Pathology – Research and Practice 207 (2011) 728–732

Contents lists available at SciVerse ScienceDirect

Pathology – Research and Practice

journal homepage: www.elsevier.de/prp

Teaching cases

Primary desmoplastic cutaneous leiomyosarcoma associated with high MIB-1 labeling index: A teaching case giving rise to diagnostic difficulties on a small biopsy specimen

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ARTICLE INFO

Article history:
Received 23 May 2011
Received in revised form 1 August 2011
Accepted 29 August 2011

Keywords:
Cutaneous leiomyosarcoma
Desmoplastic variant
Skin
MIB-1

ABSTRACT

A case of primary desmoplastic cutaneous leiomyosarcoma is reported. A flat and elevated tan plaque, measuring 30 mm × 20 mm, was noticed in the left back of a 74-year-old Japanese male 6 months before the resection. The biopsy specimen showed an overgrowth of desmoplastic fibrocollagenous stroma, focally admixed with a less cellular proliferation of spindle cells having mildly pleomorphic nuclei, but no mitotic figures, arranged in small clusters or appearing as individual cells. Based on these features, we interpreted it as a benign keloid-like lesion. A local resection was done, and gross examination revealed a poorly demarcated grayish tumor lesion, replacing the entire dermis and extending into the subcutis. Microscopic findings demonstrated a sparsely cellular proliferation of atypical spindle cells having cigar-shaped or multi-nucleated pleomorphic nuclei and abundant eosinophilic cytoplasm with few mitotic hot spots, arranged in interlacing bundles, alternating with scattered tumor cells within an abundant desmoplastic stroma. Immunohistochemically, these atypical cells were positive for α-smooth muscle actin, HHF-35, desmin, and caldesmon, and MIB-1 labeling index was greater than 10%. Therefore, we finally made a diagnosis of desmoplastic leiomyosarcoma as a very rare variant of cutaneous leiomyosarcoma. We should be aware that owing to its characteristic features, pathologists might misinterpret it as benign when examining only small or inadequate specimens. It is thus suggested that a large panel of antibodies including smooth muscle cell markers and MIB-1 in immunohistochemistry are useful and adjunctive diagnostic aids for recognizing malignancy, especially in diagnostically difficult cases such as ours.

Introduction

Among all soft tissue sarcomas, leiomyosarcomas account for 5–10% [5], whereas leiomyosarcomas of the skin are very rare, accounting for 2–3% of all superficial soft tissue sarcomas [14]. These neoplasms can be divided into three main categories: (i) primary cutaneous (dermal or intradermal) leiomyosarcomas, (ii) subcutaneous leiomyosarcomas, and (iii) secondary leiomyosarcomas arising from retroperitoneal and uterine primary lesions [5,6,18]. To date, more than 100 cases of cutaneous leiomyosarcoma have been reported in the English-language literature, and more than 30 in the Japanese-language literature [1,10,13,17].

According to some authors, we also consider each cutaneous and subcutaneous leiomyosarcoma as a single entity, because the latter has a much higher recurrence rate (50–70%) than the former and can give rise to distant metastases, more similar to their soft tissue counterpart tumors [1,10,13,16]. Moreover, the latter originates from the smooth muscle of the subcutaneous vascular wall, most probably leading to the appearance of a haphazardly intertwining and vascular growth pattern [5,6]. On the other hand, as to the former, the term 'cutaneous' should be restricted to the dermis, often subsequently extending into or invading the subcutis [1,5,8,10,13,17,18]. This might partly cause confusion between these two entities. The cutaneous leiomyosarcomas are believed to derive from the arrector pili muscle in the dermis, and show two different growth patterns: a nodular pattern shows a quite cellular proliferation of atypical smooth muscle cells with nuclear

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doi:10.1016/j.prp.2011.08.008

