Spindle Cell Carcinoma of the Tongue : Case report and immunohistochemical study

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Spindle cell carcinoma is a rare malignant tumor which is generally considered to be a variant of squamous cell carcinoma. A case of spindle cell carcinoma of the tongue occurring in a 50-year-old Chinese male is reported. Immunohistochemical technique was used as an adjunct to the diagnosis of this unusual type of carcinoma. The immunohistochemical expression of keratin was recognized in the spindle cells, as well as in the carcinomatous cells. Moreover, the spindle cell component expressed vimentin. These findings suggest an epithelial origin with squamous differentiation and mesenchymal participation in the genesis of spindle cell carcinoma. Additionally, the differential expression of low and high molecular weight keratin was demonstrated. The possible causes of coexpression of keratin and vimentin are also briefly reviewed, which may be because some epithelial tumor cells were transformed into mesenchymal (vimentin-positive) spindle cells; or due to dedifferentiation, with regression to vimentin, an embryonal type of intermediate filament; or attributed to the cellular adaptation to environmental influences; or be related to reduced cell-to-cell contact.

Key words: **spindle cell carcinoma, keratin, vimentin, immunohistochemistry**

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Introduction

Spindle cell carcinoma is a rare malignant tumor which is generally considered to be a variant of squamous cell carcinoma. It is most commonly observed in the upper aerodigestive tract, in the esophagus, and on the skin (1). In the literature, a variety of terms are used to designate these tumors, including carcinosarcoma, pseudosarcoma, sarcomatoid squamous cell carcinoma, pleomorphic carcinoma, and polypoid carcinoma (1). These diverse nomenclatures reflect the uncertain histogenesis of the spindle cell components. This paper reports a case of this unusual type of carcinoma, studied by light microscopy and immunohistochemistry.

Case Report

A 50-year-old Chinese male patient presented to the Oral Pathology Department of Kaohsiung Medical College in December 1988, complaining of an exophytic, irregular shaped, yellowish-brown, painful mass located on the left lateral border of his tongue. The mass was growing rapidly, according to the description of the patient, who was a heavy betel-nut chewer (30-40 grains/day for more than 30 years) and cigarette smoker (2 packages/day for more than 30 years). Trismus, with a maximum interincisal distance of 1 cm, was noted for about 10 years. The patient's medical history was unremarkable. The clinical impression was a lingual squamous cell carcinoma. An incisional biopsy was performed. The pre-operative diagnosis was compatible with spindle cell carcinoma. The patient, referred to an oral maxillofacial surgeon, was then admitted for a full diagnostic examination. Two courses of intra-arterial chemotherapy via the left superficial temporal artery with cisplatine, bleomycin and 5-fluouracil were done in January 1989. No radiotherapy was performed. Definite surgical treatment was carried out in March 1989, including left radical neck dissection and left hemiglossectomy. Resected margin and neck nodes were histologically free of tumor. The postoperative course was uneventful and the patient was then discharged from the hospital. He was followed closely on an outpatient basis. Unfortunately in September 1989, a recurrent tumor containing only the spindle cell components was observed in the submental region. The patient refused any further surgical intervention. The later situation of the patient could not be assessed due to his failure to keep subsequent follow-up appointments.

The surgical specimen was fixed in 10% neutral buffered formalin solution and embedded in paraffin. Sections 5 m thick were cut and stained with

Table 1: Primary antibodies used for incubation with specimen sections and immunohistochemical results

Applied antibodies	Dilution	Source	Carcinomatous area	Spindle cell area
Monoclonal mouse antibodies				
Keratin EAB-902(35 β H11)a	1:400	Enzo Biochem (NY, USA)	++++	+++
Keratin EAB-903(35 β E12)b	1:2000	Enzo Biochem	++++	+
Vimentin	1:50	Dakopatts (Glostrup, Denmark)	-	+
Leukocyte common antigen	1:50	Dakopatts	-	-
HHF35 c	1:50	Enzo Biochem	-	-
Polyclonal rabbit antibodies				
Desmin	1:1000	Dakopatts	-	-
Lysozyme	1:200	Dakopatts	-	-
S-100	1:1000	Dakopatts	-	-
Factor VIII	1:300	Dakopatts	-	-

(-): negative reaction; (+): 20-40%, (++): 40-60%, (+++): 60-80%, (++++): >80% of positive-stained cells;
a35βH11: specific for low molecular weight keratin 8(52.5kd) characteristically found in simple epithelium; b35 βE12: specific for high molecular weight keratin 5,10,11(58, 56.5, 56kd) reacting with all squamous epithelia; c HHF35 : a muscle actin specific monoclonal antibody

