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Robert E. Garola

Children's Mercy Hospital

Vivekanand Singh

Children's Mercy Hospital

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P16-Ki67-HMB45 Immunohistochemical Profiling May Help Discriminate Between Spitzoid Melanoma and Atypical Spitz Nevi

Robert Garola, MD and Vivekanand Singh, MD

Background

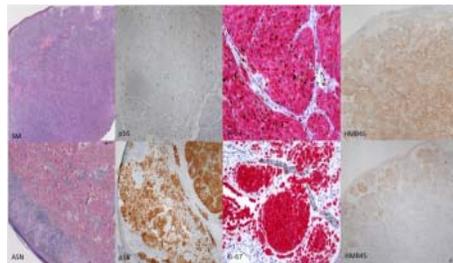
When Spitz nevi have increased vertical thickness (>1.5 MM), show ulceration and deep seated mitosis, the differential diagnostic considerations of atypical Spitz nevus (ASN) or a Spitzoid melanoma (SM) enter into consideration. While expert consultation from a dermatopathologist is most often sought to resolve the differential diagnosis, it could be expensive and time consuming. Recently, the use of molecular genetic testing has also been advocated in the work group up of atypical melanocytic proliferations. On the contrary, immunohistochemistry is a more routinely used technique in most pathology centers may be more simple to apply. A single immunohistochemical marker may not be accurate enough to differentiate benign from malignant melanocytic lesions. Recently, one study (Ref. 1) employed the combination of p16, Ki-67 and HMB45 (PKH) immunohistochemistry on adult melanomas and proposed a combination of the three markers with scoring in discriminating SM and ASN in children. In this study we applied the methodology of the published study to atypical Spitzoid lesions and Spitzoid melanomas.

Methods

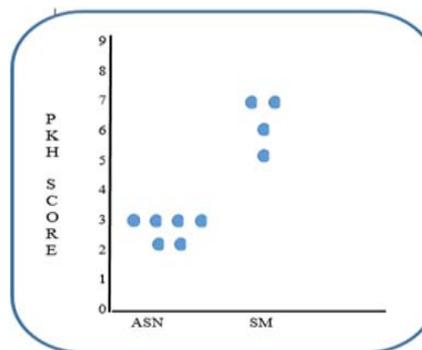
- Institutional review board approval was obtained for this HIPAA-compliant study.
- We retrospectively reviewed 10 cases (4 SM and 6 ASN) from children (age range 1.5-12 years, 6 females and 4 males).
- H&E stained slides and immunohistochemical stains for PKH were independently interpreted by two pathologists.
- The extent of IHC expression in the lesional cells were scored following published criteria comprised as follows:
 - P16 scored as 0; >50% stained cells, 1; 11-50%, 2; 1-10%, 3; 0%
 - Ki-67 scored as 0; <2%, 1; 2-5%, 2; 6-10%, 3; 11-20%, 4; >20%
 - HMB45 scored as 0; gradient present, 1, doubtful/inconclusive gradient, 2; gradient absent
- The total PKH score for the combination of the 3 antibodies for any case could vary from 0 to 9.

Results

- Four cases of SM had total PKH scores: 7, 6, 7 and 5.
- Six cases of ASN had PKH scores of 3, 2, 3, 2, 3 and 3.
- In our study all cases of SM had a total score of >4 and all ASN scored <4.
- HMB45 was completely negative in one case each of SM and ASN.
- Where aCGH was done, heterozygous loss of 9p correlated well with low P16 immunostain positive cell numbers in one case.



Each case three parameters scoring				
Type	p16	Ki-67	HMB45	PKH Score
SM	1	2	2	5
SM	2	3	2	7
SM	0	4	2	6
SM	2	4	1	7
ASN	0	2	1	3
ASN	0	0	2	2
ASN	0	2	1	3
ASN	0	2	0	2
ASN	2	0	1	3
ASN	3	0	0	3



Conclusions

- Our study replicates the findings of the published study of adult melanomas and nevi that showed a total PKH score of equal/or>4 is seen in melanoma.
- A single immunostain could be misleading as Ki-67 labeling index tended to be higher in young children (<2 years of age) and HMB45 was occasionally negative in both ASN and SM, and P16 could be completely lost in ASN.
- We suggest routine use of PKH immunohistochemistry in the work up of atypical Spitzoid lesions in children.

References

- Uguen, A., et al. A p16-Ki-HMB45 immunohistochemistry scoring system as an ancillary diagnostic tool in the diagnosis of melanoma. *Diag Pathol* 2015; 10: 195-1005.

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