnosis

• MIS with regression
Atypical Junctional Melanocytic Proliferations in Benign Lichenoid Keratoses

Differentiating regressed melanoma from regressed lichenoid keratosis

Aegean H. Chan, Kenneth J. Shulman, Bonnie A. Lee

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Differentiating regressed melanoma from regressed lichenoid keratosis

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J Cutan Pathol. 2017;44:338–341
Methods

- 20 actively inflamed LPLK
- 12 LPLK with regression
- 15 melanomas with regression
- H&E, Melan-A, microphthalmia transcription factor (MiTF) and cytokeratin (AE1/AE3)
Results

- Complete or near complete loss of epidermal melanocytes
  - 40% of regressed melanomas
  - 8% of regressed LPLK

- Necrotic keratinocytes were seen in the epidermis in
  - 33% regressed melanomas as opposed to
  - 100% of regressed LPLK

- A dense infiltrate of melanophages in the papillary dermis was seen in 40% of regressed melanomas, a feature not seen in regressed LPLK
Conclusions

• Complete or near complete loss of melanocytes within the epidermis strongly favors a regressed melanoma.

• Necrotic epidermal keratinocytes (LK) and the presence of a dense band-like distribution of dermal melanophages (MM) can be helpful in differentiating these lesions.
Thank you!

Watch out of hidden melanomas