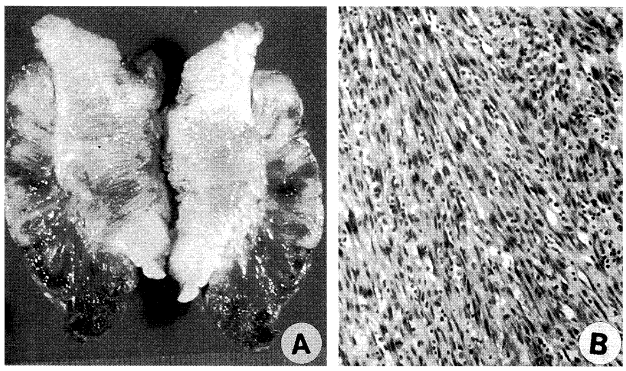

Fig.1: (A) Grossly, the overall configuration of the tumor was that of a polypoid growth. (B) The H-E staining of the resected tumor was comprised of predominantly bizzare, basophilic, hyperchromatic, pleomorphic spindle cells with frequent prominent mitotic figures (×100).

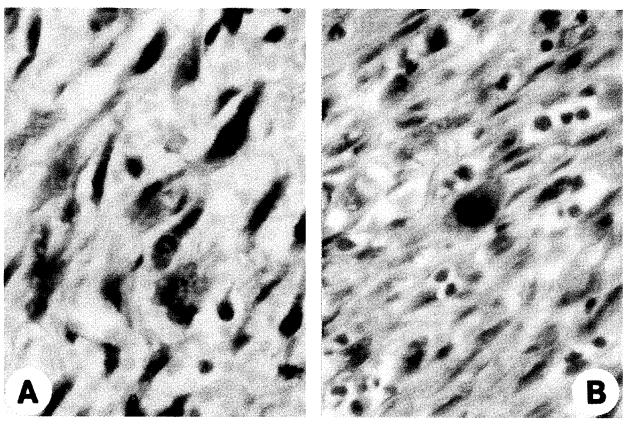

Fig. 3A & B: ABC immunostaining of the spindle cell component of the lesion with 35 β H11 (A×100) & 35βE12 (B×100).

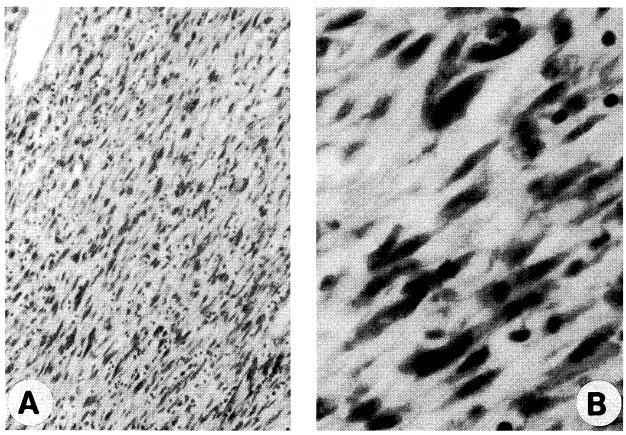

Fig. 2A & B: ABC immunostaining of the spindle cell component of the lesion with vimentin (×100).

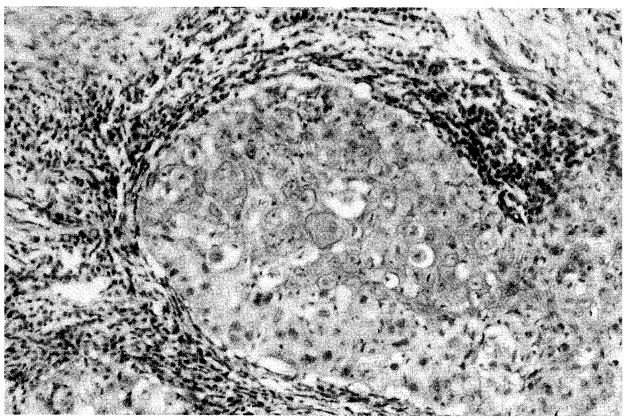

Fig. 4: ABC immunostaining of the carcinomatous component of the lesion with 35 β H11 (×100); a similar result is observed with 35 β E12 staining.

hematoxylin and eosin (H-E). Additional sections were incubated with various antibodies, according to the avidin-biotin-peroxidase complex (ABC) method of Hsu and coworkers (2) (Table 1). Appropriate positive control tests were done, and internal controls for the staining of the various antibodies were evaluated in the non-neoplastic component present on each slide. Negative control tests were carried out by substituting non-immune mouse serum for monoclonal mouse antibodies and non-immune rabbit serum for polyclonal rabbit antibodies.

