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Case Report

Desmoplastic Malignant Melanoma of the Gingiva: Case Report and Review of the Literature

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A rare case of desmoplastic melanoma arising from the maxillary gingiva of a 66-year-old woman is reported. This tumour metastasised to the submandibular lymph node 5 years after extirpation, and local recurrence was observed 2 years later. The gingival tumour showed the histopathological characteristics of desmoplastic melanoma and the metastasised tumour cells were immunohistochemically positive for S-100 protein, neuron specific enolase, HMB-45 highly specific for conventional melanoma, and Fontana–Masson staining. The gingival tumour, originally regarded as benign clinically, was actually a desmoplastic melanoma. Copyright © 1996 Elsevier Science Ltd

Key words: desmoplastic melanoma, gingiva, S-100 protein, NSE, HMB-45

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INTRODUCTION

Conley *et al.*, in 1971 [1], first categorised desmoplastic malignant melanoma (DPM) as a variant of malignant melanoma. Desmoplastic malignant melanoma develops most commonly in the head and neck, but only four DPMs primarily arising from the oral tissues have been reported [2–5]. The benign-looking clinical and histological features occasionally allowed us to consider this disease as a benign tumour [6].

We report here a case of gingival DPM, which clinically appeared to be a pedunculated fibrous epulis, but metastasised to the submandibular lymph node 5 years after extirpation and locally recurred 2 years later. The histological diagnosis of DPM was confirmed by the immunohistochemical analysis using a battery of antibodies.

CASE PRESENTATION

A 66-year-old female visited our clinic in September 1986, with complaints of maxillary gingival swelling and ill-fitting denture. A pedunculated fibrous lesion, measuring 3.5 × 2.5 cm, was found on the right molar gingiva of the edentulous upper jaw (Fig. 1). Its surface was smooth but partially ulcerated by the denture. An X-ray film revealed no local bone resorption. The lesion was simply extirpated under the diagnosis of fibrous epulis.

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In March 1991, the right submandibular lymph node gradually enlarged and the swollen lymph node was extirpated. After that, any involvement of other lymph nodes was not observed.

In January 1994, a pedunculated fibrous tumour was found to recur at the original site. The tumour tip was necrotic and the gingiva around the tumour base was pigmented. The tumour was extirpated with wide resection of the gingiva and the superficial part of the alveolar bone, despite no apparent bone resorption. There has been no evidence of recurrence or metastasis for 20 months following the wide resection.

HISTOPATHOLOGY AND IMMUNOHISTOCHEMISTRY

Histologically, deparaffinised sections from formalin-fixed tissues of the primary, metastatic and recurrent tumours were stained with haematoxylin and eosin, and Masson–Fontana stains. Additional sections were tested with antibodies (Table 1) to S-100 protein, neuron specific enolase (NSE), human melanoma (HMB-45), epithelial membrane antigen (EMA), vimentin, α-smooth muscle actin (α-SMA), cytokeratin (AE1/AE3), human macrophage (KP-1) and chromogranin A, using the avidin–biotin complex method.

Light-microscopically, the primary gingival lesion was composed of spindle cells exhibiting from mild to moderate atypia in dense fibrous tissue beneath the intact epithelium, but nuclear mitoses were less than 1/10 high-power fields (Fig. 2). No apparent pleiomorphism of the

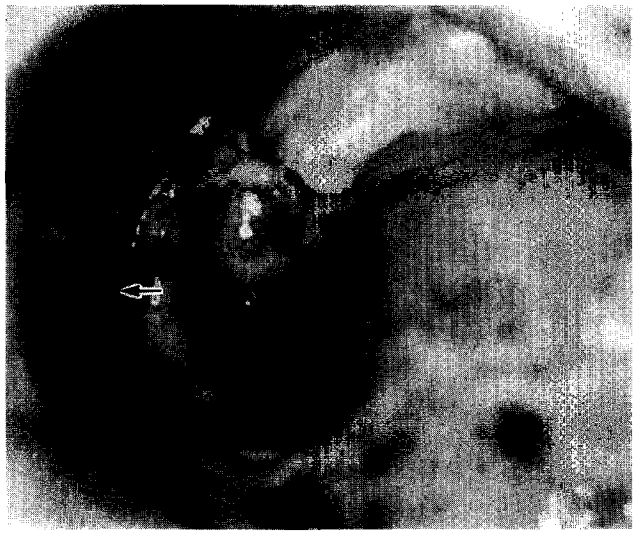

Fig. 1. Macroscopic view of the original tumour. This pedunculated tumour is partly ulcerative (arrow-head) by the denture edge and the ulcerated portion is black because of bleeding (arrow).

