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Case Report

A case of desmoplastic melanoma that was difficult to distinguish from malignant peripheral nerve sheath tumor

Kenji Yorita [a,*], Satoka Yoshii [b], Naoto Kuroda [a], Yuichi Senzaki [b], Koji Nakagawa [b], Jun Iwata [c], Takanori Hirose [d], Ichiro Murakami [e]

[a] Department of Diagnostic Pathology, Japanese Red Cross Kochi Hospital, Kochi, Japan
[b] Department of Cosmetic Surgery, Japanese Red Cross Kochi Hospital, Kochi, Japan
[c] Department of Diagnostic Pathology, Kochi Health Sciences Center, Kochi, Japan
[d] Department of Diagnostic Pathology, Hyogo Cancer Center, Hyogo, Japan
[e] Deptartment of Pathology, Kochi Medical School, Kochi, Japan

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ABSTRACT

The clinical and pathological diagnosis of desmoplastic melanoma is difficult, because almost 50% of desmoplastic melanoma cases involve non-pigmented lesions and the tumor cells can resemble fibroblasts or Schwannian cells based on their frequent amelanotic features. Moreover, desmoplastic melanoma typically has low positive rates for melanoma markers, with the exception of the S-100 protein. We report the case of an 81-year-old Japanese man with an 8-mm desmoplastic melanoma. He initially noticed a painless and non-pigmented skin lesion that did not grow noticeably for 6 months. It was unlikely that he had von Recklinghausen disease, and the mass was initially considered a dermatofibroma. Excisional biopsy revealed an intradermal mass, with the superficial portion mimicking neurofibroma and the deeper portion exhibiting nodular growth of sarcomatoid spindle cells. The tumor region lacked intradermal proliferation of atypical melanocytic cells, intracytoplasmic melanin, and expression of melanoma markers (except S-100 protein and Sox10). Although a malignant peripheral nerve sheath tumor derived from neurofibroma was possible, the slow growth with diffuse and strong immunoreactivity to the S-100 protein and Sox10 favored a diagnosis of desmoplastic melanoma. Pathologists should recognize that desmoplastic melanoma may not involve *in situ* lesions or the immunohistochemical expression of standard melanoma markers.

1. Introduction

Desmoplastic melanoma (DM) accounts for 1–4% of all melanomas [1] and is histologically characterized by spindle cells with associated collagen production. DM is usually found in the head and neck region of elderly patients with chronically sun-damaged skin. The clinical and pathological diagnosis of DM is difficult, because almost 50% of cases involve a non-pigmented lesion, the tumor cells are usually amelanotic [1], and the disease can lack an *in situ* component [2]. In addition, the low sensitivity of melanoma markers (except the S-100 protein and Sox10) [3,4] exacerbates the difficulty of histologically diagnosing DM. We recently encountered a case of DM in which the tumor was located at a common site for DM; the tumor did not involve *in situ* melanoma, melanin-laden tumor cells, or immunohistochemical expression of representative melanoma markers, such as melanosome, melan A, microphthalmia transcription factor (MiTF), and tyrosinase. Thus, we report the clinicopathological data from our case and discuss the differential diagnoses, as we experienced difficulty in differentiating the tumor from malignant peripheral nerve sheath tumor (MPNST).

2. Case presentation

An 81-year-old Japanese man was referred to our hospital for the diagnosis and treatment of a forehead mass. He had noticed the lesion 6 months earlier, but the lesion's size had not noticeably changed. The patient's medical history was unremarkable and he did not have a history of melanoma. The tumor's appearance was a slightly erythematous, firm, and non-tender nodule with a maximum diameter of <10 mm and no fixation to the epicranial aponeurosis. The mass was subsequently diagnosed as a dermatofibroma and excisional biopsy was performed. After the pathological diagnosis, no metastasis was found during a radiological examination that included computed tomography

* Corresponding author at: Department of Diagnostic Pathology, Japanese Red Cross Kochi Hospital, 2-13-51, Shinhonmachi, Kochi-city, Kochi 780-8562, Japan.
E-mail address: kenjiyorita@gmail.com (K. Yorita).

