Superficial Atypical Melanocytic Proliferations

II. Lentigo Maligna Melanoma and Simulants
Maui January 2020
Superficial Atypical Melanocytic Proliferations

• RGP Melanomas
  • SSM, LMM, ALM, MLM

• Intermediate lesions
  • Dysplastic nevi, Atypical lentiginous proliferations in high CSD skin; Atypical Acral lentiginous nevi

• Superficial atypical melanocytic proliferations
  • Pagetoid plaque-like Spitz nevi; pigmented spindle cell nevus (Reed)
  • Special site nevi (genital, breast, scalp, ear, flexural, etc).

• Superficial atypical melanocytic proliferations of uncertain significance
  • Atypical/unusual/uncertain examples of all of the above
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  • Atypical/unusual/uncertain examples of all of the above
High CSD Melanomas and Simulants.

D Elder, Maui, HI Jan 2020

Lentigo maligna melanoma
Atypical lentiginous nevi/proliferations
High CSD: Lentiginous Nevi and Lentigo Maligna Melanoma and Simulant(s)

- Lentiginous Melanoma of Sun-Damaged Skin
  - LMM in situ
  - LMM invasive
  - Distinction from Dysplastic Nevi (Dysplastic Nevus-like Melanoma/Nevoid Lentigo Maligna)

- Lentiginous Nevi of the “Elderly” (i.e. CSD Skin)

- Solar (actinic) lentigo, pigmented AK, SK...
CSD Melanomas (Pathways 1-III)


SSM is commonly associated with a precursor nevus

BRAF V600E is the usual driver mutation

LMM has no easily recognized precursor (atypical lentiginous nevus of sun-damaged skin?)

NRAS, BRAF non V600E, KIT, NF1 are possible driver mutations
<table>
<thead>
<tr>
<th>High UV Pathway II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High-CSD Melanoma (LMM)</strong></td>
</tr>
<tr>
<td>Severe CSD (exposed skin, outdoor work)</td>
</tr>
<tr>
<td>High Tumor Mutation Burden (TMB)</td>
</tr>
<tr>
<td>UV signature mutations</td>
</tr>
<tr>
<td>Lentigo maligna melanoma in situ before invasive melanoma, may progress to vertical growth phase</td>
</tr>
<tr>
<td>Lentigo Maligna Melanoma: Continuous basal &quot;lentiginous&quot; proliferation of uniformly atypical melanocytes.</td>
</tr>
<tr>
<td>NRAS, BRAF ( \text{non-V600E} ), KIT, (gain of function, activated oncogenes, mutually exclusive)</td>
</tr>
<tr>
<td>NF1 (Loss of function)</td>
</tr>
<tr>
<td>TERT (promoter mutation), CDKN2A, TPS3, PTEN (Loss of function)</td>
</tr>
<tr>
<td>RAC1</td>
</tr>
</tbody>
</table>


**SSM v LMM**
- Low pigment
- Low scatter
- Low nesting
- Poor circumscription
- Thinned epidermis
- Smaller cell size
- Similar nuclear size
- Spindle > epithelioid cells
- HIGH CSD
Melanocytic tumours in chronically sun-exposed skin

Lentigo maligna melanoma

Definition
High-risk melanomas—melanomas in chronically sun-exposed skin with 1 or more of the following: naevus of compressive growth, angiosarcoma, or dermal melanocytic naevus (DMN) with or without lentigo maligna. Lentigo maligna melanomas (LMMs) are a type of high-risk melanoma characterized by lentigines in the upper dermis that may or may not extend into the subcutaneous fat. LMMs are associated with increased risk of progression to invasive melanoma.

Clinical features
Lentigo maligna melanoma is an aggressive form of melanoma that typically occurs on chronically sun-exposed skin. It is characterized by the presence of a distinct clinical feature known as the “age-related” lentigo maligna. The lesions are usually solitary, and they tend to be more common in areas of the body that are frequently exposed to sunlight, such as the face, neck, and hands.

