Practical Management of Atypical Melanocytic Lesions

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AAD Forum F045, March 3, 2016, Orlando, FL, 3:30-5:30 pm
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


Benign nevus

Mild dysplasia ▶ Mod dysplasia ▶ Severe dysplasia

???
Atypical/ Dysplastic Nevi and Risk of Melanoma

• ~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: ?????

Tsao et al. *Arch Dermatol* 2003; 139(3):282-2
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
Use of Dermoscopy in US

Published survey studies:

2002: 23%
2013: 94%

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

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
Clinical Pearls

• Look for signatures and the ugly duckling
• Use dermoscopy
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• 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
When you biopsy suspicious atypical pigmented lesions, what method do you tend to use the most?

1. Incisional shave biopsy: most atypical part
2. Excisional scoop shave w/ 1-3 mm clear clinical margin
3. Incisional punch biopsy: most atypical part
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**

<table>
<thead>
<tr>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred biopsy technique is narrow excisional biopsy that</td>
<td>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.</td>
</tr>
</tbody>
</table>

*From the Academy*
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
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
Atypical Nevi

Management in US: 2002

Questionnaire mailed to 1216 fellows of AAD: 456 responded

--86% of respondents intend to do total removal when performing biopsy of AN
--75% use margins of 2mm or less
--67% prefer to re-excite AN when margins positive, some use histologic atypia as criterion

Outcomes: Observation

The role of observation in the management of atypical nevi


• 55 previously biopsied atypical nevi that were not re-excised
  --26 with at least 1 involved margin; 29 with clear margins
• Followed for at least 5 years, mean 6.12 years
• No melanomas observed to arise within pre-existing atypical nevi in both groups
Dysplastic nevi with positive margins

Low rates of clinical recurrence after biopsy of benign to moderately dysplastic melanocytic nevi


- 69 dysplastic nevi with positive margins—no melanomas after 2 yr f/u
- Dysplastic nevi and benign nevi had similar rate of clinical recurrence (~3%)

Favorable long-term outcomes in patients with histologically dysplastic nevi that approach a specimen border


- 115 patients, average f/u 17.4 years. (71% followed longer than 10 years)
- 66/115 mild dysplasia
- 42/115 moderate dysplasia
- 7/115 severe dysplasia
- No patient developed melanoma or metastatic melanoma at site of biopsy
Outcomes of Surgical Excision and Association With Melanoma

Atypical (Dysplastic) Nevi
Outcomes of Surgical Excision and Association With Melanoma

Kavitha K. Reddy, MD; Michele J. Farber, MD; Jag Bhawan, MD; Roy G. Geronemus, MD; Gary S. Rogers, MD

Published online June 12, 2013.

Histologic Outcomes of Excised Moderate and Severe Dysplastic Nevi

Maria V. Abello-Poblete, MD, Lilia M. Correa-Selm, MD, Danielle Giambrone, BS, Frank Victor, MD, FAAD, and Babar K. Rao, MD, FAAD

Dermatol Surg 2013;1–6 ● DOI: 10.1111/dsu.12391

The utility of re-excising mildly and moderately dysplastic nevi: A retrospective analysis

Lauren Strazzula, BA, Priyanka Vedak, BA, Mai P. Hoang, MD, Arthur Sober, MD, Hensin Tsao, MD, PhD, and Daniela Kroshinsky, MD, MPH

(J Am Acad Dermatol 2014;71:1071-6.)
<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>
</tr>
<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>
</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>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, Severe: 16</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, Mild-moderate: 137, Moderate: 342</td>
<td>Unstated</td>
<td>0.2% upgraded from Mod to Severe</td>
<td>0</td>
</tr>
</tbody>
</table>

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

Total 211

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

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>Clear margins</th>
<th>Obs</th>
<th>Reexc</th>
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<tbody>
<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>
<thead>
<tr>
<th>Positive margins</th>
<th>Obs</th>
<th>Reexc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>79%</td>
<td>21%</td>
</tr>
<tr>
<td>Mod</td>
<td>19%</td>
<td>81%</td>
</tr>
<tr>
<td>Severe</td>
<td>5%</td>
<td>95%</td>
</tr>
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Degree of clinical concern and dysplasia affect biopsy technique and management of dysplastic nevi with positive biopsy margins: Results from a survey of New England dermatologists

Lana X. Tong, MD, MS, Peggy A. Wu, MD, and Caroline C. Kim, MD

J Am Acad Dermatol
February 2016

Total Surveyed: 620 email addresses
Total responded: 213 (34%): 189 in full, partial: 24 surveys
Comparison between Chicago dermatologist study and 2014 New England dermatologists survey

<table>
<thead>
<tr>
<th></th>
<th>Observe or other</th>
<th>Reexcise</th>
<th>New England positive margins</th>
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<tbody>
<tr>
<td></td>
<td>Chicago positive margins</td>
<td></td>
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<td>39%</td>
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<tr>
<td>Mod-Sev</td>
<td></td>
<td></td>
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<tr>
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<td>5%</td>
<td>95%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Tong L, Wu P and Kim CC (JAAD 2016)
Management of dysplastic nevi: A 14-year follow-up survey assessing practice trends among US dermatologists

Richard R. Winkelmann, DO,* and Darrell S. Rigel, MD, MS†
JA M ACAD DERMATOL December 2015

<table>
<thead>
<tr>
<th>Do you intend to do total removals when performing biopsies of DN to achieve clear margins?</th>
<th>2001 (%)</th>
<th>2015 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>86</td>
<td>69</td>
</tr>
<tr>
<td>No</td>
<td>14</td>
<td>31</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>If DN margins are positive, do you typically re-excise?</th>
<th>2001 (%)</th>
<th>2015 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>67</td>
<td>98</td>
</tr>
<tr>
<td>Observe</td>
<td>28</td>
<td>67</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Do not re-excise</td>
</tr>
</tbody>
</table>

*From the Department of Dermatology, University of New Mexico, Albuquerque, New Mexico. †From the Department of Dermatology, Stanford University, Stanford, California. Supported by the Melanoma Research Fund no. 2301722.
• 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
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
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Thank you!

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