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and magnetic resonance imaging. No skin lesions suggestive of malignant melanoma were identified in any other regions. The patient received a 1-year treatment using regional injections of interferon-β to reduce the possibility of local recurrence and metastasis, and remained free from disease for 18 months after the tumor resection.

2.1. Microscopic findings

The extirpated tissue was subjected to hematoxylin and eosin (HE) staining, and we observed that the 8-mm multinodular lesion was mainly located in the dermis (Fig. 1A). The superficial portion exhibited neurofibroma-like features and the deeper portion exhibited a sarcomatous growth pattern of mitotically active spindle cells. The superficial portion had mild-to-moderately atypical spindle cells that were loosely associated with collagen fibers, lymphocyte infiltration, plasma cells, mast cells, and a delicate fibromyxoid stroma (Fig. 1B, C). The deeper portion had increasing pleomorphic spindle cellularity, and the spindle cells had frequent mitotic figures (approximately 6 per 10 high-power fields; Fig. 1D). Some fascicular arrangements of the sarcomatous tumor cells were observed in the deeper portion. The superficial portion had lymphoplasmacytic infiltration and lymphoid aggregates were particularly evident at the periphery (Fig. 1E). We did not observe cytoplasmic melanin, perineural invasion of the tumor cells, intratumoral dense fibrosis, or nuclear palisades. The epidermis covering the lesion was normal (Fig. 1F) and appeared to be spared from the lesion. Solar elastosis in the superficial dermis was mild, and solar keratosis was absent. Malignant spindle cell tumor was suggested, and MPNST arising from the neurofibroma was suspected. The differential diagnoses included spindle cell carcinoma, atypical fibroxanthoma, dermatofibrosarcoma protuberans, and malignant melanoma. Immunohistochemical testing was performed using the BenchMark XT autostainer (Ventana Medical Systems Inc., Arizona), and the antibodies are summarized in Table 1.

The immunohistochemistry findings from the superficial and deep portions revealed spindle cells that were diffusely and strongly positive for the S-100 protein (Fig. 2A, B) and Sox10 (Fig. 2C). However, the specimens were negative for pan-cytokeratin (CAM5.2), keratin 903, CD31, alpha-smooth muscle actin, CD10, factor XIIIa, melanosome, melan A (Fig. 2D, E), tyrosinase, BRAF V600E, neurofilament, Wilms' tumor-1 protein (WT-1), and glypican-3 (GPC3). The tumor cells were nearly negative for MiTF, although several tumor cells were weakly positive (<1%; Fig. 2F). The sarcomatous component was negative for CD34, but 40% of the neurofibroma-like area exhibited fingerprint-like immunostaining for CD34. The sections that were stained using melanoma markers did not exhibit abnormal localization or proliferation of atypical intraepidermal or junctional melanocytes. The resection margin was free from tumor cells, but was close to the edge of the tumor.

Based on these findings, the patient was diagnosed with DM, and we suggest that he had "combined" DM based on the presence of a non-desmoplastic solid component [5]. Spindle-cell melanoma might also be possible, as desmoplasia was inconspicuous within the tumor. After the excisional biopsy, we performed wide resection of the biopsied site, and the pathological testing confirmed that the tumor cells were contained within a peripheral nerve in the subcutaneous tissue, which suggested neurotropism.

Table 1
The antibodies that were used for the immunohistochemistry.