Table 1. Results of immunohistochemical staining

	Original tumour	Metastasised lymph node	Recurrent tumour
S-100 protein	+	+	+
NSE	+	+	+
HMB-45	–	++	–
EMA	–	–	–
Vimentin	++	++	++
Fontana–Masson	–	+	–

+ +, Strongly positive; +, weakly positive; –, negative.

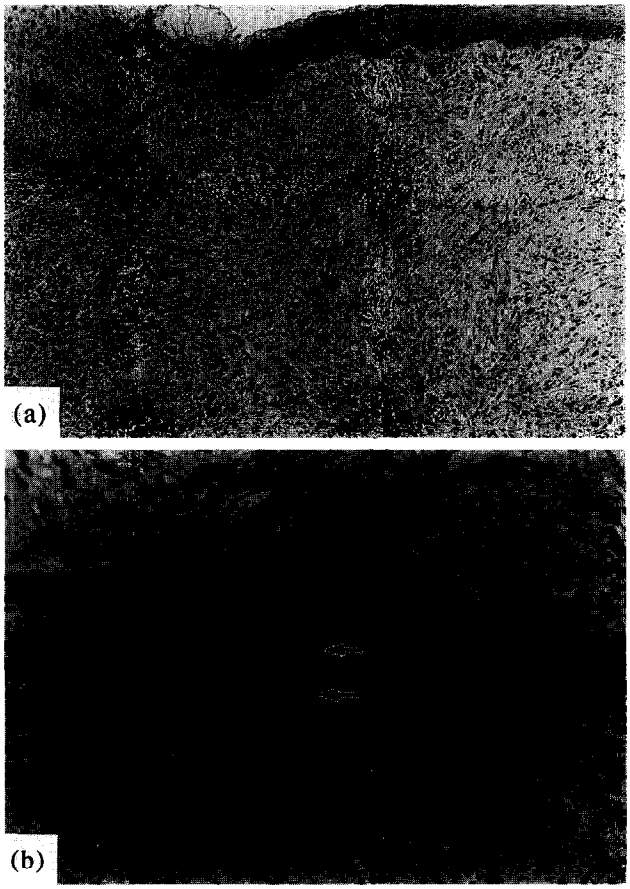

Fig. 2. Microscopic views of the primary gingival tumour. The tumour is encapsulated with the normal epithelium and tumour cells are proliferating in the desmoplastic tissue (a). Spindle cells showing mild atypia (arrow) proliferate with desmoplasia (b). The H-E stain; original magnification, (a) ×40; (b) ×200.

proliferating cells was seen, and Masson–Fontana stain did not demonstrate melanin production of the cells. Immunohistochemically, atypical spindle cells were positive for S-100 protein, NSE and vimentin (Table 2), but negative for the other markers tested. Thus, we diagnosed the lesion as DPM.

The metastatic tumour of the lymph node histologically revealed features of conventional malignant melanomas which consisted of large polygonal tumour cells having marked atypical nuclei with prominent nucleoli (Fig. 3). The tumour cells were positive for HMB-45 as well as S-100 protein and vimentin (Table 2) and occasionally they possessed melanin pigments positive for Masson–Fontana stain. While the recurrent tumour revealed the characteristics of DPM (Fig. 4); atypical spindle cells predominantly proliferated in the fibrous tissue. Although the cellularity became much higher than that of the primary tumour, the immunostaining revealed similarities with those of the primary tumour; positive for S-100 protein, NSE and vimentin, but negative for HMB-45 (Table 2).

Table 2. Immunostaining results in primary, metastatic and recurrent DPMs

Tumour		S-100 protein	NSE	HMB-45	Vimentin
Primary					
	Ours	+	+	–	++
	Kurihara *et al.*	+	+	NE	NE
	Chen JH *et al.*	+	NE	NE	+
Metastatic					
	Ours	+	+	++	++
Recurrent					
	Ours	+	+	–	++
	Kurihara *et al.*	+	–	NE	NE

+ +, Strongly positive; +, weakly positive; –, negative; NE, not examined.

