

Clinical Pearls will help prepare residents for the future by providing them with pearls about what they should know about a specific subject area by the time they complete their residency.

## Melanocytic lesions

By Vikas Shrivastava, MD, FAAD

### 1. Understand the report.

Histopathologic reports for melanocytic lesions can be complicated. One must understand what is being said and what testing was performed. You must agree with the pathologist's interpretation before discussing management and prognosis.

### 2. Establish a relationship.

Histopathologic analysis via H+E staining is the gold diagnostic standard<sup>i</sup>. Key features include cytologic atypia, lentiginous hyperplasia, Pagetoid scatter, lack of maturation, and inflammation.

Borderline lesions are challenging. Panels of immunohistochemical stains can help establish a diagnosis and include SOX10 (or other sensitive melanocytic stain), HMB-45 (lack of deep staining reassuring), p16 (retention reassuring) and Ki67 (low proliferation index reassuring)<sup>iii</sup>. Furthermore, p53, has been shown to help distinguish desmoplastic melanoma from neurofibroma (negative reassuring)<sup>iv</sup>.

If you do not agree with your pathologist, frank discussion is paramount.

### 3. Don't over-rely on PRAME.

Nuclear immunoreactivity for PRAME is seen in up to 90% of melanomas and may be used to identify precursor nevus, highlight residual melanoma, and delineate background melanocytic hyperplasia.

That said, desmoplastic melanoma is typically PRAME negative and benign lesions may have some staining. Interpretation must account for intensity (weak-strong) and number of nuclei staining (1-25%, 26-50%, 51-75%, 76-100%).

Spitzoid lesions are difficult to classify using PRAME alone. McAfee et al showed the combined utility of p16 (positive reassuring) and BRAF V600E (negative reassuring) in this group while Boutko et al described a role for TERT-promoter mutation analysis (negative reassuring)<sup>vi, vii</sup>.

For concerning lesions with discordant staining, FISH or CGH may be performed<sup>viii</sup>.

### References:

- i. Lam GT, Martini C, Brooks T, Prabhakaran S, Hopkins AM, Ung BS, Tang J, Caruso MC, Brooks RD, Johnson IRD, Sorvina A, Hickey SM, Karageorgos L, Klebe S, O'Leary

JJ, Brooks DA, Logan JM. Insights into Melanoma Clinical Practice: A Perspective for Future Research. *Cancers (Basel)*. 2023 Sep 19;15(18):4631. doi: 10.3390/cancers15184631. PMID: 37760601; PMCID: PMC10526186.

- ii. Lam GT, Prabhakaran S, Sorvina A, Martini C, Ung BS, Karageorgos L, Hickey SM, Lazniewska J, Johnson IRD, Williams DB, Klebe S, Malone V, O'Leary JJ, Jackett L, Brooks DA, Logan JM. Pitfalls in Cutaneous Melanoma Diagnosis and the Need for New Reliable Markers. *Mol Diagn Ther*. 2023 Jan;27(1):49-60. doi: 10.1007/s40291-022-00628-9. Epub 2022 Dec 7. PMID: 36477449.
- iii. Uguen A, Talagas M, Costa S, Duigou S, Bouvier S, De Braekeleer M, Marcorelles P. A p16-Ki-67-HMB45 immunohistochemistry scoring system as an ancillary diagnostic tool in the diagnosis of melanoma. *Diagn Pathol*. 2015 Oct 26;10:195. doi: 10.1186/s13000-015-0431-9. PMID: 26503349; PMCID: PMC4623282.
- iv. Elsensohn A, Shiu J, Grove N, Hosking AM, Barr R, de Feraudy S. Distinguishing Neurofibroma From Desmoplastic Melanoma: The Value of p53. *Am J Surg Pathol*. 2018 Mar;42(3):372-375. doi: 10.1097/PAS.0000000000000978. PMID: 29112020; PMCID: PMC6095644.
- v. Lezcano C, Jungbluth AA, Nehal KS, Hollmann TJ, Busam KJ. PRAME Expression in Melanocytic Tumors. *Am J Surg Pathol*. 2018 Nov;42(11):1456-1465. doi: 10.1097/PAS.0000000000001134. PMID: 30045064; PMCID: PMC6631376.
- vi. McAfee JL, Scarborough R, Jia XS, Azzato EM, Astbury C, Ronen S, Andea AA, Billings SD, Ko JS. Combined utility of p16 and BRAF V600E in the evaluation of spitzoid tumors: Superiority to PRAME and correlation with FISH. *J Cutan Pathol*. 2023 Feb;50(2):155-168. doi: 10.1111/cup.14342. Epub 2022 Nov 4. PMID: 36261329; PMCID: PMC10099989.
- vii. Boutko A, Asadbeigi S, Roth A, Lampley N, Olivares S, Dittmann D, Dittmann D, Jennings L, Gerami P. TERT Promoter Mutational Analysis as an Ancillary Diagnostic Tool for Diagnostically Challenging Melanocytic Neoplasms. *Am J Dermatopathol*. 2023 May 1;45(5):289-299. doi: 10.1097/DAD.0000000000002366. Epub 2023 Feb 17. PMID: 36898007.
- viii. Nagarajan P, Tetzlaff MT, Curry JL, Prieto VG. Use of New Techniques in Addition to IHC Applied to the Diagnosis of Melanocytic Lesions, With Emphasis on CGH, FISH, and Mass Spectrometry. *Actas Dermosifiliogr*. 2017 Jan-Feb;108(1):17-30. English, Spanish. doi: 10.1016/j.ad.2016.05.005. Epub 2016 Jun 22. PMID: 27344067. DR



**Vikas Shrivastava, MD, FAAD**, is a dermatopathologist and the dermatology residency program director at the Naval Medical Center in San Diego.

The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States government.

### More Clinical Pearls online!

Visit the archives at [www.aad.org/member/publications/more/dir/clinical-pearls](http://www.aad.org/member/publications/more/dir/clinical-pearls).