Dysplastic Nevus
Atypical Mole...
Typical Role?

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What Should I Call You?

- Dysplastic Nevus
- Atypical Mole
- BK Mole syndrome
- Familial atypical mole syndrome
- Nevus with architectural disorder
- Nevus with atypical melanocytic hyperplasia
- Atypical melanocytic proliferation
What Do I Call You?

- Blinded study, expert dermatopathologists, utilizing previously agreed upon criteria, reviewed histologic slides of atypical melanocytic nevi

- Excellent inter-observer concordance and reproducibility
In a controlled setting where criteria are agreed
Morphologic Confusion

- Standardized criteria are not adhered to by all pathologists
- About 20% of clinically benign nevi, with no “dysplastic” features, will exhibit histologic changes, indistinguishable from classic dysplastic nevi OR
- Dysplastic nevi are not dysplastic-instead represent the common acquired *Clark’s nevus*
Terminologic Confusion

- Benign melanocytic lesions may exhibit considerable and disturbing cytologic and architectural features that taken alone, could be part of a melanoma
- Spitz nevi exhibit an alarming degree of cytologic atypia, complete with atypical mitotic figures
- Deep penetrating nevus, will exhibit atypical melanocytes, situated deep within the reticular dermis
Terminologic Confusion

- Desmoplastic melanomas may exhibit only focal or minimal cytologic atypia, easily misdiagnosed as a scar.
Histologic Confusion

- Six histologic features analyzed in 253 melanocytic nevi with different clinical appearances
  - Dimension > 5 mm
  - Lentiginous proliferation
  - Disordered nested pattern
  - Melanocytic dyskaryosis
  - Dermal lymphocytic infiltrate
  - Suprabasal melanocytes

Histologic Confusion

- Numeric value of 1 was assigned when each of the studied parameters was present and a value of 0 was assigned when each of these parameters was absent; on the basis of the final scores, nevi were divided in six different classes (classes 0-5).
- Diagnostic categories such as dysplastic nevi and common nevi seem to be inappropriate.
- Do not reflect the real histologic complexity of such lesions.
Clinical Confusion

- Fifty-eight nevi from 26 volunteer subjects were excised and examined:
  - 5 mm or less in diameter
  - Symmetric
  - Round or slightly oval
  - Uniform pigmentation
  - Distinct and regular margins
  - No erythema

- 87.8% one or more of the histologic features
  - 69% two or more present
  - 29.3% all three histologic features

- Histologic features of dysplastic nevi occur in clinically benign common acquired nevi

Who Are You?

- Phenotype of increased number of atypical nevi in melanoma-prone kindreds.
- Original biopsies of these nevi led to the designation of melanocytic dysplasia.
- By 1982, the presence of histologic dysplasia was considered sufficient for a diagnosis of the dysplastic nevus syndrome.
What Are You?

- Risk factor for melanoma
- Need careful physical examination, with emphasis on biopsy evaluation of other pigmented lesions
- Patients with multiple pigmented lesions are at definite risk for the development of melanoma
- Problem quantifying the risk
  - Case control studies have found one clinical dysplastic nevus associated with a 2 fold risk
  - 10 or more associated with a 12 fold risk.

"Doctor, I have a suspicious looking mole on my shoulder."
NIH Consensus Conference

- Architectural disorder with asymmetry
- Shoulder phenomenon (intraepidermal melanocytes extending single or in nests beyond the main dermal component)
Histopathologic Criteria

- Melanocytes
- Papillae
- Dermis
Melanocytes

- Lentiginous melanocytic hyperplasia with spindled or epithelioid cell nests aggregating in nests of variable size and forming bridges between adjacent rete ridges
- Melanocytic atypia may be present to a variable degree
- Atypical melanocytes are frequently spindle shaped
- MF infrequent
Dermal Papillae

- Subepidermal (concentric eosinophilia and/or lamellar) fibroplasia
Dermis

- Nests extend downward into the upper dermis with the long axis of the nests lie parallel to the ED interface
- Dermal lymphocytes may be present
- Inflammatory infiltrate with melanophages is common
Grading the Atypia

