Practical Management of Atypical Melanocytic Lesions

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Disclosures

No relevant conflicts of interest

Relationships
Hoffmann-La Roche, Ltd.
Investigator, Consultant
Overview:
Practical Management of Atypical Melanocytic Lesions

1. Background
2. Examination of the atypical nevus patient
3. Management/biopsy
Atypical Nevi

Background:

--First described in 1978: clinicopathologic entity, which identified patients at increased risk for melanoma

- Mole larger than 5 mm
- Variegated pigmentation
- Irregular borders

Pathology features:

Architecture:
- nests bridge rete ridges
- elongated rete ridge

Cytology:
- larger, atypical cells
- larger nucleoli

Host response:
- lymphocytic infiltrate

Atypical Nevi (Dysplastic Nevi)

Background:

- Clinical term: *Atypical nevus*
- Pathologic term: *Nevus with architectural disorder*

*Dysplastic nevus*
Atypical/ Dysplastic Nevi

Significance:

Increased risk of developing MM

- General population: ~1.93% lifetime risk
- Atypical nevi: ~2-12 x risk
- Atypical Mole Syndrome:
  --10 yr cumulative risk for developing MM
  10.7% vs. 0.62% for controls

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Atypical/ Dysplastic Nevi and Risk of Melanoma

• ~50-75% of melanomas arise de novo
• Similar rate may be observed of melanoma arising in association with dysplastic nevi (21-56%) vs. common nevi (44-79%)
• Actual transformation rate of dysplastic nevus cells into melanoma: ???
Examination of the Atypical Nevus Patient
Clinical Pearls

• Look for signatures and the ugly duckling!
Clinical Pearls

• Look for signatures and the ugly duckling
• Use dermoscopy
Epiluminesence Microscopy

- Clinical exam alone: 65-80% melanomas correctly diagnosed
- With dermoscopy: 70-95%

Training necessary!

Without training, dermoscopy decreased rate of melanoma detection

- Mayer 1997
- Binder et al. 1997
Dermoscopy: Beauty and the Beast

Clinical Pearls

• Look for signatures and the ugly duckling
• Use dermoscopy
• Beware of de novo and changing lesions
Clinical Pearls

• Look for signatures and the ugly duckling
• Use dermoscopy
• Beware of de novo and changing lesions
• A picture is worth a thousand words
Total Body Digital Photography

-- can detect subtle changes and de novo lesions: detection of early melanoma
--can reduce the number of lesions excised
--can reduce patient anxiety

Canfield Scientific, Inc.


Total Body Digital Photography

-- can detect subtle changes and de novo lesions: detection of early melanoma
-- can reduce the number of lesions excised

• Reviewed records of all patients in 2 pigmented lesion clinics who received TBP and had 2 or more f/u visits over at least 2 years.
• Before PLC/TBP vs. after PLC/TBP:
  -- mean rate of biopsies: 1.62 per year vs. 0.34 per year.
  -- 3.8-fold reduction in nevus biopsies

Diagnosis

Future directions:

Further development of diagnostic devices:

-- Multispectral imaging / computer analysis
-- Confocal microscopy
-- Automated change detection
-- Optical coherence tomography
-- Teledermoscopy
-- Smartphone applications
-- Artificial intelligence
Clinical Pearls

• Look for signatures and the ugly duckling
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• Beware of de novo and changing lesions
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• Listen to the patient!
Management / Biopsy
Atypical Nevi

Education:
--significance of AN (avoid word “precancerous”)
--rationale for biopsy/excisions
--self-skin exam:
  * abcds, ugly duckling
--sun protection
--notify family members

Follow-up:
q6 or 12 mo
Decide if total body photography would be beneficial
Consider sharing care with a local pigmented lesion clinic
Atypical Nevi

When to biopsy?