Epidemiology
The incidence of lentigo maligna melanoma is highest in individuals who have a history of chronic sun exposure. The risk of developing this condition increases with age, and it is more common in individuals who have a fair complexion and who spend a lot of time in the sun. It is estimated that about 20% of all melanomas are associated with chronic sun exposure.

Pathology
Lentigo maligna melanoma is characterized by the presence of atypical melanocytes in the dermis. These melanocytes are typically arranged in a lentiginous pattern, and they may extend into the subcutaneous fat. The lesions are often multiple, and they tend to be more common in areas of the body that are frequently exposed to sunlight. Lentigo maligna melanoma is characterized by the presence of atypical melanocytes in the dermis. These melanocytes are typically arranged in a lentiginous pattern, and they may extend into the subcutaneous fat. The lesions are often multiple, and they tend to be more common in areas of the body that are frequently exposed to sunlight.
SSM v LMM, Summary

<table>
<thead>
<tr>
<th>Superficial Spreading Melanoma (SSM)</th>
<th>Lentigo Maligna Melanoma (LMM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Low CSD (Solar Elastosis)</td>
<td>• High CSD, High TMB</td>
</tr>
<tr>
<td>• Precursor nevus common</td>
<td>• Ill-defined precursors</td>
</tr>
<tr>
<td>• Well circumscribed</td>
<td>• Poorly circumscribed</td>
</tr>
<tr>
<td>• Often pigmented</td>
<td>• Often amelanotic</td>
</tr>
<tr>
<td>• Pagetoid scatter and nesting</td>
<td>• Lentiginous basal proliferation</td>
</tr>
<tr>
<td>• <em>BRAFV600E</em></td>
<td>• <em>NRAS, BRAF nonV600E, KIT, NF1</em></td>
</tr>
<tr>
<td>• Epithelioid or Spindle Cell VGP (nondesmoplastic)</td>
<td>• Often a desmoplastic VGP</td>
</tr>
<tr>
<td>• Better responses to targeted therapy (anti V600E)</td>
<td>• Better responses to Immune therapy (checkpoint inhibitors)</td>
</tr>
<tr>
<td>High UV</td>
<td>Pathway II</td>
</tr>
<tr>
<td>---------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td></td>
<td>High-CSD Melanoma (LMM)</td>
</tr>
<tr>
<td>? IMP</td>
<td>? IMP</td>
</tr>
<tr>
<td>? IAMP</td>
<td>? IAMP</td>
</tr>
<tr>
<td>Lentigo maligna melanoma in situ</td>
<td>Melanoma in situ</td>
</tr>
<tr>
<td>Lentigo Maligna Melanoma</td>
<td>Desmoplastic Melanoma</td>
</tr>
<tr>
<td>NRAS, BRAF non-V600E, KIT, NF1</td>
<td>NF1, ERBB2, MAP2K1, MAP3K1, BRAF, EGFR, MET,</td>
</tr>
<tr>
<td>TERT, CDKN2A, TP53, PTEN, RAC1</td>
<td>TERT, NFKBIE, NRAS PIK3CA, PTPN11</td>
</tr>
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LMM v SSM

- Low pigment
- Low scatter
- Low nesting
- Poor circumscription
- Thinned epidermis
- Smaller cell size
- Similar nuclear size
- Spindle > epithelioid cells
- HIGH CSD
Case 1

12438

F64 Lesion of back
Your Diagnosis?

