Pitfalls in melanoma diagnosis & how to potentially avoid them

10:30-11:15
Saturday 10th July 2010
(45 minutes)

Ashfaq A. Marghoob, M.D.
Memorial Sloan-Kettering Cancer Center


- 8 of the most common scenarios encountered in litigation cases
  1) NM misdiagnosed by clinician
  2) NM misdiagnosed by pathologist
  3) Partial biopsy issues
  4) MM misdiagnosed as DN
  5) MM misdiagnosed as Spitz
  6) Unrecognized desmoplastic MM
  7) Inadvertent destruction of a presumed benign lesion that turned out to be MM
  8) Missed melanoma – “failure to diagnose”

Pitfall #1
Nodular melanoma misdiagnosed as nevus by clinician

- Why?
  - Nodular MM often lacks the ABCDs of MM

Potential methods to avoid misdiagnosing nodular melanoma

- “ABCDE” for evolving may help
- Evolving
  - Patient history: change symptoms
  - TBP: help detect new lesions some of which may be subtle early NM
- Examine all outlier (UD) lesions & all lesions highlighted by the patient
  - dermoscopy may sway you to biopsy NM lacking clinical ABCDs

Self Skin Examination
Why is it so critical?

Rate of growth of melanoma subtypes: Median melanoma growth in mm per month

Patient claims that this new 'mole' appeared approximately 3 weeks ago.

**Red-brown structureless areas at periphery**

**BWS over raised area**

**FINAL DX: Nodular melanoma 0.6mm**
How can Dermoscopy Help?

Outlier lesion on arm

Patient has a history of melanoma & BCC. This lesion is on the forearm and was found by the clinician during routine skin cancer surveillance.

Expect to see

Homogeneous blue pigmentation

Blue white veil

Brown structureless area

Heterogeneous brown pigment (blotch)

Nodular 0.8mm melanoma
**Historical, Clinical, and Dermoscopic Characteristics of Thin Nodular Melanoma**

**Background:** Nodular melanoma (NM), representing 15–30% of all melanomas, constitutes roughly half of all melanomas diagnosed in the United States. It is characterized by a slow clinical course, a large initial size, and frequent dermoscopic features of thin NM. The lesions are often deeply invasive with advanced stage at presentation. Thin NM lacks specific ABCD criteria.

**Observations:** The 3 to 4 mm lesions we examined lacked characteristic architectural arrangements. Histologically, they demonstrated dermoscopic patterns with less than 4 mm criteria. On dermoscopy, the lesions were featureless with asymmetric atypical vessels in association with atypical vessels. Pigmented variant reveals:

- BWV
- Multiple colors
- Chrysalis
- Atypical vessels

Amelanotic variant reveals:

- Atypical vessels
- Chrysalis

NM pattern is:

- Homogeneous disorganized
- Featureless with vessels

**Pitfall # 2**

Nodular melanoma misdiagnosed as nevus by pathology

- Why?
  - NM may manifest a nevoid appearance under histopathology
  - Partial biopsy may not capture the diagnostic portion of lesion
  - Technical error (inadequate sectioning / mixed specimens)

**What can a clinician do to potentially correct this error?**

- Question yourself as to why you biopsied the lesion
  - You must reconcile your clinical impression with the pathology diagnosis
- If there is discordance then:
  - Ask for step-sectioning / stains / 2nd opinion
- If you did a partial biopsy:
  - Re-excite
• Why did you biopsy? R/O BCC, PG
• Pathology = nevus (clinical-pathology discordance)
• Log book (with images) – reconcile clinical dx & path report
  • Pathology report should never be read in a vacuum
  • Clinician’s degree of concern will be questioned in court of law (both the clinician and pathologist pay)
• Stop – question / step section / stains – pursue until you are able to reconcile clinical & pathology diagnosis.

2 biopsies done on the same patient & on the same day: arm and back

An example of the importance of reconciliation

Arm
R/O amelanotic MM

Back
R/O BCC

R/O MM (larger of the 2)
R/O BCC

• Path states invasive MM on back and BCC on arm.
• Review of the images shows that this cannot be correct.
• Asked path to look at lesions and see which has crust/ulcer and which is larger.
• Thus, clinician was able to correctly identify the mistake and correct it: MM was on arm & BCC on back.
• Mix-up occurred somewhere: placement in incorrect labeled bottle, incorrect labeling, grossing bench mix-up, pathologist error.
Pitfall #3  
Partial biopsies

• Why?
  – Partial biopsy may sample nondiagnostic area or miss the prognostically worst portion of the lesion
  – Of claims involving a missed diagnosis of melanoma, the pathology review revealed that:
    • 83% were shave, punch or incisional biopsies
    • Only 17% were excisional biopsies

How to prevent this pitfall?