Antigen	Clone	Dilution	Supplier
Pancytokeratin	CAM5.2	Prediluted	Becton Dickinson, CA
Keratin 903	34betaE12	1:200	Enzo, NY
S-100 protein	Polyclonal	1:400	DAKO, Glostrup, Denmark
Sox10	SP267	Prediluted	Roche, Diagnostics
CD31	JC70A	1:40	DAKO, Glostrup, Denmark
CD34	My10	1:20	Becton Dickinson, CA
CD10	56C6	Prediluted	Novocastra Laboratories Ltd., Newcastle, UK
Alpha-smooth muscle actin	1A4	1:3200	DAKO, Glostrup, Denmark
Factor XIIIa	E980.1	Prediluted	Biocare Medical, CA
Melanosome	HMB45	Prediluted	DAKO, Glostrup, Denmark
Melan A	A103	1:25	Novocastra Laboratories Ltd., Newcastle, UK
Tyrosinase	T311	1:200	Cell Signaling Technology, Danvers, MA
MiTF	D5	Prediluted	Thermo Scientific, Fremont, CA
BRAF V600E	VE1	1:50	Spring Bioscience, Pleasanton, CA
Neurofilament	2F11	1:100	DAKO, Glostrup, Denmark
WT-1	6F–H2	1:50	DAKO, Glostrup, Denmark
Glypican-3	1G12	Prediluted	Nichirei, Tokyo, Japan
Ki-67	MIB-1	1:100	DAKO, Glostrup, Denmark

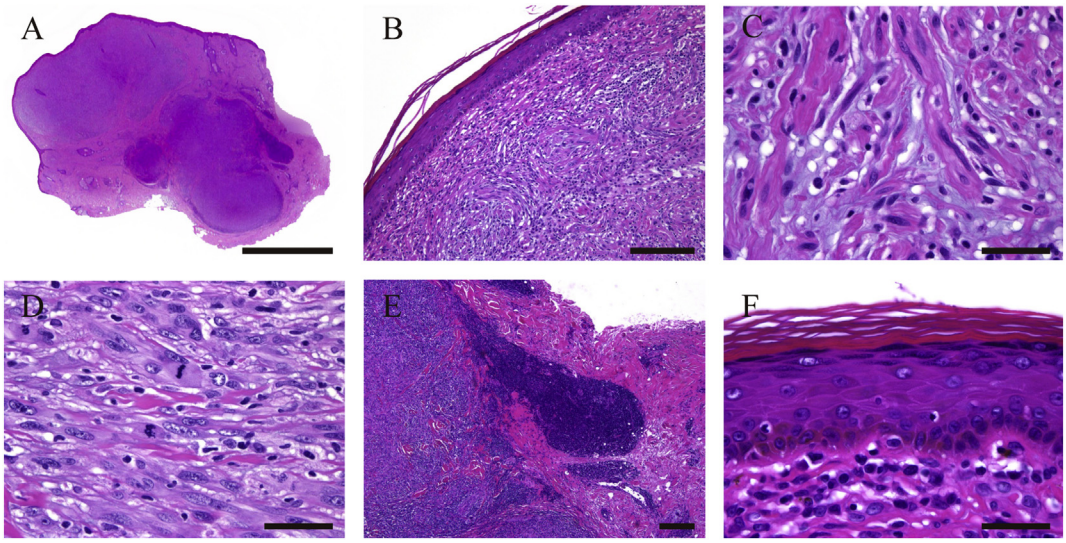

Fig. 1. Histological findings from the specimen of the forehead desmoplastic melanoma. A section stained using hematoxylin-and-eosin reveals the nodular lesion with a somewhat multinodular appearance (A). The superficial portion of the tumor has increased spindle cells with elongated nuclei that are accompanied by basophilic fine fibrils and inflammatory infiltrates (B, C). The deeper portion of the tumor exhibits a sarcomatous growth pattern with pleomorphic spindle cells and frequent mitotic figures (D). The periphery of the tumor has nodular lymphoid aggregates (E). The epidermis covering the tumor appears to be intact (F). Bars represent 2 mm in A; 200 μm in B, E, and F; and 50 μm in C, D, and F.