The influence of p16 immunohistochemistry on diagnosis and management recommendation of melanocytic neoplasms by dermatopathologists: A single institution prospective study

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INTRODUCTION

- Early diagnosis of melanoma is imperative for improved survival
- The diagnosis of melanoma is based on histopathologic evaluation but lacks interobserver agreement in up to 10-25% of cases[1], showing the diagnostic difficulty in a subset of melanocytic neoplasms
- Improved molecular diagnostic markers are needed, which may impact diagnosis and treatment recommendations[2]
- p16, the protein product of *CDKN2A*, is a gene frequently mutated in melanomagenesis[3,4]
- p16 immunohistochemistry (IHC) is becoming a commonly used marker for evaluating challenging melanocytic neoplasms
- Prospective studies on the impact of p16 IHC on the diagnosis, diagnostic confidence, and treatment recommendations by dermatopathologists of melanocytic neoplasms are lacking

AIM

- The aim of the study was to determine the impact of p16 immunohistochemistry stain on dermatopathologists' diagnosis, diagnostic confidence, and treatment recommendations of melanocytic neoplasms

MATERIALS AND METHODS

- Institutional Review Board approval was obtained at University of California Davis prior to the initiation of the study
- All three board-certified dermatopathologists at the University of California, Davis participated in the study
- All cases of melanocytic neoplasms between October 2017 and June 2019 where a dermatopathologist ordered a p16 IHC stain were prospectively included
- For each case, the dermatopathologist completed a survey to assess their favored diagnosis, diagnostic confidence, and treatment recommendation before and after the p16 IHC stain (Figure 1)

MATERIALS AND METHODS

- Exclusion criteria included if p16 was obtained for non-melanocytic neoplasms or if the pre- or post-test survey was not returned
- Changes in diagnosis, confidence in diagnosis, and treatment recommendations were calculated
- Two and three category change indicator variables were generated based on the values of the difference, *i.e.*, changed (difference $\neq 0$) and unchanged (difference = 0) and no change (difference = 0), upgrade (difference > 0) and downgrade (difference < 0) changes
- Frequency tables were generated to show the proportions of cases with or without changes
- Chi-squared test or Fischer's exact test (if any cell <5) were used to explore the association of confidence with consultation

RESULTS

- There were 84 cases with a response rate of 88% (74/84), of which 81% (68/84) met criteria
- Pre- and post-test diagnoses are outlined in Table 1
- Overall, nearly half of the cases (33/68, 48.5%) showed an increase in confidence after the p16 IHC stain (Table 1, Table 2)
- The diagnosis and treatment recommendations changed in 12.5% (8/64) of cases and 17.7% (11/62) of cases, respectively (Table 1, Table 2)
- Notably, 56/65 (86%) cases were shared in consultation, though no association was found with confidence (p=0.7)

Table 1: Pre- and post-test survey characteristics

	Pre-test	Post-test
Diagnosis		
Benign	22/64 (34.4%)	20/64 (31.3%)
Malignant	20/64 (31.3%)	20/64 (31.3%)
Indeterminant	22/64 (34.4%)	24/64 (37.5%)
Confidence		
Very unsure	0/68 (0%)	0/68 (0%)
Unsure	12/68 (17.6%)	2/68 (2.9%)
Somewhat unsure	15/68 (22.1%)	12/68 (17.6%)
Neutral	2/68 (2.9%)	10/68 (14.7%)
Somewhat confident	20/68 (29.4%)	15/68 (22.1%)
Confident	19/68 (27.9%)	26/68 (38.2%)
Very confident	0/68 (0%)	3/68 (4.4%)
Treatment recommendation		
No further treatment necessary; Close clinical surveillance	20/62 (32.3%)	17/62 (27.4%)
Excision; Wide local excision; Evaluation for metastasis and/or sentinel node biopsy	42/62 (67.7%)	45/62 (72.6%)

Table 2: Post-test survey changes

Diagnosis change	
Benign to malignant	0
Malignant to benign	0
Benign to indeterminant	4
Indeterminant to benign	2
Malignant to indeterminant	1
Indeterminant to malignant	1
Confidence change	
No change	34
Increased	33
Decreased	1
Treatment recommendation change	
No change	51
More aggressive	7
Less aggressive	4

CONCLUSIONS

- Our study found that obtaining a p16 IHC stain for ambiguous melanocytic neoplasms correlated with increased diagnostic confidence
- This supports the notion that utilization of ancillary tests may increase diagnostic accuracy of challenging melanocytic neoplasms
- IHC staining is readily available and commonly used in most dermatopathology laboratories, though validation studies are rarely published and often lab-specific
- Most cases were shared with other pathologists in consultation, likely creating an additional influence on the diagnostic confidence, especially given the known benefit that expert review has on the diagnosis of melanocytic neoplasms[5]
- While prospective, our study is limited by the number of participating pathologists at a single institution
- Therefore, further studies are warranted in multiple clinical settings and institutions to assess for any possible differences

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ACKNOWLEDGEMENTS

The authors are grateful to Candie Westwood-Olmstead, Cesar Garcia and Tenille Baker for their support in this study.