Dysplastic Nevus - IAMP?
Melanoma?
Our Diagnosis

Case 1  12438

Lentigo maligna melanoma in situ
<table>
<thead>
<tr>
<th>Feature</th>
<th>Melanoma</th>
<th>Dysplastic Nevus</th>
<th>Superficial Nevus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>larger</td>
<td>intermediate</td>
<td>smaller</td>
</tr>
<tr>
<td>Symmetry</td>
<td>poor</td>
<td>good</td>
<td>good</td>
</tr>
<tr>
<td>Elastosis</td>
<td>moderate-severe</td>
<td>mild-moderate</td>
<td>minimal- mild</td>
</tr>
<tr>
<td>Rete ridges</td>
<td>irregular</td>
<td>uniformly elongated</td>
<td>uniform</td>
</tr>
<tr>
<td>Junctional Melanocytes</td>
<td>epithelioid</td>
<td>mixed (neviod /epithelioid)</td>
<td>nevoid</td>
</tr>
<tr>
<td>Poor circumscription</td>
<td>often</td>
<td>less common</td>
<td>uncommon</td>
</tr>
<tr>
<td>Distribution of Nests</td>
<td>variable, irregular</td>
<td>predominant, regular</td>
<td>predominant, regular</td>
</tr>
<tr>
<td>Distribution of Nests</td>
<td>coalescent (confluent)</td>
<td>bridging</td>
<td>discrete</td>
</tr>
<tr>
<td>Size of Nests</td>
<td>variable</td>
<td>uniform</td>
<td>uniform</td>
</tr>
<tr>
<td>Lentiginous</td>
<td>continuous</td>
<td>discontinuous</td>
<td>minimal</td>
</tr>
<tr>
<td>Pagetoid</td>
<td>high, extensive</td>
<td>low, focal, minimal</td>
<td>minimal</td>
</tr>
<tr>
<td>Nuclear atypia</td>
<td>uniform atypia, severe ( &gt; 1.5x)</td>
<td>random atypia, mild-moderate</td>
<td>minimal</td>
</tr>
<tr>
<td>Mitoses – junctional</td>
<td>about 1/3 of cases</td>
<td>almost always absent</td>
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<td>Fibroplasia</td>
<td>diffuse</td>
<td>concentric</td>
<td>minimal</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>bandlike, lichenoid</td>
<td>patchy, perivascular</td>
<td>minimal</td>
</tr>
<tr>
<td>Regression</td>
<td>frequent, extensive</td>
<td>rare, minimal</td>
<td>absent</td>
</tr>
<tr>
<td>Dermal Cells</td>
<td>uniform atypia</td>
<td>random or no atypia</td>
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<tr>
<td></td>
<td>limited maturation</td>
<td>maturation</td>
<td>maturation</td>
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<tr>
<td></td>
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A large pigmented lesion of the back in a 74-year-old man.

I called this lesion a dysplastic nevus. The clinician then calls back to inform us that this is a 2.2 cm irregular pigmented lesion. Now looking at the deepers we think this might be a “lentiginous melanoma”.
Description

- Shave biopsy of a broad lesion with a dermal component and a moderately cellular junctional component.
- Lesion is ill-defined (poorly circumscribed) at each periphery, with features overlapping with those of actinic lentigo.
- Subtle increase of melanocytes along the dermal-epidermal junction, with mild to moderate but relatively uniform cytologic atypia.
- Pagetoid scatter is minimal.
- Focally there are elongated rete ridges, overlapping with features of dysplastic nevus, however these changes are focal within the lesion rather than being symmetrically distributed at shoulders adjacent to a dermal component.
Lentiginous nevus versus lentiginous melanoma

- Poorly circumscribed at each periphery
• Junctional IAMP
• Patchy lymphocytic infiltrate
• Solar elastosis
Your Diagnosis?

Melanoma?
Nevus?
### Criteria for Melanoma vs. Nevi

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**Diagnosis. Case 2, M74**

Skin, mid back: Superficial atypical melanocytic proliferation of uncertain significance, most consistent with melanoma in situ, lentiginous type (nevus lentigo maligna), versus atypical lentiginous nevus of the elderly, see comment.