--Diagnosis of atypical nevus can be made clinically
--Biopsy suspicious lesions concerning for melanoma

--Removal also option for nevi in areas difficult to monitor
Biopsy

Variable types of biopsies performed

my.webmd.com
Guidelines of care for the management of primary cutaneous melanoma

Table IV. Recommendations for biopsy

Preferred biopsy technique is narrow excisional biopsy that encompasses entire breadth of lesion with clinically negative margins to depth sufficient to ensure that lesion is not transected, which may be accomplished by elliptical or punch excision with sutures, or shave removal to depth below anticipated plane of lesion. Partial sampling (incisional biopsy) is acceptable in select clinical circumstances such as facial or acral location, low clinical suspicion or uncertainty of diagnosis, or very large lesion. Repeat biopsy is recommended if initial biopsy specimen is inadequate for diagnosis or microstaging of primary lesion.
High suspicion for melanoma: narrow excisional biopsy preferred

1-3 mm margins

2 mm margins in saucerization method: ~87% of excisional biopsies had clear pathologic margins

Partial/incisional biopsy:

- Facial or acral areas
- Very large lesions
- Low suspicion

Be aware of limitations of partial / incisional biopsy
Clinical Pearls

• Look for signatures and the ugly duckling
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• Listen to the patient!
• Excisional biopsies for lesions suspicious for melanoma are preferred / be aware of limitations of partial biopsies.
Clinical Pearls

- Look for signatures and the ugly duckling
- Use dermoscopy
- Beware of de novo and changing lesions
- A picture is worth a thousand words
- Listen to the patient!
- Excisional biopsies for lesions suspicious for melanoma are preferred / be aware of limitations of partial biopsies.
- Think about your biopsy / think ahead
Dysplastic nevi: after the biopsy

Pathology result:
--grading system is variable
dysplastic vs severely DN

Mild, mod, severely DN

Mild, mild-mod, mild-focal mod, mod-focal severe, mod-severe, severe

No guidelines on indications for reexcision
Pathology interobserver variability:

Pathologists’ diagnosis of invasive melanoma and melanocytic proliferations: observer accuracy and reproducibility study

Elmore JG et al. BMJ. 2017 Jun 28

- Skin biopsy cases (n=240), Pathologists from 10 US states were randomized to independently interpret the same set on two occasions (phases 1 and 2), at least 8 months apart

- Diagnosed in 5 classes: I (eg, nevus or mild atypia)
  - II (eg, moderate atypia)
  - III (eg, severe atypia or melanoma in situ)
  - IV (eg, pathologic stage T1a (pT1a) early invasive melanoma)
  - V (eg, ≥pT1b invasive melanoma).

- Reproducibility was assessed by intraobserver and interobserver concordance rates
Pathology interobserver variability:
Pathologists’ diagnosis of invasive melanoma and melanocytic proliferations: observer accuracy and reproducibility study
Elmore JG et al. BMJ. 2017 Jun 28

• Intraobserver concordance: highest for class I 76.7% and class V 82.6%).

• However, the intraobserver reproducibility was lower for class II (35.2%), class III (59.5%), and class IV (63.2%).

• Average interobserver concordance rates were lower, but with similar trends.

• Efforts to improve clinical practice should include using a standardized classification system, acknowledging uncertainty in pathology reports, and developing tools such as molecular markers to support pathologists’ visual assessments.
<table>
<thead>
<tr>
<th>Publication</th>
<th># DN with positive margins observed or re-excised</th>
<th>Distribution of atypia</th>
<th>Duration of follow up</th>
<th>#/% recurrence (AN)</th>
<th>#/% recurrence (MM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kmetz et al. 2009</td>
<td>26 observed</td>
<td>unstated</td>
<td>6.12 years</td>
<td>unstated</td>
<td>0</td>
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<tr>
<td>Goodson et al. 2009</td>
<td>69 observed</td>
<td>Mild: 65</td>
<td>At least 2 years</td>
<td>3-4%</td>
<td>0</td>
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<tr>
<td>Hocker et al. 2013</td>
<td>115 observed</td>
<td>Mild: 66</td>
<td>17.4 years</td>
<td>unstated</td>
<td>0</td>
</tr>
<tr>
<td>Fleming et al. 2016</td>
<td>159 observed</td>
<td>Moderate: 42 Severe: 7</td>
<td>5.5 years</td>
<td>1 (AIMP favor early MMIS)</td>
<td></td>
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<tr>
<td>Reddy et al. 2013</td>
<td>127 re-excised</td>
<td>Mild: 2</td>
<td>unstated</td>
<td>N/A</td>
<td>2/127 (1.5%) (both from mod-severe DN biopsies)</td>
</tr>
<tr>
<td>Abello-Poblete et al. 2013</td>
<td>91 re-excised</td>
<td>Mod: 75</td>
<td>2-16 weeks, majority after 4 weeks</td>
<td>N/A</td>
<td>0</td>
</tr>
<tr>
<td>Strazzula et al. 2014</td>
<td>495 re-excised</td>
<td>Mild:16</td>
<td>Unstated</td>
<td>0.2% upgraded from Mod to Severe</td>
<td>0</td>
</tr>
</tbody>
</table>

