THE IMPORTANCE OF USING SOX10 FOR EXACT DIAGNOSIS OF DESMOPLASTIC MELANOMA

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Abstract

Desmoplastic malignant melanoma is a rare variant of spindle cell melanoma commonly seen in older adults on sun-exposed areas. It accounts for 1–4 % of all cases of cutaneous melanoma. The common location of the desmoplastic melanoma is the head and neck region, whereas other sites are less common. A 45-year-old male presented with an proliferative growth on nose, after a trauma that was diagnosed as tumor. Histopathological examination with the help of wide panel of immunohistochemical methods and with emphasis on SOX10, was, after a broad differential diagnosis concluded as a desmoplastic melanoma.

Key words: desmoplastic melanoma, spindle-cell variant, immunohistochemistry, SOX10, differential diagnosis

INTRODUCTION

Desmoplastic melanoma (DM) is a variant of spindle cell melanoma in which the malignant cells are separated by collagen fibers or fibrous stroma. DM account for 1–4 % of melanomas in populations with a predominance of pale-skinned individuals. As is the case with other melanoma subtypes, males are more often affected, with a male-to-female ratio of 1.75 : 1. The median age at diagnosis (cca 65 years) is slightly higher for desmoplastic melanoma for the most common melanoma subtypes. Clinical, epidemiological, and genomic findings, including the common localisation of DM in severely sun-damaged skin, very high mutation load, and UV radiation mutation signatures, implicate UV irradiation as the predominant etiological agent in the majority of cases. DM most commonly involves chronically sun-exposed skin, most frequently that on the head and neck region (including nose and lip). In men, the ears and bald scalp are commonly affected. However, these tumours can also occur in sites with minimal or no evidence of UV radiation-induced damage (1). Early correct diagnosis of desmoplastic melanoma is associated with a favourable outcome because of its slow growing nature, although most of the cases present in later stages.

CASE REPORT

A 45-year-old male patient was referred for surgical therapy. Pathologic lesion was clinically painless, 11 mm small, irregular, seminodular tumor in the skin of the nasal radix.

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He had a history of trauma at the tumor site. This scar-like skin thickening without pigmentation, was evaluated by a surgeon as a scar, basal cell carcinoma, dermatofibroma, or other lesion. Biopsies of these lesions were reported as infiltrative dermal spindle-shaped cells resembles fibroblasts or myofibroblasts in and between fine collagen bundles. Distribution of spindle cells was haphazard, but the cells occasionally form paralel bundles or storiform areas (Fig. 1). The overlying epidermis was thin and adjacent superficial dermis showed solar elastosis. Characteristically, there are accompanying small or moderate aggregates of lymphocytes. The cytological atypia of spindle cells usually varies from minimal to moderate. A few lager or more-elangated hyperchromatic nuclei were presented. The mitotic index was 9/1 mm² using method for PHH3 (Fig. 2). The Breslow index was greater than 2 mm histologically and dermatoscopically (2).

Fig. 1 Desmoplastic melanoma. The increased cellularity in the dermis is mainly due to spindled melanocytes (HE, 120x)

Fig. 2 Desmoplastic melanoma. Mitotic figure and marked nuclear atypia within spindled, malignant cells (HE, 480x)

Lesions and changes such as lentigo maligna described in literature were not present in our examination. Neurotropism, as a characteristic feature of DM, was not found, first because of shallowness of, excision (3). The tumor cells was positive for S-100 protein (Fig. 3), vimentin and focal for SMA. Negative result was examined for Melan A (MART1), HMB-45, CD34, CD10. In the second step, we used the SOX10 method for differential diagnostics. We found high nuclear positivity of this marker in the spindle cell population of the tumor (Fig. 4). This examination helped to resolve varied differential-diagnostic embarrassment and close the case as desmoplastic melanoma (4). Further immunohistochemical examinations are presented in tab. 1 and tab. 2.

Fig. 3 Desmoplastic melanoma. S-100 protein positivity of spindle malignant cells (S-100 protein, 120x)

Fig. 4 Desmoplastic melanoma. SOX10 nuclear positivity of malignant cells. The most important differential diagnostic factor.

