Important Pitfalls in the Diagnosis of Melanocytic Tumors

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Melanocytic Tumors

One of the most challenging and controversial areas in diagnostic dermatopathology

One of the most frequent causes of litigation

Important to remember: Perspective

Majority of melanocytic lesions no diagnostic challenge

• Majority of nevi are common acquired nevi
• Majority of melanomas are conventional subtypes
Melanocytic Tumors

Issues:

Clinical information (or lack thereof):
  Age, site, size, clinical presentation and level of concern

Type of biopsy: Is it representative?

Wide morphological spectrum of melanocytic lesions, both malignant and benign

Diagnostic pitfalls
Melanocytic Tumors

Age

Increasing risk for melanoma with age
Melanoma before age 10 years exceptionally rare
Melanocytic Tumors

Anatomic Site

Both nevi and melanoma may show site specific features

• Genital
• Acral
Melanocytic Tumors

Clinical presentation

Asymmetry
Irregular Borders
Colour variation
Diameter >5mm
Evolution (any change in appearance, including ulceration and bleeding)
Melanocytic Tumors

Type of biopsy
Preferably excisional or large incisional biopsy

Important to visualize peripheral edges and deeper aspects of the tumor to comment on circumscription and maturation

Is the biopsy representative?
Melanocytic Tumors
-Histological assessment-

Lesional outlines:
Circumscription, symmetry

Junctional component:
Lentiginous vs nested growth
Orderly distribution
Pagetoid spread
Cytological atypia (confluent vs scattered)
Ulceration
Melanocytic Tumors
-Histological assessment-

Dermal component:
Cytological atypia
Maturation with depth (cytological and architectural)
Mitotic activity
Fibrosis and inflammation
Pigmentation
Melanocytic Nevi
-Morphological Spectrum-

May resemble melanoma

- Architecture (symmetry, circumscription, maturation, junctional disorder, Pagetoid spread)
- Cytology (atypia, Spitzoid features)
- Mitotic activity
Morphological Spectrum of melanocytic tumors
Case

40 yo M

Pigmented lesion on the left lateral thigh for 2-3 years
Diagnosis

Deep penetrating nevus
Deep penetrating nevus

Wide age range; adolescence and early adulthood

Face, neck, extremities

Darkly pigmented to grayish symmetrical papule/nodule <1cm

Mutations in beta catenin and MAP kinase

Deep Penetrating Naevus

Concerning features:

• Melanocyte atypia
• Lack of maturation
• Scattered mitotic activity
• Deep pigmentation
• Growth along neurovascular bundles
• Extension into subcutis
Deep Penetrating Naevus

BUT:

• Circumscription
• Wedge-shaped architecture
• No severe or confluent atypia
• No atypical mitoses
• No expansile growth
• No necrosis
Clonal/inverted type-A Naevus

Naevus with focal atypical epithelioid component

• Closely related to DPN
• Similar clinical setting
Case

16 yo F
Pigmented lesion on the left buttock
Immunohistochemistry

S100 focal pos
Melan A pos
HMB45 pos
Diagnosis

Cellular blue nevus
Cellular blue nevus

Wide age range, adulthood

F>M

Wide anatomic distribution, predilection for lower back and scalp

1-2 cm heavily pigmented nodules

GNAQ/GNA11 mutations
Case

45 yo F

Large pigmented lesion on the scalp
Diagnosis

Plaque-type blue nevus
Plaque-type Blue Naevus

• Longstanding variably pigmented plaque
• Multiple cm
• Predilection for scalp
• Young adulthood

Plaque-type Blue Naevus vs Desmoplastic Melanoma

• Similar clinical setting on scalp of adults

• Significant histological overlap with deep extension

but

• no cytological atypia and areas of conventional blue naevus

• Melan A and HMB-45 positivity and weak and focal S100 expression

• GNAQ and GNA11 mutations
Case

30 yo F

Pigmented lesion on the right labium majus
Diagnosis

Pigmented epithelioid melanocytoma
Pigmented epithelioid melanocytoma

• Unusual distinctive melanocytic tumor
• Reminiscent of melanomas in grey horses
• “Animal- / Equine-type Melanoma”
• Significant morphological overlap with epithelioid blue nevus in Carney complex
• “Pigmented Epithelioid Melanocytoma”
• Loss of expression of Protein Kinase A Regulatory Subunit 1a (PRKAR1A) in sporadic PEM and EBN in patients with Carney complex

Pigmented Epithelioid Melanocytoma
Clinical Presentation

Deeply pigmented tumours
Extremities, head & neck, trunk
Mucosa, genital sites
Young adults (20-30 yrs)
Wide age range including congenital onset
M=F
Pigment Synthesising Melanoma
Clinical Behavior

Overall favourable prognosis

High rate of LN metastasis (30-50%)

Rare distant metastasis to liver

Rare documented mortality (limited follow up)

Antony FC Histopathology 2006;48:754-762
Case

40 yo F

Deeply pigmented nodular tumor on the trunk
Diagnosis

Malignant blue nevus
Malignant Blue Nevus

• Rare variant of melanoma (<100 cases)
• 40-50 yrs
• M>F (2:1)
• Head and neck (scalp) > trunk > extremities
• Darkly pigmented nodules and plaques
• ~ 2.5 cm in diameter
• H/o recent change/enlargement

Malignant Blue Nevus

Morphologically heterogeneous group

1. Melanoma arising in association with blue naevus (cellular blue > common blue > N. of Ota/Ito)

2. *De Novo*; without precursor lesion
   (melanoma showing growth pattern and cytology reminiscent of cellular blue nevus)
Malignant Blue Nevus

Prognosis

Deeply invasive tumors (median 5.5m, level V)

Overall poor prognosis:
- 40% distant metastasis
- 40% mortality

Outcome comparable to conventional melanoma using age matched controls

Breslow thickness best predictive histological feature

Martin RCW et al Cancer 2009; 115: 2949-2955
Case

18 year old male

1 year history

Leg lesion with dark veil

On methotrexate for severe bilateral panuveitis
Case

Deep Penetrating Naevus-like Melanoma in the setting of immunosupression
Case

Positive SLN biopsy and clearance

Disseminated metastases and

Death form disease 2 years after presentation
Melanocytic Tumors

Correct/best diagnosis:
• Use all available information
  Clinical data, levels, immunohistochemistry, genetics
• Awareness of morphologic spectrum and variants of nevi and melanoma
• Index of suspicion
• Ask for help
• Call if things don’t add up
• Expression of doubt/level of certainty
• Do what’s right for the patient