(i.e. “SAMPUS”)
Diagnosis. Case 2, M74

• Overall Comment.
  • There are overlapping features among atypical actinic lentigines, lentiginous junctional nevi with and without atypia, and lentiginous or “nevoid” lentigo maligna.
  • Lesions in a high CSD environment must be interpreted with circumspection.
  • Overdiagnosis should be avoided as even atypical lentiginous junctional nevi of the elderly seem to be biologically low grade (non-metastasizing but perhaps locally recurring potential).
  • It is judicious to completely excise these lesions in order to be sure that they have been completely examined histologically and also to minimize any possibility of local persistence, recurrence or future progression.
LENTINGINOUS DYSPLASTIC NAEVI IN THE ELDERLY: A POTENTIAL PRECURSOR FOR MALIGNANT MELANOMA

- Australas J. Dermatol 1991; 32: 27-37 •
- STEVE KOSSARD, CHRIS COMMENS, MICHAEL SYMONS AND JOHN DOYLE
- Sydney

SUMMARY
- Seventy-seven skin biopsies diagnosed histologically as lentiginous junctional naevi from individuals aged over 60 years were reviewed.
- Seventy-three specimens showed a primarily nested pattern with disordered architecture concentrated within the rete ridges conforming to the pathology of a lentiginous dysplastic naevus.
- In 28 biopsies this was combined with a melanoma in situ. The latter was reflected by a focal loss of the rete ridge system, confluent melanocytic hyperplasia and single cell invasion of the epidermis by atypical melanocytes.
- Four biopsies showed lentiginous junctional naevi with only isolated naevus cell nests without a disordered architecture or cellular atypia.

- The pathological diagnosis of dysplastic lentiginous naevi in the elderly needs to be recognised as having a high association of melanoma-in-situ.
Atypical lentiginous junctional naevi of the elderly and melanoma.


- Atypical lentiginous junctional naevi may be seen as isolated lesions and may merge with lesions that are indistinguishable from lentigo maligna.

- The predominant site distribution of such lesions on the trunk and limbs and the presence of a nested naevoid pattern on biopsy differs from classical lentigo maligna, which develops mainly on the head and neck.

- Atypical lentiginous junctional naevi of the elderly may evolve to lentigo maligna and in some cases to small cell (naevoid) melanomas.

- Such lesions have been previously classified as dysplastic naevi, atypical melanocytic hyperplasia, atypical melanocytic proliferation, atypical lentiginous melanocytic proliferation or premalignant melanosis.

- The current definition of lentigo maligna appears too narrow and the pathway to lentigo maligna in the elderly skin may include a naevoid subset.
Nevoid Lentigo Maligna/Lentiginous Melanoma
(Lentiginous Nevus)

• Clinical diagnosis may vary
  • e.g. lentigo maligna, atypical nevus, pigmented basal cell carcinoma, seborrheic keratosis and lentigo.

• Biopsies may mimic junctional nevus or dysplastic nevus, at least focally
  • Lentiginous proliferation of melanocytes at the dermo-epidermal junction both as single cells and as small nests with areas of confluent growth, extending to the edges of the biopsy.
  • Rete ridges maintained
  • Pagetoid spread of melanocytes was not prominent in H&E-stained sections.

• Diagnosis of melanoma more easily recognized in the complete excision specimens; similar atypical melanocytic proliferation occurring over a broad area flanking the prior biopsy sites.

• Stains for MITF and Mart-1 highlight continuous basal melanocytic proliferation as well as foci of pagetoid scatter.
Lentiginous Melanoma
King, Page, Googe, Mihm. Mod Pathol 2005

• Initial biopsies mimicked lentiginous nevus or dysplastic nevus
• Lentiginous proliferation of melanocytes at DEJ both as single cells and as small nests with areas of confluent growth, extending to the edges of the biopsy.
• Retiform epidermis was maintained and pagetoid spread of melanocytes was not prominent in H&E sections.

• Immunohistochemical stains for MITF and Mart-1 highlighted the extent of the basalar melanocytic proliferation as well as foci of pagetoid spread by melanocytes.