Grossly, the overall configuration of the lesion was that of a polypoid growth, measuring about 4.5 cm in diameter (Fig. 1A). The H-E staining of the resected tumor was comprised of predominantly bizzare, basophilic, hyperchromatic, pleomorphic spindle cells

with frequent prominent mitotic figures (Fig. 1B). The immunohistochemical findings are summarized in Table 1. For the spindle cell component, 20 to 40% of the cells demonstrated positive vimentin (Figs. 2A & B) and 35βE12 (high molecular weight, HMW, keratin) stainings (Fig. 3B); 60% to 80% of the cells showed positive staining for 35βH11 (low molecular weight, LMW, keratin) (Fig. 3A). Nearly all of the carcinomatous component showed positive immunoreactivities to both 35βH11 and 35βE12 antibodies (Fig. 4), while a totally negative result to vimentin was observed. Therefore, the pathological diagnosis of this lesion was spindle cell carcinoma arising in the tongue.

Discussion

Spindle cell carcinoma may involve any squamous epithelium lined body surface but inside the oral cavity it is located predominantly on the lips, tongue, and the mandibular alveolus; only a small number of lesions have been reported in the maxilla (3). To the best of our knowledge, not many cases of lingual spindle cell carcinoma were reported in the English language literature (3-7). In this report, a case of histologically biphasic spindle cell carcinoma arising from the tongue with immunohistochemical study was presented.

Due to the relatively superficial infiltrative growth pattern of this often exophytic polypoid tumor, the prognosis for this tumor type had once been assumed better than the classic squamous cell carcinoma (8). However, the tumor in the current case demonstrated an aggressive behavior with metastasis to the submental region within a short period after surgical intervention.

Our clinical data suggests that the spindle cell component of this lesion is not radiation-induced. Radiotherapy, therefore, does not seem to be a major pathogenetic factor, at least in this case. The spindle cell nature of this lesion is most likely to be attributable to chemotherapy, which selected a chemotherapy-resistant clone of spindle cells.

In the oral cavity, differential diagnoses include malignant fibrous histiocytoma, amelanotic spindle cell malignant melanoma, minor salivary gland neoplasm, neural malignant tumor, rhabdomyosarcoma, and malignancy of lymphocytic or endothelial cell origin. The negative stainings of lysozyme, S-100 protein, desmin, actin, leukocyte common antigen and factor VIII-related antibodies precluded the spindle cell component being histiocytic, melanocytic, myoepithelial, muscular, lymphocytic or endothelial in origin. These immunohistochemical findings suggest an epithelial origin with squamous differentiation and mesenchymal participation in the genesis of spindle cell carcinoma.

Two types of keratin antibodies (35βH11 & 35βE12) were employed in the present study. The staining patterns of the spindle cell component differed between these two keratin antibodies. The percentage of the positive spindle cells demonstrated by 35βH11 monoclonal body was significantly higher than that shown by 35βE12. A loss of high molecular weight keratin in tumor tissues has been confirmed in both animal and human carcinoma studies (9,10). Therefore, a significantly greater number of spindle cells showing positive 35βH11 staining are probably due to the disappearance of high molecular weight keratin corresponding to the carcinomatous changes. To our knowledge, this may be the first report to show the differential expression of low and high molecular weight keratin in oral spindle cell carcinoma.

The squamous cells component usually comprises carcinoma in situ of the overlying epithelium but may seen as islands of dysplastic squamous epithelium within the spindle cell components. Direct transition between the two cell types may also be observed (3). However, no transition zone can be observed in this lesion.

Not all the spindle cells showed a positive result for the two keratin antibodies. The possible explanation for the negative staining of the keratin antibodies may be due to the fact that some spindle cells were non-epithelial origin. On the other hand, it may also be possible that some of the original epithelial spindle cells had experienced a disappearance of keratin (especially HMW) expression upon neoplastic changes. Therefore, a positive result to keratin staining may help to establish the diagnosis of spindle cell carcinoma. However, a negative result does not absolutely exclude a malignant epithelial neoplasm.

Both keratin (an intermediate filament, IF, of epithelial origin) and vimentin (an IF of mesenchymal origin) were demonstrated in the spindle cells component; this suggests that certain spindle cells show coexpression of keratin and vimentin. Such coexpression has been reported in some epithelial tumors of the thyroid (11) and the salivary gland (12). Although the exact causes of the coexpression of keratin and vimentin in tumor cells remain enigmatic, several hypotheses have been proposed. It is possible that, under certain not yet identified epigenetic or genetic factors, some epithelial tumor cells are transformed into mesenchymal (vimentin-positive) spindle cells (13). On the other hand, the coexpression may be due to dedifferentiation, with regression to vimentin, an embryonal type of intermediate filament (14). Furthermore, experiments with cultured cells (15) and cells shed into body cavities (16) indicate that the coexpression may be a consequence of cellular adaptation to environmental influences or related to reduced cell-to-cell contact. Therefore, histologic examination of all spindle cell carcinomas regarding coexpression of keratin and vimentin in the spindle cell component should be performed to find further evidence for the proposed hypotheses on their pathogenesis.

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