Table 3. Summary of clinical features of oral DPMs reported

Cases reported	Age/sex	Site	Size (cm)	Ulceration	Peduncule	Pigmentation	Clinical diagnosis	First treatment	Local recurrence/ metastasis	Follow-up
1. Batsakis *et al.* (1979) [2]	60/M	Gingiva*	0.5	—	—	—	Fibroma	Simple excision	—/—	ND‡
2. Jain and Allen (1989) [3]	51/M	Buccal mucosa	1.5	ND	ND	—	ND	Simple excision	Intracranial invasion/—	Died (0.3 years)
3. Chen *et al.* (1989) [5]	24/M	Palate	3.0	—	—	—	ND	Simple excision	Widespread after maxilloectomy/—	Died (0.4 years)
4. Kurihara *et al.* (1992) [4]	58/M	Gingiva*	1.5	—	+	—	Epulis	Simple excision	—/—	Alive (2.5 years)
5. Ueta *et al.* (present case)	66/F	Gingiva*	3.5	—	+	—	Epulis	Simple excision	+/+†	Alive (0.9 years)

*Maxillary molar region. †Submandibular lymph node. ‡ND, not descriptive.

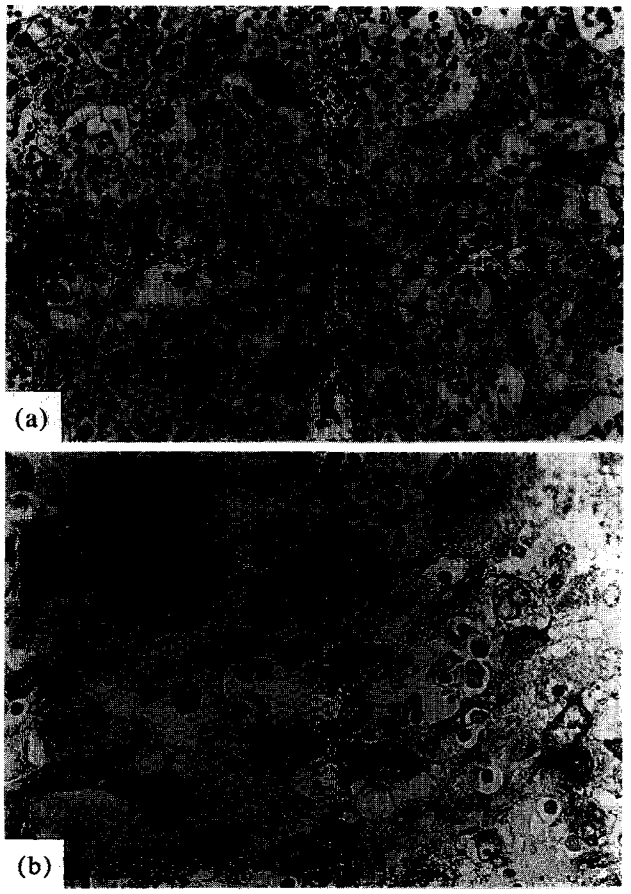

Fig. 3. Microscopic views of the metastasised tumour. The tumour resembles conventional malignant melanoma. (a) The H-E stain; original magnification ×100 and the metastasised tumour is positive for HMB-45. (b) Original magnification ×200.

