

Supplementary Online Content

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eAppendix. Histopathological Feature Descriptions

eTable. Interobserver Agreement for Each Studied Variable

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Histopathological Feature Descriptions

1. Pagetoid Spread. Melanocytes scattered in the epidermis and in the follicular epithelium in a pattern similar to that of Paget disease (1). The proportion of intraepidermal melanocytes present above the basal layer was graded from 0 to 3 (2):

- **0:** essentially all melanocytes situated at the dermo-epidermal junction, with only rare melanocytes in higher epidermal layers.
- **1:** most melanocytes (75% –100%) situated at the dermoepidermal junction, with some present in higher epidermal layers.
- **2:** roughly equal proportions of intraepidermal melanocytes present at the dermo-epidermal junction and in higher epidermal layers.
- **3:** most (>50%) of the intraepidermal melanocytes situated in the upper layers of the epidermis.

2. Nest formation of intraepidermal melanocytes. Intraepidermal melanocytes were defined as arranged in nests when they formed clusters of five or more cells no matter where they were located (within the basal epidermis or in higher layers of the epidermis). The degree of nesting was quantified as:

- **0:** intraepidermal melanocytes present almost exclusively as single cells with only rare nests.
- **1:** intraepidermal melanocytes predominantly arranged as single cells with no more than 25% of cells in nests.
- **2:** 25%–50% of the intraepidermal melanocytes in nests.
- **3:** 50% of the intraepidermal melanocytes in nests.

3. Solar elastosis. Presence of “elastotic fibers” in the normal skin surrounding the melanoma. We classified it in two different forms, the first one was graded from 0 to 3:

- **0:** Absence of “elastotic fibers”.
- **1:** Slight (isolated “elastotic fibers” between the collagen bundles).
- **2:** Moderate (disperse conglomerates of “elastotic fibers”).

- **3:** Severe (deposit of amorphous blue - gray “elastotic fibers” without the presence of a fibrillar structure).

Elastosis was also classified in (3):

- **0 (Non – CSD):** Slight to moderate elastosis. Essentially isolated fibers and a few of them forming conglomerates. (1 to 2)
- **1 (CDS):** severe solar (2 to 3), major density deposit of elastotic fibers, forming conglomerates and inclusive amorphous masses. Of note, all of our cases had moderate or severe elastosis.

4. Epidermal contour. The contour of the epidermis involved by the radial growth phase of the melanoma was compared to the adjacent normal epidermis. Then it was scored from 0 to 4:

- **0 (atrophic):** markedly thinned epidermis with effacement of rete ridges.
- **1 (thinned):** thinned epidermis with partial attenuation of rete ridges.
- **2 (normal):** epidermal silhouette similar to the adjacent uninvolved epidermis.
- **3 (thickened):** slight to moderate epidermal hyperplasia with elongation of the rete ridges resulting in a maximum 2-fold increase in epidermal thickness.
- **4 (hyperplastic):** marked epidermal hyperplasia resulting in a greater than 2-fold increase in epidermal thickness.
- **5 (other):** No predominant subtype or at least 2 different subtypes with a 50% distribution.

5. Lateral circumscription. Lateral circumscriptio was assessed by examining the transition of the intraepidermal growth portion of the tumor to normal skin at the tumor periphery. The area with the most gradual transition in any of the tissue pieces was scored from 0 to 2 (2, 3):

- **0 (discontinuous):** areas of apparently uninvolved epidermis interspersed with tumor. Areas of uninvolved epidermis apparently caused by regression were considered tumor.
- **1 (gradual but continuous):** continuous decrease of the number of intraepidermal melanocytes making it difficult to pinpoint the transition to normal skin to within one or two rete ridges or 0.1 mm,

- 2 (abrupt): transition from involved epidermis to the adjacent normal skin easily determined within one or two rete ridges or 0.1 mm.

6. Melanocytes confluent along the junction forming rows: melanocytes are more numerous and aligned in lines composed of single units along the basal layer which can be focally replaced by these cells.

7. Extensive involvement of adnexal epithelium: adnexa extensively involved with the melanocytes reaching the deepest portion of the follicular epithelium.

8. Multinucleated melanocytes. Presence vs. absence.

9. Presence of Melanophages: the presence of histiocytes with phagocytosed melanin.

10. Subepidermal Clefts: when melanocytes are confluent along the junction, subepidermal clefts can occur reflecting loss of the integrity of the junctional zone.

eTable. Interobserver Agreement for Each Studied Variable

	Kappa value*
Pagetoid extension	0.5
Nest formation of intraepidermal melanocytes	0.6
Solar elastosis in surrounding healthy skin (4 categories)	0.7
Solar elastosis, 2 categories (CSD/non CSD)	0.8
Epidermal contour	0.4
Lateral circumscription	0.4
Melanocytes confluent along the junction forming rows	0.6
Presence of extensive involvement of adnexal epithelium	0.6
Presence of multinucleated melanocytes	0.5
Presence of melanophages	0.8
Presence of subepidermal clefts	0.7

*Agreement among the two groups was assessed using the Cohen's kappa (κ) coefficient statistic for dichotomous categories. In the case of ordinal variables Cohen's weighted kappa was used instead.

References

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