Table 1. Immunohistochemical methods used in diagnosis of desmoplastic melanoma and their findings

EPITHELIAL MARKERS		MESENCHYMAL MARKERS		NEURO/MELANOMA MARKERS		OTHER (PROLIFERATIVE OR PROGNOSTIC MARKERS)	
Cytokeratins EMA	Negat. Negat.	Vimentin Desmin MSA SMA CD31 CD34	Positive Negat. Negat. Fok. positive Negat. Negat.	S-100 MelanA HMB45 CD56 SOX10	Positive Negat. Negat. Negat. Positive	PHH3 MIB-1	9/1 mm² Positive (cca 35%)

Legend: Positivity (bold) or negativity of the tumorous spindle cell. Abbreviations in the table are commonly used in the practice. (all antigens are from Fa DAKO)

Table 2. Markers for differential diagnosis of spindle cell tumors. Loosely adapted to Liu, Liu 2014 (9)

Tumours	CK	S-100	Vim	SMA	DES	CD34	SOX 10
DFSP	–	–	+	–	–	+	–
Fibrosarcoma	–	–	+	–	–	–	–
Kaposi’s sarcoma	–	–	+	–	–	+/–	–
Neuro- tumours	–	+	+	–	–	–	+/–
SFT	–	–	+	–	–	+	–
Smooth muscle tumours	–	–	+	+	+	–	–
Spindle cell carcinoma	+	–	+/–	–	–	–	–
Desmoplastic melanoma	–	+	+	–/+	–	–	+

Legend: CK – cytokeratins, Vim – vimentin, SMA – smooth muscle actin, Des – desmin, DFSP – dermatofibrosarcoma protuberans, SFT – solitary fibrous tumor

DISCUSSION

The diagnosis of DM is complicated when only a superficial biopsy is available, as was in our case. The lesion is commonly misdiagnosed as a reactive process, for example superficial nodular fascitis, fibromatosis, and scars, which threatened our patient who had a history of injury. Scar tissue may be a particular problem, especially in recurrent lesions. Pointers toward the latter include horizontal orientation of the fibroblast population, absence of adnexa, loss of the rete – ridges pattern, and vertically oriented dermal blood vessels. Examples showing storiform or “herringbone” morphology have sometimes been confused with atypical fibrous histiocytoma, dermatofibroma protuberans, or fibrosarcoma (5). Of interest was the tumor cell positivity using mesenchymal SMA otherwise antigen supporting myofibrous origin of the cells. This mood has been noticed in diagnosis by several authors and is explained by the presence of myofibroblasts in DM tumor tissue (6). Sry-related HMG-BOX gene 10 (SOX10) is a nuclear transcription factor that plays an important role in schwannian and melanocytic cell differentiation, it has recently been shown to be a

useful marker in the diagnosis of melanocytic and schwannian tumors. This staining supports evidence of a common embryonic origin of these cells. Fibroblasts and histiocytes that could histopathologically mimic melanoma cells often express S100 protein, which complicates the evaluation of melanoma excision specimens for residual tumor. Distinguishing melanoma cells from immature fibrocytes or histiocytes is made more challenging in desmoplastic melanoma excision specimens. Our results showed that SOX10 was strongly expressed by DM. Furthermore, SOX10 was less likely than S100 protein to be expressed by background fibrocytes and histiocytes within scars (7, 8)

Prognosis and predictive factors for DM tends to be diagnosed at a more advanced local stage than other melanoma subtypes, with a median tumour thickness >2.0 mm in most series. As is the case for other melanoma subtypes, prognosis is worse with increased tumor thickness, increased mitotic rate, male sex, and older age. Our patient was a younger adult, but the mitotic index was higher (9 / 1mm²) (9). However, DMs tend to have a better prognosis than do other melanoma subtypes of similar tumor thickness. Local recurrence are common, in particular after incomplete excision or marginal excision <10mm or when neutropism is present. The excision we investigated was sufficient, without neutropism. Regional node field metastasis is less frequent in DM than in other melanoma subtypes, and lung metastasis is more common as the initial site of metastasis. No distant organ metastases or metastases in biopsy-examined regional lymph nodes were detected in our patient.

CONCLUSION

Desmoplastic melanoma presents diagnostic challenges due to histologic mimics and limited immunohistochemical staining. Although S100 protein usually stains DM, other melanoma markers (HMB-45 and Melan-A) are often negative. Dermal/subcutaneous mimics of DM spindle cell/poorly differentiated squamous cell carcinoma, dermatofibrosarcoma protuberans, fibrosarcoma, Kaposi's sarcoma, other types of spindle cell tumours/ sarcomas show negative or unreliable immunohistochemical staining. Recently, SOX10 expression has shown to be a sensitive and specific marker of DM. Correct histopathologic diagnosis of malignant tumor leads to a successful therapy of the patient (10, 11)

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