Diagnostic Utility and Comparative Immunohistochemical Analysis of MITF and SOX10 in Melanoma In-Situ: A Clinicopathological and Immunohistochemical Study of 50 Cases

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Introduction

Pigmented actinic keratosis is one of the simulators of early melanoma in situ from severely sun-damaged skin. Close inspection of H&E stained section does not always allow an unequivocal diagnosis, because it is sometimes difficult to distinguish pigmented keratinocytes from melanocytes. We have recently encountered lesions with subtle features of actinic keratosis where we were unable to exclude a superimposed melanoma in situ. The diagnosis of melanoma in situ may be challenging on purely histological grounds, especially in cases in which there is minimal tissue available for inspection.

Sry-related HMG-BOX gene 10 (SOX10) is a transcription factor involved in the development of melanocytes. Microphthalmia-associated transcription factor (MITF) is a regulator of melanocyte development, differentiation, and survival. Both MITF and SOX10 are nuclear immunostains, facilitating diagnosis over cytoplasmic staining as in other melanocytic markers such as MART-1. In small tissue samples MART-1 can create diagnostic confusion, especially in cases where there is extensive melanocytic hyperplasia associated with actinic damage, as melanocytes show a cytoplasmic membranous staining and pigmented keratinocytes may show also a false positive cytoplasmic staining.

The purpose of this study was to compare the immunohistochemical staining characteristics of MITF and SOX10 in cases of melanoma in-situ and actinic keratosis with intraepidermal melanocytic hyperplasia to characterize their immunoprofile and diagnostic utility.

Materials and Methods

Seventy cases, including 50 melanoma in-situ and 20 actinic keratosis with melanocytic hyperplasia were the basis of our study. Cases were collected from the dermatopathology files at the Medical College of Wisconsin and MD Anderson Cancer Center. All tissues were fixed in neutral buffered formalin and embedded in paraffin for histologic processing. Sections were stained in hematoxylin and eosin (H&E) for routine histopathological evaluation. Representative paraffin-embedded tissue blocks were cut and processed for immunohistochemical studies.

From 1 to 5 histologic sections stained with hematoxylin and eosin (H&E) were analyzed in each case. Immunohistochemical staining was performed in a DAKO autostainer using a standard ABC method (avidin-biotin peroxidase complex technique). Heat-induced epitope retrieval was applied as pre-treatment for selected markers. The chromogen, diaminobenzidine, was utilized for antigen localization. The antibodies employed were MITF and SOX10. Appropriate positive and negative controls were run concurrently for each marker tested.

Results

Melanoma in-situ

Fifty cases of melanoma in-situ including both superficial spreading and lentigo maligna were analyzed (M:F 0.72:1, average age: 58.8).

The cases of melanoma in-situ were characterized by a wide intradermal melanocytic lesion composed of asymmetric growth, single cell proliferation, pagetoid upward migration, atypical nests and melanocytes with severe cytologic atypia.

All cases of melanoma in-situ showed strong nuclear positivity for MITF and SOX10 (50/50) in a confluent distribution. The proportion of atypical melanocytes with SOX10 showing strong nuclear positivity was variable, and did not approach that seen in MITF.

Actinic Keratosis

Twenty cases of actinic keratosis were analyzed (M:F 1.5:1, average age: 70.7).

The cases of actinic keratosis were characterized by basal layer atypia of the keratinocytes, focal parakeratosis, and dermal solar elastosis with several cases exhibiting intraepithelial melanocytic hyperplasia, which in smaller samples were difficult to distinguish from an incipient melanoma in situ.

There was scattered cytoplasmic false positive staining for both MITF and SOX10 in the pigmented keratinocytes. In cases where there was intraepithelial melanocytic hyperplasia, the melanocytes showed strong nuclear positivity but melanocytes were mostly present at the lower levels of epidermis and were equidistant from each other.

Conclusion

In summary, MITF exhibits superior sensitivity over SOX10 in cases of melanoma in-situ. In addition, both MITF and SOX10 can be used to accurately differentiate melanoma in-situ from actinic keratosis with intraepidermal melanocytic hyperplasia.

MITF is an effective immunostain for the identification and quantification of melanocytes in the setting of melanoma in-situ, especially in cases where there is limited tissue and in cases where there is actinic damage with intraepidermal melanocytic hyperplasia.