• UNCERTAINTY IS COMMON!
• PROGNOSIS IS GOOD IF LESION IS SUPERFICIAL
• IMPORTANT TO COMPLETELY EXCISE
  • FOR FULL EXAMINATION AND TO MINIMIZE ANY POTENTIAL FOR LOCAL PERSISTENCE, RECURRENCE AND PROGRESSION
Case 3.

Part 2-3. 14474

Clinical Information.
Left posterior shoulder, F81.

Reason for Consultation.
Favor a junctional Clark’s nevus (see enclosed report).
- Broad lesion, poorly circumscribed, sparse cellularity, single and nested melanocytes.
- Mainly near the dermal-epidermal junction, focal pagetoid scatter
- Moderate chronic CSD.
- Some bridging, few nests that hang down in a droplet-like pattern.
- Cytologic atypia mild but relatively uniform.
Your Diagnosis?

Melanoma?
Nevus?
Diagnosis Case 3, F81

• “Difficult to interpret”.

• Cytologic atypia is mild to moderate rather than severe, with somewhat concerning architectural changes.

• “One is somewhat more concerned about a lesion in chronically sun-damaged skin of older subjects”.

• **Skin, left posterior shoulder, shave biopsy:** Intraepidermal atypical melanocytic proliferation of uncertain significance (IAMPUS), most consistent with atypical lentiginous junctional nevus (of the elderly/CSD skin), cannot r/o evolving or early established melanoma in situ.

• Complete excision recommended (MPATH-Dx 2 or 3)
Case 4.

Part 2-3. **14474**

*Clinical Information.*
Left posterior shoulder, F84.

*Reason for Consultation.*
Favor a junctional Clark’s (mildly dysplastic) melanocytic nevus (see enclosed report). There is mild melanocytic atypia, and that the peripheral and deep margins of the specimen were negative in the plane of sectioning.
Your Diagnosis?

Melanoma?
Nevus?
Diagnosis Case 4, F81

- Recurrence of Case 8
- Shave biopsy of similar sun-damaged skin
- Somewhat more cellular proliferation of nevoid and nevoid to epithelioid melanocytes, focally exhibiting severe and uniform cytologic atypia.
- Some of these cells are confined to the epidermis above the scar, while others appear to extend some distance beyond the periphery of the scar.
- This latter feature raises some concern for evolving melanoma in situ extending beyond the scar.
Skin, left posterior shoulder, shave biopsy (recurrence): Intraepidermal atypical melanocytic proliferation of uncertain significance, extending to specimen margins, see description and comment.

Comment: Cannot rule out an evolving more significant lesion, suggest complete excision
Case 5.

Part 2-3. 14474

Clinical Information.
Biopsy from posterior shoulder of an 85 year old female.

Reason for Consultation.
This specimen, in my opinion, has histologic features concerning for melanoma because of the architectural symmetry, ill-defined borders, contiguous proliferation of atypical solitary melanocytes, and some pagetoid spread of melanocytes within the epidermis. I do not see definitive features of a scar consistent with a prior biopsy site.
• Broad
• Moderately cellular
• Moderate to severe CSD
• Poorly circumscribed
• Few bridging nests
• Diffuse fibroplasia
• Cells in dermis
• Moderately cellular
• Moderate to severe CSD
• Nests hanging down
• Diffuse fibroplasia (not a scar)
- Moderately cellular
- Moderate to severe CSD
- Nests hanging down
- Diffuse fibroplasia (not a scar)
- Nests in dermis
- No maturation
Melan-A Stain

- Moderately cellular
- Continuous basal proliferation
- Nests hanging down
- Low level pagetoid scatter
- Nests in dermis
- No maturation
Your Diagnosis?

Melanoma?
Nevus?
Our Diagnosis

Malignant melanoma, lentigo maligna type ("lentiginous melanoma", Clark level II, Breslow thickness 0.85 mm)
Updated History Cases 3-5.

- **Clinical Information.**

  - Three separate biopsies from left posterior shoulder of an 85-year-old female over a period of three years. The biopsies were performed 4 years and 1 year ago, and recently.

