P75 nerve growth factor receptor staining is superior to S100 in identifying spindle cell and desmoplastic melanoma

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Background: Spindle cell melanoma (SCM) including desmoplastic melanoma (DM) is a rare variant of malignant melanoma that may present diagnostic difficulties particularly when staining with S100 is negative, weak, focal, or a combination of these. Conventional melanocytic markers in SCM are usually negative.

Objective: We sought to compare the staining of p75 nerve growth factor receptor (NGF-R) and S100 in SCMs.

Methods: We evaluated the staining of p75 NGF-R and S100 in 13 cases of SCMs: 3 SCMs without desmoplasia, 5 pure DMs, and 5 combined DMs with a conventional component.

Results: Staining with p75 NGF-R was positive in 13 of 13 (100%) cases of SCMs. In 3 cases the intensity of staining and the percentage of cells staining with this marker were greater than those with S100. One case of SCM was negative for S100 but demonstrated strong expression of p75 NGF-R. One case was focally and weakly positive with S100 but expressed strong positive staining with p75 NGF-R. Absence of staining with p75 NGF-R was noted in the conventional round cell component of two of 5 (40%) combined DMs whereas the same areas were strongly positive for human melanoma black (HMB)-45 and Melan-A. In 5 of 5 (100%) cases of combined DMs the desmoplastic component stained positive with p75 NGF-R, demonstrating an inverse relationship with the staining of conventional melanocytic markers.

Limitations: Small study size was a limitation.

Conclusion: p75 NGF-R exhibits superior staining characteristics and greater sensitivity in identifying SCM and DMs than S100. P75 NGF-R may be a useful diagnostic and ancillary stain in addition to S100. (J Am Acad Dermatol 2010;63:852-8.)

Key words: desmoplastic; desmoplastic melanoma; nerve growth factor receptor; p75; spindle cell melanoma.

Spindle cell melanoma (SCM) is an uncommon variant of malignant melanoma. Desmoplastic melanoma (DM) is an uncommon but distinct variant of SCM accounting for only 1% of all subtypes of melanoma.[1] On histologic examination both SCM and DM are composed of spindle melanocytes frequently extending deep into the dermis and subcutaneous tissue in a fascicular pattern. The tumor cells infiltrating the dermis show variable pleomorphism, are often cytologically bland, and have a low mitotic index. In DM the malignant cells are surrounded by a densely fibrotic or collagenous stroma and may exhibit neurotropic tendencies.[2-5] Many but not all SCMs and DMs have an associated atypical intraepidermal melanocytic component.[6]

Abbreviations used:

DM:	desmoplastic melanoma
HMB:	human melanoma black
NGF-R:	nerve growth factor receptor
SCM:	spindle cell melanoma

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SCM and DM remain a diagnostic pitfall for both clinicians and histopathologists leading to delays in diagnosis, recurrences, poor outcome, and, often, legal complications. As SCM and DM often pose a diagnostic challenge on routine histology, using immunohistochemistry is critical in arriving at the correct diagnosis. Melanocytic markers such as human melanoma black (HMB)-45, tyrosinase, and Melan-A stain the melanocytes of conventional melanoma. However, they are frequently negative in DM.[7] It is well known that S100 protein is a highly sensitive marker for malignant melanoma including the spindle cell variants. Recent studies have shown that approximately 10% of DMs exhibit nonuniform weak staining or may not stain at all with this marker.[8-10] In this scenario an additional marker that may be used to confirm the diagnosis of SCM or DM would be of paramount importance.

CAPSULE SUMMARY

- P75 nerve growth factor receptor is a superior stain compared with S100 for identifying spindle cell and desmoplastic melanoma.
- P75 nerve growth factor receptor is a useful confirmatory immunohistochemical stain in addition to S100 in cases of spindle cell and desmoplastic melanoma.
- P75 nerve growth factor receptor and S100 should be used together to increase their diagnostic sensitivity and to assure more reliable and accurate diagnosis.

Reports of p75 nerve growth factor receptor (NGF-R) expression in SCM and DMs have raised the possibility of its usefulness as an ancillary stain to S100.[10-14] The purpose of our study was to compare the staining of p75 NGF-R and S100 in SCM and DM.

METHODS

We reviewed all cases of SCM in a 19-year period from the files of Yale Dermatopathology Laboratory, New Haven, CT. This yielded 11 cases of SCM on which tissue was available for immunohistochemical analysis, all of which were included in the study. Two additional cases from the Department of Dermatology, University of Cologne, Germany, were also included in the study. Five of the 13 cases were pure DMs, 3 were SCMs without desmoplasia, and 5 were combined DMs as defined by Busam at al,[15] in which densely cellular tumor foci without stromal fibrosis constituted more than 10% of the tumor in conjunction with classic DM histology comprising greater than 10% but less than 90% of the entire tumor. All tumors were diagnosed according to established histologic criteria. We also compared the staining of p75 NGF-R and S100 in 20 cases of immature scars.

Immunohistochemical studies were performed on 4-μm formalin-fixed paraffin-embedded sections using an autostainer (Dako, Carpinteria, CA) with the antibodies summarized in Table I and the Labeled Strep Avidin Biotin 2 kit (Dako). Epitope retrieval methods were used to optimize immunoreactivity for all antibodies via Heat-induced Epitope Retrieval pH6.0 (Dako). For this study we used prediluted S100 polyclonal rabbit antibody (Dako). We coupled this with a peroxidase blocking kit and the lsab2 detection kit with diaminobenzidine as a chromogen (Dako). Appropriate negative and positive controls were included. Staining of the outer root sheath epithelium, peripheral nerves, and perivascular cells was used as internal positive control for p75 NGF-R.

The staining results were reported as a Staining Intensity Score on a scale of 0 to 9. Scores were calculated by multiplying a score for staining intensity (0 = negative, 1 = weak, 2 = moderate, 3 = strong) by a score of 0 to 3 of the percentage of cells staining: 0 (no cells staining), 1 (<10% of cells staining), 2 (10%-50% of cells staining), and 3 (>50% of cells staining).

RESULTS

The clinical and histopathologic characteristics of the cases are summarized in Table II. The age of the patients ranged from 67 to 99 years (median 83 years). The locations included scalp, face, upper extremity, back, neck, and shoulder. The male to female ratio was 3:1. The melanomas were Clark levels IV and V and Breslow thickness ranged from 1.5 to 10 mm (median 4.5 mm). Ten of the 13 SCMs had associated lentigo maligna (melanoma in situ). Expression of S100, Melan-A, HMB-45, p75 NGF-R, and Ki-67 in SCMs is summarized in Tables III and IV.

All cases, 13 of 13 (100%), of SCM and DM stained strongly positive for p75 NGF-R whereas 12 of 13 (92%) stained positive for S100. Case 2, one of 13 (8%), was negative for S100 (Fig 1). Case 13 was only weakly and focally positive for S100 (Fig 2). In these two cases with minimal or no expression of S100 the majority of the malignant spindle cells stained intensely positive with p75 NGF-R (Figs 1 and 2). In 3 cases the intensity of staining and the percentage of cells staining with p75 NGF-R were both quantitatively and qualitatively superior to S100 and demonstrated a higher Staining Intensity Score (Table IV).