**Total** 517

**Mild:** 131
**Mod:** 47
**Severe:** 7
**?:** 26

**Total** 713

**Mild:** 18
**Mild-Mod:** 146
**Mod:** 469
**Mod-sev:** 55
**Sev:** 25
Comparison between Chicago dermatologist study and 2014 New England dermatologists survey

<table>
<thead>
<tr>
<th></th>
<th>Observe or other</th>
<th>Reexcise</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2009 Chicago positive margins</td>
<td>2014 New England positive margins</td>
</tr>
<tr>
<td>Mild</td>
<td>79%</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>21%</td>
<td>5%</td>
</tr>
<tr>
<td>Mod</td>
<td>19%</td>
<td>39%</td>
</tr>
<tr>
<td></td>
<td>81%</td>
<td>61%</td>
</tr>
<tr>
<td>Mod-Sev</td>
<td></td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>95%</td>
<td>95%</td>
</tr>
<tr>
<td>Severe</td>
<td>5%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>95%</td>
<td>100%</td>
</tr>
</tbody>
</table>


Tong L, Wu P and Kim CC (JAAD 2016)
Other recent survey studies

Management Strategies of Academic Pigmented Lesion Clinic Directors in the United States.
Nelson KC et al. JAAD Jan 2018

• Survey of pigmented lesion clinic directors in U.S.; 40 directors identified, 38 responded (95%)
• Recommended management of moderate DN with + histologic margins, no clinical residual:
  No re-excision: 43%; 1-2 mm margins: 27%; 3-4 mm margins: 21%.

A Survey Analysis on the Management of Moderately Dysplastic Nevi Among Academic Dermatologists Across the United States
Tessitore et al. JAAD May 2018

• Survey emailed to 385 members of Association of Professors Dermatology
• 131 responses (34%) showed varied responses for scenarios
• Absence of visible pigment in a positive biopsy margin (lateral, deep or deep and lateral) markedly increased the percentage of respondents who chose clinical monitoring (45%, 40%, 37% respectively)
• Mild + margins without pigment → Observation
• Moderate + margins without pigment → Observation may be reasonable, more data needed
• Severe + margins without pigment → Re-excision
• Monitor all biopsy sites for unusual regrowth

Pigmented Lesion Subcommittee
MPWG/ECOG/SWOG
Need for large-scale data to further investigate role of observation vs. re-excision of dysplastic nevi

Pigmented Lesion Subcommittee
MPWG/ECOG/SWOG
Multi-center study
Role of Observation for Excisionally Biopsied Moderately Dysplastic Nevi with Positive Histologic Margins and Risk of Development of Future Melanoma

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On behalf of the Pigmented Lesion Subcommittee, Melanoma Prevention Working Group
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# These authors contributed equally

Presented at the Society of Investigative Dermatology Annual Meeting 2018
Recurrent Pigmentation

- **Recurrent nevi**: tend to develop within 8 months with pigmentation confined to scar

- **Melanomas**: tend to recur more than 20 months after biopsy, in patients older than 30 years, and with pigmentation crossing into normal skin

Summary

Management of atypical nevus patients can be challenging

Clinical pearls:

Look for signatures and the ugly duckling

- Use dermoscopy
- Beware of de novo and changing lesions
- A picture is worth a thousand words
- Listen to the patient!
- Excisional biopsies for lesions suspicious for melanoma are preferred / be aware of limitations of partial biopsies.
- Think about your biopsy / think ahead
- Recurrent pigmentation

Dysplastic nevi with positive margins:

- Recent data on observation of dysplastic nevi with positive margins: observation may be reasonable option for excisionally biopsied mildly and moderately DN without clinical residual pigment but with + histologic margins.
- Follow all biopsy sites clinically for any unusual regrowth, educate patients.
Thank you!

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