Practical Management of Atypical Melanocytic Lesions

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AAD Forum F003, July 27, 2017, New York, NY, 9:00-11:00am
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


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: ????

Sagebiel RW. J Invest Dermatol 1993;100:322S-5S.
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
Epiluminescence 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
“Signature” Nevi
Use of Dermoscopy in US

Published survey studies:

- Noor O 2nd et al. A dermoscopy survey to assess who is using it and why it is or is not being used. Int. J. Dermatol 2009 Sept; 28(9): 951-2.
Dermoscopy: Beauty and the Beast


Thus, knowledge of these benign patterns may be helpful in identifying those melanocytic lesions that deserve further diagnostic work-up.

Melanoma, symbolized by the beast, is by definition a melanocytic lesion that deviates from one of the nine benign patterns described above.

Melanomas almost invariably display at least some degree of asymmetry of pattern, color, and structure and elicit a sense of displeasure in the viewer. In addition, most melanomas will display at least one of the following dermoscopic structures: atypical network, atypical dots and globules, streaks (radial streaming or pseudopods), off-center blotches, blue-white veil, negative pigment network, regression structures, and/or ominous vascular structures.

Strictly requiring the presence of a melanoma-specific structure, however, should not be mandatory in all cases. As dermatologists we do not practice in a vacuum; patient history, patient age, lesion location, clinical examination including examination of surrounding lesions, history of evolution of the lesion (changes observed over time), and gut feeling all play an integral part in arriving at a correct diagnosis.

Thus, prudence may dictate obtaining biopsies of melanocytic lesions that fail to conform to one of the nine benign patterns, even in the absence of any melanoma-specific structures.

Exceptions of course exist. It has been demonstrated that the specificity of dermoscopic diagnosis of melanoma ranges from 79% to 98%.

Indeed, many dysplastic nevi can be categorized into one of the nine benign patterns, obviating the need for a biopsy. However, some dysplastic nevi are dermoscopically indistinguishable from the beast (i.e., a sheep in wolf’s clothing).

Benign patterns

Malignant patterns
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 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
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!
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
When you biopsy suspicious atypical pigmented lesions, what method do you tend to use the most?

1. Incisional shave biopsy
2. Excisional scoop shave w/ 1-3 mm clear clinical margin
3. Incisional punch biopsy
4. Punch excision w/ 1-3 mm clear clinical margin
5. Elliptical excision w/ 1-3 mm clear clinical margin
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. |

From the American Academy of Dermatology, Inc.
High suspicion for melanoma: narrow excisional biopsy preferred
1-3 mm 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
- 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.
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
Think about your biopsy

- Degree of suspicion for melanoma
- Possible need for wide local excision and sentinel lymph node biopsy
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
For what level of dysplasia do you re-excise dysplastic nevi with + histologic margins?

1. ALL dysplastic nevi (mild, moderate, severe) + margins
2. ALL moderate, severe + margins
3. ALL severe + margins, SOME moderate + margins depending on patient/level of concern
4. ALL severe + margins
5. None of the above/ my pathologist does not grade
<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>% recurrences (AN)</th>
<th>% recurrences (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, Moderate: 4</td>
<td>At least 2 years</td>
<td>3-4%</td>
<td>0</td>
</tr>
<tr>
<td>Hocker et al. 2013</td>
<td>115 observed</td>
<td>Mild: 66, Moderate: 42, Severe: 7</td>
<td>17.4 years</td>
<td>unstated</td>
<td>0</td>
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<tr>
<td>Fleming et al. 2016</td>
<td>159 observed</td>
<td></td>
<td>5.5 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reddy et al. 2013</td>
<td>127 re-excised</td>
<td>Mild: 2, Mild-moderate: 9, Moderate: 52, Moderate-Severe: 55, Severe: 9</td>
<td>Unstated</td>
<td>NA</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, Severe: 16</td>
<td>2-16 weeks, majority after 4 weeks</td>
<td>N/A</td>
<td>0</td>
</tr>
<tr>
<td>Strazzulla et al. 2014</td>
<td>495 re-excised</td>
<td>Mild: 16, Mild-mod: 137, Moderate: 342</td>
<td>Unstated</td>
<td>0.2% upgraded from Mod to Severe</td>
<td>0</td>
</tr>
</tbody>
</table>

**Total**

Mild: 131
Mod: 47
Severe: 7
?: 26
Fleming et al.
JAMA Derm: 159

Mild: 18
Mild-Mod: 146
Mod: 469
Mod-sev: 55
Sev: 25

**Total** 370

**Total** 713
Clinical decision making based on histopathologic grading and margin status of dysplastic nevi

2009 Survey of 158 members of the Chicago Dermatologic Society: 101 (58%) responded

<table>
<thead>
<tr>
<th>Grading</th>
<th>Clear margins</th>
<th>Positive margins</th>
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<tbody>
<tr>
<td></td>
<td>Obs</td>
<td>Reexc</td>
</tr>
<tr>
<td>Mild</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Mod</td>
<td>91%</td>
<td>9%</td>
</tr>
<tr>
<td>Severe</td>
<td>45%</td>
<td>55%</td>
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</table>

Comparison between Chicago dermatologist study and 2014 New England dermatologists survey

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

Tong L, Wu P and Kim CC (JAAD 2016)
Pigmented Lesion Subcommittee
MPWG/ECOG/SWOG

- 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
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

• 58 yo F, h/o prior stage IB melanoma
  --history of biopsy of left thigh OSH: mod-severe DN
  --had re-excisional biopsy 3 years later left thigh: mod-severe DN, recurrent nevus extending within 0.1 mm of margin
  --pt did not agree to additional re-excision
  --clinical f/u: scar was clear of pigment
  --gap of 1.5 years lost to f/u
  --f/u 4 years after last re-excision
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

Dysplastic nevi with positive margins:
• Recent data on observation of dysplastic nevi with positive margins: small, underpowered: observation may be reasonable option for lower grade dysplastic nevi but more data needed
• Larger scale data needed
Thank you!

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