• Excisional biopsy, if feasible, is the preferred method of biopsy for melanocytic lesions
  
• If excision is not possible then
  – Sample "enough" tissue so that the pathologist is not placed at a disadvantage
    • Saucerization / deep shave biopsy
    • Multiple partial biopsies

Diagnosis: Intradermal nevus with congenital features

Diagnosis: Melanoma

Final diagnosis: Melanoma in association with congenital nevus
Problem with partial biopsies

- Partial biopsy "assumption" is that a clinician can consistently predict the portion of a suspicious pigmented lesion that will have the worst representative histology
    - 40% of excised melanomas had worse pathology compared to initial punch biopsy.
    - 20% of melanomas revealed invasion which was not seen in initial punch biopsy
  - Karimipour et al. JAAD 2005;798-802
    - Incisional biopsy mean thickness 0.66mm
    - Excision of above lesion mean thickness 1.07mm
    - Upstaged in 21% of cases
    - 10% became candidates for SLNB

Ideal Biopsy (if feasible)

- Orient axis along lines of lymphatic drainage
- Step section
- Excisional biopsy with 2-3mm margin
  * Limit sampling error
  * Remove DN completely – prevent recurrence
  * Better predict Breslow depth

Importance of step-sectioning

- Thorough block sampling MM resulted
  - Increased thickness in 43% of cases (by mean of 0.16mm)
  - 10% cases had a change in stage and treatment

Remember

- Even when step-sectioned, <2% of lesion is evaluated
  - Thus, focus of MM can still get missed
Help your pathologist

- Clinical / dermoscopic guidance can help highlight areas for the pathologist to focus on.

Examples: help direct pathologist

Sometimes it is not feasible to do an excisional biopsy: what to do?

- Prevent the pathologists from assuming that the biopsy specimen represents the entire lesion
  - Indicate the fraction of the lesion biopsied
  - Adding an image can help orient the pathologist

- Remember that the area sampled may not be the "worst" or most diagnostic area on histopathology
  - In large lesions consider obtaining multiple biopsies

Pitfall #4
Melanoma misdiagnosed as "Dysplastic nevus involving margins"

- How could this happen?
  - DN diagnosis may be incorrect
  - Focus of MM may have been missed
    - Focus missed clinically
    - Focus missed on histology step-sectioning
  - MM may develop from residual cells

What can you do to minimize this error?

- Consider re-excising "nevus" if the margins are positive, especially if the lesion was suspicious under dermoscopy or has unconventional features under histopathology
  - Decision will be based heavily on
    - your sense of the pre-test probability for the lesion being a MM
    - How small a biopsy was taken (how much of the lesion is still remaining on the patient)
  - At a minimum - follow-up the patient for clinical recurrence of pigmentation
If pigment recurs, think that

• Diagnosis of nevus may have been incorrect

• Focus of MM may have been missed (at the pathology laboratory or during partial biopsy)

• MM may have developed from residual cells

• Always ask for review of original biopsy slides of “recurrent nevi”.

Recurrent (persistent) Melanomas:

Initial path Dx: DN with + margins

History: Re-pigmentation

Re-biopsy: Melanoma

Review original path: Melanoma

*Initial diagnosis of DN was incorrect.

Pathology is an imperfect gold standard!

Original biopsy report: DN + margins

2 years later: re-pigmentation noted

Original path reviewed: DN + margins

Re-biopsy: ?

Melanoma

- Focus of MM was missed on original biopsy
  or
  - MM developed from residual nevus cells
Another Clue to MM:

- Pigment recurs months to years later
- Pigment crosses from the scar tissue into normal skin

Surgical management of dysplastic nevi

When asked about their intent during biopsy, 380 (86.0%) indicated that most often they intend to remove the dysplastic nevus completely, whereas only 61 (13.8%) stated that it is not usually their intention to remove the lesion completely. These two groups

<table>
<thead>
<tr>
<th>Intention to Remove</th>
<th>100%</th>
<th>86%</th>
<th>13.8%</th>
</tr>
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<tbody>
<tr>
<td>Complete removal</td>
<td>380</td>
<td>335</td>
<td>45</td>
</tr>
<tr>
<td>Partial removal</td>
<td>47</td>
<td>55</td>
<td>84</td>
</tr>
<tr>
<td>Not intended</td>
<td>47</td>
<td>55</td>
<td>84</td>
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Pitfall #5
Melanoma misdiagnosed as Spitz nevus

- Why does this happen?
  - The morphology of Spitz nevi & MM can overlap clinically and histologically
Spitz vs MM

Spitzoid lesions

- There is poor agreement among pathologists when evaluating Spitzoid melanocytic lesions (28%-30%)\(^1\)\(^-\)\(^3\)
- Even in those instances where several pathologists agreed with the diagnosis of Spitz nevus or atypical Spitzoid tumors, some of the cases had fatal outcomes


How to potentially prevent a bad outcome in this scenario?

- All Spitz nevi should be completely excised (at least in adults)!
  - Why?