  - The original biopsy was called a junctional Clark’s (mildly dysplastic) melanocytic nevus, might have been better interpreted as a lentiginous nevus of the elderly/sundamaged skin, with mild to moderate atypia.
    - The peripheral and deep margins of the specimen were said to be negative in the plane of sectioning.

  - The next biopsy at presumably the same anatomic location was signed out as an atypical melanocytic proliferation consistent with a persistent/recurrent Clark's (dysplastic) nevus, involving the peripheral edge of the biopsy.
    - It was mentioned that the differential diagnosis included early melanoma in situ evolving within a pre-existing nevus, and a reexcision was recommended.

  - The most recent specimen was concerning for melanoma because of the architectural symmetry, ill-defined borders, contiguous proliferation of atypical solitary melanocytes, and some pagetoid spread of melanocytes within the epidermis.

  - Additional procedure warranted to ensure that the lesion has been completely removed.
• Broad lesion, poorly circumscribed, sparse cellularity, single and nested melanocytes.
• Mainly near the dermal-epidermal junction, focal pagetoid scatter
• Moderate chronic CSD.
• Cytologic atypia mild but relatively uniform.
• POTENTIAL PRECURSOR (low risk) VS ACTUAL PRECURSOR (hindsight bias)
• Manage by excision or follow-up
• Case 5

• Second recurrence of a lesion that originally had only “mild” atypia (but moderate to severe architectural disorder)

• Diagnosis of dysplastic nevus should be made with caution in elderly/CSD skin

• Complete excision is appropriate for “atypical lentiginous nevus of elderly/sundamaged skin”.
Next Case.

Part 2-7. 12150

Clinical Information.
Lesion of right shoulder, r/o melanoma versus nevus in a 76 y.o. man

Reason for Consultation.
Is this anything other than a moderately atypical neurotized compound nevus?
• A relatively broad lesion with irregular thickening and thinning of rete ridges and a sparsely cellular infiltrate in the dermis.
• Generally sparsely cellular
• Moderate to severe CSD
Poorly circumscribed
• Pigmented melanophages in the dermis
• Increased number of melanocytes in the epidermis, many of them suprabasal
• Cells in the papillary dermis are delicate spindle cells and there is a sprinkling of lymphocytes.
• Cells in the papillary dermis are delicate spindle cells and there is a sprinkling of lymphocytes.
S100 stain highlights the increased cellularity in the epidermis and also labels the spindle cells in the papillary dermis.
• Melan-A stain highlights the junctional component but the dermal spindle cells are negative.
Case 6

- Skin, right superior shoulder: Malignant melanoma, lentigo maligna type, nonulcerated, with pure desmoplastic vertical growth phase, Clark level IV, Breslow thickness not < 0.64 mm, extending close to the specimen base, see Comment 3.

- Comment
  - Changes extend close to the base and to a peripheral margin of the specimen.
  - It is unusual to see a small desmoplastic melanoma at this early stage of its evolution.
  - Should be excised locally in order to prevent any possibility of persistence, recurrence, or future progression of it.
  - Based on its microstaging attributes, the prognosis for this lesion should be excellent. The prognosis for “pure” desmoplastic melanoma is if anything better than that for melanomas of similar thickness.
  - This lesion could be managed with a relatively generous wide local excision – MPATH DX Category 4 (or 5).
<table>
<thead>
<tr>
<th><strong>High UV Pathway III</strong></th>
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</thead>
<tbody>
<tr>
<td><strong>Desmoplastic Melanoma</strong></td>
</tr>
</tbody>
</table>

- Skin with Severe CSD
- High Tumor Mutation Burden
- Melanoma in situ, or may be no in situ lesion
- Infiltrative spindle cells separated by “desmoplastic” collagen
- NF1 (loss of function)
  - ERBB2, MAP2K1, MAP3K1, BRAF, EGFR, MET (amplifications)
  - TERT, NFKBIE, NRAS PIK3CA PTPN11