- **Nucleus**
  - Area
  - Variability
  - Chromatin
  - Nucleolus

- **Cytoplasm**
  - Quantity
  - Quality
## Nuclear Changes

<table>
<thead>
<tr>
<th>Degree of Atypia</th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area</td>
<td>Normal (N) 1/2-2/3 area of a basal keratinocyte</td>
<td>1.5-2N</td>
<td>&gt;2N</td>
<td>&gt;2N</td>
</tr>
<tr>
<td>Variability</td>
<td>Minimal</td>
<td>Marked</td>
<td>Marked</td>
<td>Marked</td>
</tr>
<tr>
<td>Chromatin</td>
<td>Small, regular, aggregates in finely granular homogenous background</td>
<td>Condensed, with loss of all detail</td>
<td>Attenuated, widely spaced aggregates in pale background with condensation on nucleolar membranes</td>
<td>Few, large, irregular aggregates with pale, almost empty background, and condensation on nuclear membranes</td>
</tr>
<tr>
<td>Nucleolus</td>
<td>Not visible</td>
<td>Not visible</td>
<td>Large, pale, often multiple</td>
<td>Lavender, often multiple</td>
</tr>
</tbody>
</table>
# Cytoplasmic Changes

<table>
<thead>
<tr>
<th>Degree of Atypia</th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Features</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quantity</td>
<td>Rarely visible</td>
<td>Small rim, eccentric around nucleus</td>
<td>Increased, eccentric around nucleus</td>
<td>Fully expanded around nucleus</td>
</tr>
<tr>
<td>Quality</td>
<td>Densely pink</td>
<td>Pink, pale, finely granular</td>
<td>Pink and finely granular, often bipolar staining</td>
<td></td>
</tr>
</tbody>
</table>
Conceptual Framework

- Melanocytes are neural crest derived cells.
- As melanocytes proliferate at the dermo-epidermal junction, progressive changes in architecture and cytologic atypia lead to a fibro-inflammatory host response.
- Degree of atypia can be viewed as a spectrum of changes encompassing the architecture, cytology, and host response.
- Term atypical melanocytic hyperplasia has been coined and the atypia graded with a three-tiered system.
- Overall schema is not significantly different from the other grading systems.
IPOX Help

- p53
- MIB1 (Ki67)
p53

- Positive reactivity
  - Seven (35%) metastatic MMs
  - Eight (31%) primary MMs
  - Two (7%) SNs, only one showed strong nuclear staining
  - None of the CNs

- Immunohistochemical detection of p53 protein with strong nuclear reactivity may prove to be an adjunctive tool in the histopathologic differentiation of MM from SN

Am J Dermatopathol 1995 Dec;17(6):547-50
Ki-67/p53

- Negligible Ki-67 and p53 labeling was seen in CN, SN
- Radial growth-phase SSMMs and LMMs similar to those of melanocytic nevi
- Largest proportion in NMMs, followed by SSMMs
- Ki-67 threshold index of 10% and a p53 index of 5%
  - Correctly indicated the presence of vertical growth in 75% of NMMs
  - Only 8% of radial growth phase melanomas of other types were colabeled at the same levels of reactivity for the two markers

Mod Pathol 2000 Mar;13(3):217-22
Differential Diagnosis

- Nevi arising in certain body locations
  - Elbow
  - Ear
  - Ankle
  - Genital Skin
  - Umbilicus
Summary

- Sporadic dysplastic nevus is common
- May be associated with increased risk of melanoma, especially in high-risk individuals
- Considerable histologic variability
- Ki-67/p53 may be helpful
Questions

- I know that you believe that you understood what you think I said, but I am not sure you realize that what you heard is not what I meant.

Robert McCloskey, Former State Department spokesman
References

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- Cancer 1980;46:1787-1794
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- J Am Med Assoc 1997;277:1439-1444
- Mod Pathol 1989;2:306-319