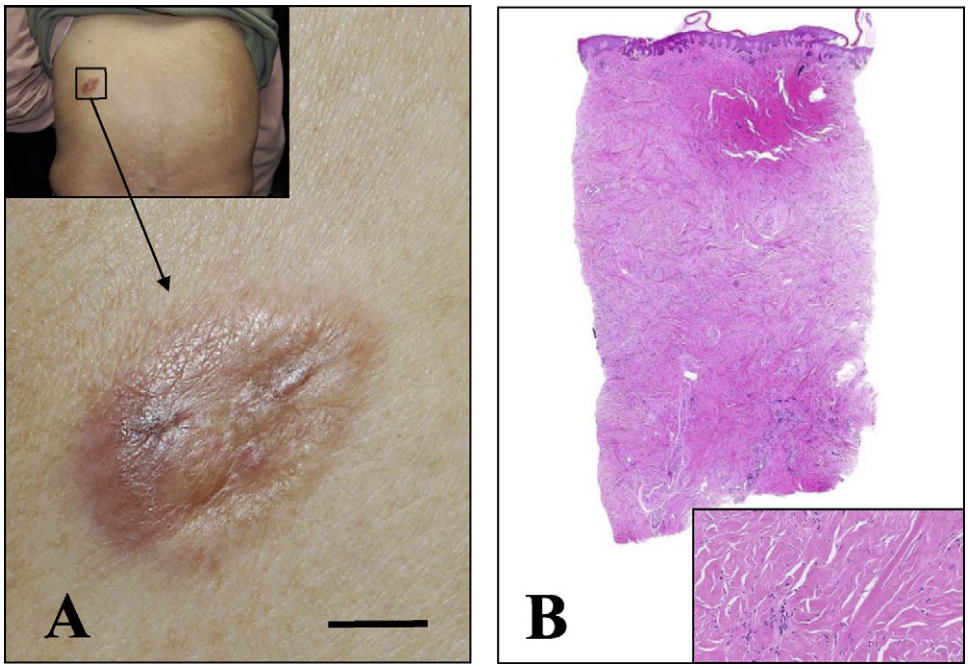

Fig. 1. Clinical finding and microscopic examination of the biopsy specimen. (A) A flat and elevated tan plaque, measuring 30 mm × 20 mm (inset), was recognized in the left back. (B) The biopsy specimen predominantly showed a dermal overgrowth of desmoplastic fibrocollagenous stroma, focally admixed with a less cellular proliferation of spindle cells having sometimes mildly pleomorphic nuclei, but no mitotic figures, arranged in small clusters or appearing as individual cells (H&E stains). Based on these features, we first made a diagnosis of a benign keloid-like lesion. Each bar = 10 mm.

pleomorphism, admixed with pockets of greater mitotic activity, namely mitotic 'hot spots'. The other one is a diffuse pattern displaying less cellular proliferation with well-differentiated tumor cells and very low mitotic activity [5,7,10,13,18]. These tumors are more common between the fifth and seventh decades and occur mostly on the extensor surfaces of the extremities and, to a lesser extent, on the scalp and trunk [6,10,18]. Most of them are solitary, firm, and usually asymptomatic nodules, measuring 0.5–3 cm in diameter when first detected [6,9,18]. Among the cutaneous leiomyosarcomas, desmoplastic leiomyosarcoma is one of the very rare variants, which was first described by Karroum et al. in 1995 [12], and only 6 cases have been reported in the literature [2–4,11,12]. This unique desmoplastic variant clinically presents as an indurated plaque and histologically reveals the presence of tumor cells within an abundant desmoplastic stroma, mimicking other cutaneous desmoplastic lesions [2–4,11,12].

We report an extremely rare case of desmoplastic cutaneous leiomyosarcoma, which originated from the dermis of the left back and involved the dermis to superficial subcutaneous fat as an ill-defined nodular lesion.

Clinical summary

The patient was a 74-year-old Japanese man who had a history of cerebral infarction 2 years ago. There was no history of malignancy, immunosuppressive disorders, use of immunosuppressive medications, or unusual infections.

He noticed a flat and elevated tan plaque, measuring 30 mm × 20 mm, in the left back (Fig. 1A) 6 months before the resection. Since no effects were recognized against the long external application of steroids, a biopsy was performed, followed by a local resection. Moreover, an additional wide resection was done under the diagnosis of desmoplastic cutaneous leiomyosarcoma, based on the histological features of the resected specimen. Laboratory data, including blood cell count and chemistry, were within normal limits, except for modestly low levels of albumin (3.3 g/dL) and hemoglobin (12.1 g/dL), and there was no evidence of tumor or tumor-like lesions in the CT scannings of chest and abdomen. The patient was alive and well at 2 years after the operation.

Pathological findings

The biopsy specimen predominantly showed an overgrowth of desmoplastic fibrocollagenous stroma in the dermis, focally admixed with a less cellular proliferation of spindle cells having sometimes mildly pleomorphic nuclei, but no apparent mitotic figures, arranged in small clusters or as individual cells (Fig. 1B). Based on these features, we first diagnosed it as a benign keloid-like lesion, and an ordinary local resection was performed. On gross examination, the cut surface revealed a solid and whitish to grayish tumor lesion, measuring 28 mm × 7 mm, replacing the entire dermis (Fig. 2A). A scanning magnification of it showed a solid and patchy growth of tumor cells in a cellular or acellular fashion, replacing the upper to lower layer of dermis, including lateral and deep surgical margins, associated with central artifacts due to the previous biopsy (Fig. 2A). Microscopic findings of the sparsely cellular areas demonstrated a proliferation of atypical spindle-shaped stromal cells having hyperchromatic and cigar-shaped pleomorphic nuclei, as well as abundant eosinophilic cytoplasm with few pockets of greater mitotic activity (2 or more mitotic figures per 10 high-power fields), namely mitotic hot spots, arranged in interlacing bundles within an abundant desmoplastic stroma (Fig. 2B). These atypical tumor cells occasionally contained multinucleated giant cells (Fig. 2C). The covering epidermis exhibited mild to moderate acanthosis and elongated thickened rete ridge without any evidence of atypical changes, focally associated with hyperpigmentation in the basal layer, overlying these sparsely proliferating spindle tumor cells blending with a desmoplastic fibrocollagenous stroma in the upper dermis (Fig. 2D). All immunohistochemical stainings below were carried out using Dako Envision kit (Dako Cytomation Co., Tokyo, Japan) according to the manufacturer's instructions. Immunohistochemically, these