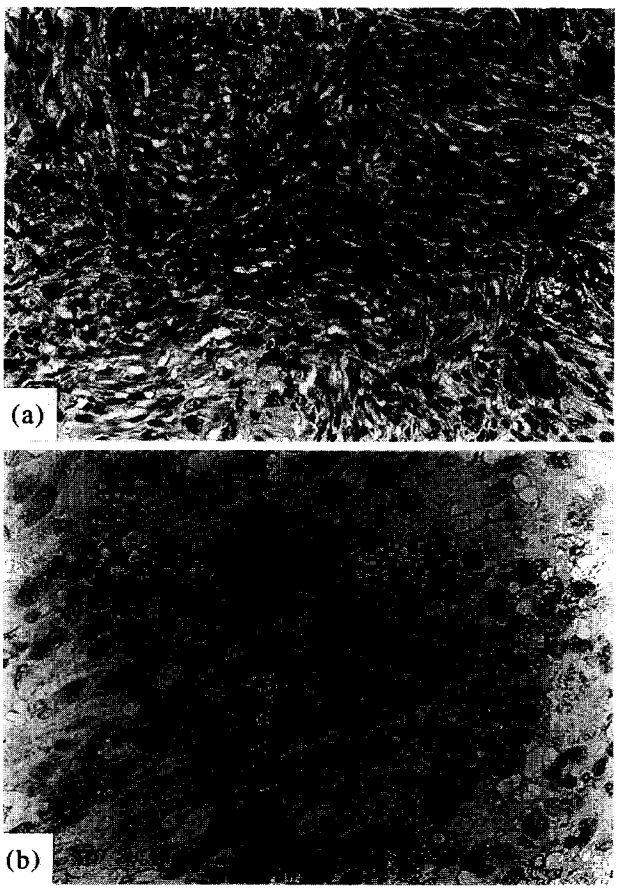

Fig. 4. Microscopic views of the recurred tumour. Tumour cells are more densely proliferating than those in Fig. 2, and nuclear chromatin is prominent. (a) The H-E stain, original magnification ×100. The recurred tumour is positive for S-100 protein. (b) original magnification ×200.

DISCUSSION

Since the first description of Conley *et al.* [1], a number of DPMs have been reported [2–11]. Although DPM frequently occurs in the sun-exposed areas of the head and neck, DPM in the oral cavity is extremely rare [6]. As far as we know, there have been only five DPMs, including our own, in English literature (Table 3). 4 cases were male and 1 female. The patients ranged from 24 to 66 years of age. The tumours were relatively small, measuring from 0.5 to 3.5 cm in diameter. Two tumours were pedunculated, but no tumour was pigmented. Because of the benign-looking clinical features, three DPMs were diagnosed clinically as benign lesions, such as fibroma and epulis, and therefore were simply extirpated. However, regional lymph metastasis and local recurrence occurred occasionally, being similar to those in DPMs arising in the head and neck [6]. The occasional erroneous diagnosis of DPM as a benign fibromatous tumour appears to be caused by the benign-looking clinical and histological features. It should be stressed that immunohistochemical examination is required for the accurate diagnosis of DPM.

Immunohistochemistry using a battery of markers is extremely useful for the diagnosis of DPM [6, 7, 9, 12], although some investigators [5, 6] have ultrastructurally demonstrated premelanosomes. As shown in Table 2, in the 5 cases of DPM of the oral cavity, three primary and two recurrent tumours with one metastatic lesion have been examined. S-100 protein and vimentin were constantly positive, and the positivity for NSE was also observed in tumours except for one recurrent tumour [4]. However, the staining results of keratins are not listed in Table 2 because of the negativity; immunohistochemical detection of keratin appears to be very important for the discrimination of DPM from desmoplastic spindle cell squamous cell carcinoma. Although one metastatic tumour (our case) was positive for HMB-45, others were negative for this antigen. These immunohistochemical results, being similar to those reported by Anstey *et al.* [12], indicate that the identification of DPM should depend on S-100 protein, vimentin and NSE, but not on HMB-45, even though it is specific and the most common antigen for conventional melanoma. The expression of HMB-45 in the metastatic tumour cells in spite of the absence in the original gingival tumour appears to indicate that clonal cells having the antigen had metastasised to the lymph node or the metastatic cells gained the productivity of the antigen increasing the tumorigenicity in the lymph node. From the staining results of our case, HMB-45 seems to be correlated with the grade of malignancy.

The line of differentiation or histogenesis in DPM remains controversial. It has been thought that DPM grows up via multiple growth and infiltration phases with fibro-

blastic differentiation of the transformed melanocytes, and tumour cells differentiate into myofibroblastic and Schwannian cells [8]. On the other hand, desmoplasia is considered to result from collagen synthesis by fibroblasts [13]. In the present case, myofibroblastic differentiation, at least, was not indicated because of the negativity of tumour cells for α-SMA. However, there is a possibility that desmoplasia might be induced by melanoma cells, although chronic mechanical stimulation by the denture might be one of the factors which accelerated the desmoplasia.

The survival rate and prognosis of DPM seems better than the conventional type of malignant melanoma, although there are some controversial reports [3, 6, 7]. Such a good prognosis might be due to the slowly proliferating activity of desmoplastic melanoma cells. In fact, local recurrence usually occurs slowly [3, 6]. In our case, the recurrent tumour developed 8 years after extirpation of the primary tumour even without safe margin. However, the tumour with low-grade malignancy may become highly invasive with rapid engrowth possessing HMB-45 antigen. In addition, DPM usually reveals a diffusely invasive pattern of neoplastic cells [6]. Therefore, resection with appropriate wide safe margin and strict long follow-up are necessary for DPM.

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