Fig. 2.5D Desmoplastic melanoma. The range of appearances is broad: some examples arise in a pigmented patch, others, like this example, are amelanotic; level with the surface (or elevated, as shown here), and (often) indurated.
Desmoplastic Melanoma

**NF1, ERBB2, MAP2K1, MAP3K1, BRAF, EGFR, MET, TERT, NFKBIE, NRAS PIK3CA PTPN11**

HIGH TUMOR MUTATION BURDEN (Potential checkpoint therapy)


“... patients with advanced desmoplastic melanoma derive substantial clinical benefit from PD-1 or PD-L1 immune checkpoint blockade therapy ... likely to result from the high mutational burden and a frequent pre-existing adaptive immune response limited by PD-L1 expression”
Desmoplastic melanoma

Definition
Desmoplastic melanoma is a variant of spindle cell melanoma in which the malignant cells are separated by collagen fibers and fibrous stroma.

S(s) code 407.94

Epidemiology
Desmoplastic melanomas account for 1% of all melanomas at all ages. As with other melanomas, they are more common in males, with a male-to-female ratio of 1.7:1. The median age at diagnosis is 63 years in patients with desmoplastic melanomas. Most desmoplastic melanomas are not the most common melanomas overall.

Etiology
Clinical, dermatologic, and genetic factors are significant. The tumor exhibits desmoplastic melanoma in nearly all cases. A high proportion of these tumors are found in patients with a history of a prior melanoma.

Localization
Desmoplastic melanomas most commonly occur in the abdomen, upper back, and neck region (including the nape and tip) in men, and the skin and soft tissues are uncommonly affected. However, these tumors can also occur in areas with minimal or no evidence of prior melanoma.

Clinical features
Most tumors present as a painless, indurated plaque or a poorly demarcated area or macule. The lesion may be surrounded by a collar of atrophic skin and may be ulcerated. The tumor is often associated with a fibrous or collagenous stroma, which may be thick and rigid. The lesion is often asymptomatic but may cause detectable pain or discomfort.

Histopathology
The desmoplastic melanoma is characterized by the presence of desmoplastic stromal changes. The tumor may be in situ or invasive, with the presence of atypical melanocytes in the dermis and subcutaneous tissues. The tumor cells may be arranged in nests, cords, or sheets, and may show evidence of atypical mitotic activity. The tumor may be associated with a fibrous or collagenous stroma, which may be thick and rigid. The lesion may be ulcerated.

Prognosis
Desmoplastic melanoma has a better prognosis than other types of melanoma, with a 5-year survival rate of 80-90%. The prognosis is influenced by the depth of invasion, the presence of ulceration, and the absence of regional lymph node metastases. The treatment of desmoplastic melanoma is surgery, with wide local excision or excision with margins of normal tissue. The use of adjuvant therapy, such as chemotherapy or immunotherapy, is controversial.

References
Case 7.

Clinical Information.
Pigmented lesion on the back of a 40 year old woman

Reason for Consultation.
Rule out melanoma?
A Lesion of the Back in a 40 Year Old Woman

• “shave biopsy under the left arm ... has caused consternation ... two of us believing that we are dealing with a ... melanoma... two others believing that although worrisome ... not yet melanoma”
Your Diagnosis?

Melanoma?
Nevus?
Your Diagnosis?

Dysplastic?
Nondysplastic?
Your Diagnosis?

