Disclosures

No relevant conflicts of interest
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

Melanoma

???
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: ???

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
Dermoscopy: Beauty and the Beast


Melanoma, symbolized by the beast, is by definition a melanocytic lesion that deviates from one of the nine benign patterns described above (Figure 2). 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 (Figure 2).

Figure 1. Nine benign patterns representing “beauty.” Experience has shown that one rarely, if ever, will encounter a melanoma that mimics one of these benign patterns (i.e., a wolf in sheep’s clothing).

Figure 2. Melanoma (“beast”) will deviate from the nine benign patterns and will often reveal one of the eight global dermoscopic patterns shown in the figure, and at least one of eight dermoscopic structures listed in the text. Exceptions, of course, exist: some dysplastic nevi are indistinguishable from the beast (i.e., a sheep in wolf’s clothing).

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).
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

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• 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
-- Artificial intelligence
Clinical Pearls

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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:**
qu6 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
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

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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
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• 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
<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>
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<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>Moderate: 4</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>Mild: 66</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>
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<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>
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<tr>
<td>Strazzulla 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>
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</tbody>
</table>

**Total 517**

- Mild: 131
- Mod: 47
- Severe: 7
- ?: 26
- 159

Hiscox et al
147

**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

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

**Consensus Statement**

Addressing the Knowledge Gap in Clinical Recommendations for Management and Complete Excision of Clinically Atypical Nevi/Dysplastic Nevi

Pigmented Lesion Subcommitteee Consensus Statement

Caroline C. Kim, MD; Susan M. Sweeter, MD; Clara Curiel-Lewandrowski, MD; James M. Grillnik, MD, PhD; Douglas Grossman, MD, PhD; Allan C. Halpern, MD; John M. Kirkwood, MD; Sancy A. Leachman, MD, PhD; Ashfaq A. Marghoob, MD; Michael E. Ming, MD, MSCE; Kelly C. Nelson, MD; Emir Velez, PhD; Suraj S. Venna, MD; Suephy C. Chen, MD, MS

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
Risk of Subsequent Cutaneous Melanoma in Moderately Dysplastic Nevi Excisionally Biopsied but With Positive Histologic Margins

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Objective:

- To determine outcomes and risk for the development of subsequent cutaneous melanoma from moderately dysplastic nevi that had been excisionally biopsied with positive histologic margins observed for ≥ 3 years (January 1, 1990-August 31, 2014)

Design:

- Multicenter (9 US academic dermatology sites) retrospective cohort study
- Patients ≥ 18 years of age with a moderately DN excisionally biopsied with + histology margins with ≥ 3 years of clinical f/u
- Central dermatopathology review: 5 representative slide cases were reviewed per site to confirm histologic grading

Main outcomes and measures:

- Development of melanoma at 1) the same biopsy site or 2) elsewhere on the body
Results:

467 moderately DN + margins from 438 patients with a mean f/u time of 6.9 years.

- No biopsy-site melanomas developed
- 100 patients (22.8%) developed a cutaneous melanoma at a separate site
- Multivariable analysis revealed that history of cutaneous melanoma was significantly associated with the risk of subsequent melanoma at a separate site (OR 11.74; 95% CI: 5.71-24.15; p<0.001) as were 2 or more prior biopsied dysplastic nevi (OR 2.55; 95% CI, 1.23-5.28, p=0.1).

Central dermatopathology review:

- Agreement in 35 of 40 cases (87.5%)
- 3 of 40 cases upgraded in degree of atypia. Of these, 1 was interpreted as melanoma in situ. That patient remains without recurrence or evidence of melanoma after 5 years of follow-up.
Conclusions:

• Close observation with routine surveillance is a reasonable management approach for moderately dysplastic nevi (excisionally biopsied) with positive histologic margins.

• However, having 2 or more biopsies dysplastic nevi (1 of which is moderately dysplastic) appears to be associated with an increased risk for melanoma at a separate site—recommend continued surveillance.
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 lower grade dysplastic nevi but more data needed
Thank you!

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