Use of MITF (Microphthalmia-Associated Transcription Factor) Immunostain for Diagnosis of Desmoplastic Melanoma

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Citation

Abstract
We are reporting a case of desmoplastic malignant melanoma that was confirmed by immunostaining for microphthalmia-associated transcription factor (MITF). A brief review of utility of MITF for diagnosis of melanoma is presented.

CASE REPORT
An 81-year-old male presented with a posterior parietal scalp lesion measuring 9 mm in greatest dimension. The lesion was a yellow crusted raised nodule presenting for an unknown period of time. Examination of the face, anterior neck, scalp, forearms and hands revealed multiple scaling and erythematosus macules consistent with actinic keratosis.

The biopsied lesion of the scalp showed a dermal spindle cell malignant neoplasm extending from the basal membrane to the deep margin of biopsy. The epidermis showed acute neutrophilic keratitis, crusting, and hyperkeratosis but no ulceration or epidermal dysplasia [Fig 1]. The dermal neoplastic cells showed significant polymorphism with dark hyperchromatic nuclei and prominent enlarged nucleoli with perinucleolar halo [Fig 2]. There was marked desmoplastic reaction in the dermis with spindle or ovoid neoplastic cells evenly distributed among the fibroelastic and vascular stroma. Numerous mitoses and atypical mitoses were identified. The neoplastic cells were strongly positive for S-100 [Fig 4] and MITF [Fig 5] but were negative for HMB-45 and Mart-1 [Fig 3].
FIGURE 3
Figure 3: Immunostains, HMB-45 and Mart-1 are negative for melanoma

FIGURE 4
Figure 4: Immunostain, S-100 is positive for desmoplastic melanoma

FIGURE 5
Figure 5: Immunostain, MITF is positive for desmoplastic melanoma

DISCUSSION
Melanoma is the most serious form of skin cancer. Although it accounts for only 4 percent of all dermatologic cancers, it is responsible for 80 percent of deaths from skin malignancy. Melanoma can be categorized into five basic types: superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma, acral lentiginous melanoma, and desmoplastic melanoma. Superficial spreading melanoma is the most common type of melanoma, accounting for 70% of melanoma cases in United States. As its name indicates, it grows superficially and develops irregular borders with a variegated color including white, pink, brown, and black.

Nodular melanoma is the most aggressive type of melanoma, accounts for about 15% of all melanoma in United States. It has unique features compared with other type of melanoma: 1) it tends to grow more rapidly in thickness, 2) may not have obvious developmental stage, 3) lentigo maligna melanoma occurs mostly on sun-damaged skin, especially on the face, neck. This melanoma may mimic benign “age spot” or “sun spot” so it could go undetected for many years. Acral lentiginous melanoma is also called “hidden melanoma” because it is located on the palms, soles, mucous membranes, and underneath nail. It is often overlooked until it is well advanced because in the early stages, it often looks like a bruise or nail streak, even plantar wart.

Desmoplastic melanoma is a rare subtype of melanoma and is usually found on the head and neck region as a spreading plaque. Sometimes, the desmoplastic melanoma is found only in the recurrence or in the metastases of more common types of melanoma. Desmoplastic melanoma has a male predominance ratio of approximately 2:1. Approximately one half of desmoplastic melanomas develop in association with a lentigo maligna. Desmoplastic melanoma may present clinically as a pigmented macule with or without a nodular component or a flesh-colored nodule without any surrounding pigmentation. Desmoplastic melanomas often spread perineurally causing pain. Most desmoplastic melanomas are deeply invasive at the time of diagnosis.

Microscopically, desmoplastic melanoma appears as a poorly circumscribed neoplasm of variable size, that in some cases extend into subcutaneous tissue, fascia and nerves. It is characterized by dermal and/or subcutaneous infiltrates of spindle-shaped cells arranged singly or in thin fascicles within a prominent collagenous or, less commonly, myxoid stroma. The overlying epidermis may or may not show any melanocytic nesting or dysplasia. Routine immunostaining
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by HMB-45 and MART-1 is usually negative. The spindle neoplastic cells are usually positive for S-100 protein indicating a neural or melanocytic type of cell. The melanocytic nature of the cells can be confirmed by positive staining for MITF.

Microphthalmia-associated transcription factor (MITF) is a melanocyte-specific transcriptional factor that plays a key role in melanocyte development, survival and differentiation. MITF appears to contribute to melanocyte survival by increasing the expression of the BCL-2 gene, a key antiapoptotic component. It also regulates the transcription of silver homologue (SILV) the melanocytic-specific genes melan-A (MLANA), whose immunohistochemical detection points to the diagnosis of melanoma. Malignant melanocytic cells possess increased copy number of MITF locus. This increase is accompanied by the amplification of the MITF protein, which subsequently enhances the expression of BCL-2 gene [1]. King et al [2] first reported that 100% malignant melanoma cells stained positively for MITF with a nuclear pattern of reactivity. MITF staining was positive for 76 specimens of melanoma that failed to stain for either HMB-45 or S-100. We recently reported a case of nodular malignant melanoma that was positive only for MITF [3]. Additional published articles [4, 5] also demonstrate that MITF is a more sensitive and specific tumor marker than traditional HMB-45 or S-100. MITF also has shown excellent sensitivity for desmoplastic/spindle-cell melanoma [6].

In our case, the presence of infiltrating pleomorphic neoplastic cells that stained positively for S-100 protein within a markedly desmoplastic stroma suggested a possible desmoplastic melanoma. MITF, a nuclear stain for melanoma cells were positive in the neoplastic cells suggesting that the neoplastic spindle cells were melanocytic rather than neural type.

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References
3. Wang JF, Sarma DP, Ulmer P. Diagnostic dilemma: HMB-45 and Melan-A negative tumor, can it be still a melanoma?: MITF (Microphthalmia-associated transcription factor) stain may confirm the diagnosis. The Internet Journal of Dermatology Volume 5 Number 1, 2007
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