High Grade?
Low Grade?
<table>
<thead>
<tr>
<th>Feature</th>
<th>Melanoma</th>
<th>Dysplastic Nevus</th>
<th>Nevus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>tend to be larger</td>
<td>intermediate</td>
<td>smaller</td>
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<tr>
<td>Symmetry</td>
<td>poor</td>
<td>good</td>
<td>good</td>
</tr>
<tr>
<td>Keratinocytes</td>
<td>irregular</td>
<td>uniform elongated rete</td>
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<td>epithelioid</td>
<td>mixed</td>
<td>nevoid</td>
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<td>variable</td>
<td>predominant</td>
<td>predominant</td>
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<td>bridging</td>
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<tr>
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<td>discontinuous</td>
<td>discontinuous</td>
</tr>
<tr>
<td>Pagetoid</td>
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<td>low, focal, minimal</td>
<td>minimal</td>
</tr>
<tr>
<td>Nuclear atypia</td>
<td>uniform atypia, severe (&gt; 1.5x)</td>
<td>random atypia, mild-moderate</td>
<td>minimal</td>
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<tr>
<td>Mitoses</td>
<td>about 1/3 of cases</td>
<td>almost always absent</td>
<td>absent</td>
</tr>
<tr>
<td>Fibroplasia</td>
<td>diffuse</td>
<td>concentric</td>
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<tr>
<td>Lymphocytes</td>
<td>bandlike, lichenoid</td>
<td>patchy, perivascular</td>
<td>minimal</td>
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<tr>
<td>Regression</td>
<td>frequent, extensive</td>
<td>rare, minimal</td>
<td>absent</td>
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</tbody>
</table>
Diagnosis Rendered

• “malignant melanoma, probably lentigo maligna type, showing Clark level III invasion with early tumorigenic but nonmitogenic vertical growth phase, at a greatest Breslow thickness of 0.30 mm ... associated nevus with congenital pattern features”
New Information!

“I received a call from the primary care physician of this patient asking me to review a biopsy from June of 2004, which I had signed out as a compound congenital melanocytic nevus. She told me that the lesion had developed repigmentation in the previous biopsy site ... ”
• “I think it is almost certain that the subsequent biopsy is a pseudomelanoma based on the fact that there was no atypia in the original shave biopsy specimen, the interval between biopsy and re-pigmentation is only three months, and the re-pigmentation is in the previous biopsy site. The lack of this additional clinical information at the time you received the biopsy was a handicap”
New Report!

“superficial atypical melanocytic proliferation, c/w recurrent nevus phenomenon, extending to specimen margins” ... “I would make only one reservation, and that is that this lesion should be re-excised again with a margin of normal skin around the scar and any residual lesion ...”
Pseudomelanoma (Ackerman)

- pigmented patch at site of prior shave biopsy of a benign compound or dermal nevus
- repigmentation occurs quickly (6 weeks)
- pigment does not extend beyond scar's borders
RECURRENT MELANOCYTIC NEVUS

Histology

- variably sized and shaped sometimes confluent nests
- single cells & nests above DEJ usually not beyond mid-spinous layer
- occasional lesional cells or nests in dermis
- slight cytologic atypia (“reactive?”), rare mitoses
- proliferation does not extend beyond scar
- original nevus should be reviewed
Lessons

• Atypia in recurrent nevi can be severe, yet is “reactive”.
  • Mitoses can be present
  • Dermal atypia can be present

• A superficial scar can mimic diffuse fibroplasia seen in many melanomas

• Keep a high index of suspicion
  • Consider a full differential diagnosis
  • Call for history if necessary
Take Home Messages

• Early/evolving LMM IS can be subtle

• Changes at periphery and at margins can be subtle
  • Confluence or continuous proliferation of uniformly atypical cells
  • Nests in epidermis overlying elastotic dermis (LeBoit)

• Focal areas in LMM IS can mimic dysplastic nevus
  • Diagnosis of dysplastic nevus in sun-damaged skin of elderly is fraught with hazard

• Diagnosis is often based more on architectural disorder (including size) than on severe cytologic atypia.
High CSD Lesions

• Cautious approach – beware of nests of melanocytes in epidermis above solar elastosis
• Caution in diagnosis of dysplastic nevus in CSD skin
• Do not overcall actinic atypia in re-excision specimens (more of a risk marker than a precursor)
• Beware of subtle spindle cells in dermal component of CSD melanomas
Thanks!