- MM 10.5mm
- Invasion of blood vessel wall
- Spindle cell

![Management of Spitz nevi: A survey of dermatologists in the United States](image)

Fig. 1. Age of patients at time of initial biopsy of lesion diagnosed as Spitz nevus that has since transformed, combined data from 35 physicians (general and pediatric dermatologists and pigmented lesion clinic directors) who responded to the questionnaire. **Variable** includes responses of physicians who would have the type of biopsy in the clinical situation (eg, size of lesion, location of lesion, age of patient).
Pitfall #6
unrecognized desmoplastic melanoma

- Why does this happen?
  - Desmoplastic MM often has a banal clinical appearing (70% amelanotic)
  - It can present only as firmness in subQ

Potential ways to help diagnose DM

- Clinical clues
  - Be suspicious of "banal" appearing lesion on chronically sun-damaged skin that are:
    - Symptomatic
    - Growing
    - Unexplained scar (no history of trauma)
    - LM with firm areas (palpation of skin!!!!!!!)
  - Dermoscopic clues
    - If any of the above lesions manifest irregular blood vessels then strongly consider a biopsy

Differential Diagnosis
(MM in diff 33% of time & not in diff 67% of the time)

- Epidermal inclusion cyst
- Eczema
- BCC
- Dermatofibroma
- Lentigo
- Seborrheic keratosis
- Neurofibroma
- Scar
Pitfall #7
Inadvertent destruction of a presumed benign lesion that turned out to be MM

- Why?
  - Judgment error
  - Clinical examination may not have been thorough enough
    - Inadequate lighting
    - Rushed
    - Lack of clinical-dermoscopy correlation

How to minimize this unfortunate error from occurring?

- Be extremely selective when removing (discarding) or destroying presumed "benign" lesions
- Be careful & selective with use of liquid nitrogen/laser on lesions not biopsied (nevus, SK, etc)
- It is my opinion that clinical-dermoscopy correlation will probably prevent most/all such cases from occurring
Pitfall #8
Missed melanoma

• How can one miss a MM?
  • Total body skin examination was not performed
  • The MM may not manifest clinically concerning features (mimic benign lesions)
  • The MM was simply missed (‘saccade vision’ scanned over it & thus ‘focused vision’ failed to get triggered)
  • The MM was too small

What can be done to minimize the chance of missing a MM?

– Periodic screening TBE sifts through all lesions and will eventually find the MM
– Listen to patient’s concerns (‘feels funny’)
– Engage & empower patients in their own care
  • PE and SSE are complementary – shared responsibility

Lawyers love this one!

• Theory of biologic necessity
  – MM must have been present for some time prior to diagnosis (not always true)
  – Failure to diagnose the MM earlier carries with it the implication that the prior MD was negligent in not finding it during their previous encounter

Reality about ‘delay’

• Widely accepted that delay in diagnosis means poorer prognosis
  – However, modest delays of up to 6 months has not been shown to effect ultimate outcomes (exception: nodular MM)


Rate of growth of melanoma subtypes: Median melanoma growth in mm per month

<table>
<thead>
<tr>
<th>Growth Rate (mm/month)</th>
<th>SSM</th>
<th>LMM</th>
<th>NMM</th>
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<tr>
<td>0.12</td>
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<td>0.49</td>
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Slow-growing melanoma: a dermoscopy follow-up study

Conclusions: This study provides evidence for the existence of a subgroup of slow-growing melanomas, which may explain the increase in the incidence of thin melanoma, despite stable rates of thick melanoma and melanoma-associated mortality.


Excised after 16 months
Screening/surveillance will help find the slower growing melanomas

Analytical
Comparative: long term

Differential
Comparative: short term

This MM grew over a course of 4 months

4.1mm nodular MM
• PE and SSE are complementary
  – MM found by MD and missed by patient
  – MM found by patient and missed by MD

“Gold standard” is clinical-dermoscopic-histopathologic correlation
• Do not accept histopathologic diagnosis at “face value” (your index of suspicion is important)
• Reconcile histopathologic diagnosis with clinical / dermoscopic diagnosis and images
• Alert pathologist of
  – Partial biopsy (particularly of larger lesion or superficial biopsy of nodular lesion)
  – Clinical-pathologic discordance
  – Focal area of concern within lesion

Concluding remarks
• Question yourself and your pathologist always
• Engage patients in their own care (shared responsibility)
  – at “this moment in time” all lesions look benign. However, if you notice a changing, symptomatic or new lesion on SSE, you need to inform us
  – SSE & PE complementary

Conclusion: “Gold standard” is clinical-dermoscopic-histopathologic correlation
• Request additional sections of tissue when discordant diagnosis occurs between you and your pathologist.
• It is acceptable to seek a second opinion.
• Consider complete excision of partially biopsied lesions
• Consider complete excision if your index of suspicion is very high even if pathologist is convinced it is benign.