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TASHIRO, Hideo

First Department of Oral Maxillofacial Surgery, Faculty of Dentistry, Kyushu University

OMURA, Ayumi

First Department of Oral Maxillofacial Surgery, Faculty of Dentistry, Kyushu University

OZEKI, Satoru

First Department of Oral Maxillofacial Surgery, Faculty of Dentistry, Kyushu University

HIGUCHI, Yoshinori

First Department of Oral Maxillofacial Surgery, Faculty of Dentistry, Kyushu University

他

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Squamous Cell Carcinoma of the Oral Cavity Consisting of Band-like Nests

Hideo TASHIRO¹⁾, Ayumi OMURA¹⁾, Satoru OZEKI¹⁾
Yoshinori HIGUCHI¹⁾ and Masanori SHINOHARA²⁾

¹⁾ First and ²⁾ Second Departments of Oral and Maxillofacial Surgery,
Faculty of Dentistry, Kyushu University 61, Fukuoka 812

Abstract Four squamous cell carcinomas of the oral cavity shared common histological and clinical characteristics. The primary lesion was situated at the floor of the mouth or the tongue. The cancer cell nests were band-like. The border between nests and stroma was smooth and distinct, with the continuity of the basement membrane being well maintained. The response to preoperative chemoradiotherapy was relatively poor. Although the lesion was locally advanced, no cervical metastasis was detected. No recurrence has occurred after the operation.

Introduction

Oral carcinomas are characterized by extreme histologic and clinical diversity. Generally, oral carcinomas are histopathologically classified based on their degree of differentiation and mode of infiltration. Separate from this classification, there is a special type of highly differentiated squamous cell carcinoma which presents with verrucous or papillomatous gross and microscopic features, a well preserved basement membrane, and does not tend to proliferate deeply or metastasize. Ackerman¹⁾ designated this type of lesion as "verrucous carcinoma".

The authors have identified another group of moderately or poorly differentiated squamous cell carcinoma of the oral cavity with features unlike those of verrucous carcinoma. These carcinomas invaded and proliferated deep regions, had a well preserved basement membrane and morphologically formed thin, band-like nests. Clinically, they responded poorly to preoperative combined treatment with bleomycin chemotherapy and radiotherapy, and

did not show metastasis.

Patients

During the 11 years from 1981 to 1991, the authors treated 244 primary squamous cell carcinomas of the oral cavity. Histologically, the tumor cell nests of 4 of these carcinomas displayed a band-like pattern throughout the entire lesion. The pathologic characteristics, preoperative therapy and metastases of these four lesions are presented in Table 1 and 2. All patients were men, ranging in age from 57 to 73 years, and had a history of moderate smoking and alcohol consumption. The lesions were mainly situated at the floor of the mouth or the lateral under surface of the tongue. All tumors were relatively large, and primarily showed an endophytic pattern of proliferation and ulceration (Fig. 1). Upon palpation, the lesions were found to have a relatively distinct, indurated border. X-ray examination of Case 1, in which the tumor invaded into the anterior alveolar region of the mandible, revealed a relatively distinct and smooth border around the resorbed area (Fig. 2, 3). Both bleomycin chemotherapy

Table 1 Patient Summaries

Patient	Age	Sex	Site	T	N	Largest Diameter (mm)
Case 1	65	M	Floor of mouth Lower gum	4	2 c	34
Case 2	57	M	Floor of mouth	4	2 c	45
Case 3	58	M	Tongue Floor of mouth	2	1	38
Case 4	73	M	Floor of mouth Tongue Lower gum	3	2 b	55

Table 2 Preoperative Treatment, Neck Dissection and Results

Patient	Preoperative Treatment	Histological Effect	Neck Dissection	Metastasis	Follow-up, Status
Case 1	BLM 110 mg ⁶⁰ Co 22.5 Gy	Minimal	Bilat.*	None	11 yrs Died of lung cancer
Case 2	BLM 90 mg ⁶⁰ Co 22.5 Gy	Partial	Bilat**	None	11 yrs 9 mos Alive
Case 3	BLM 110 mg Linac 22.5 Gy	Partial	Unilat.	None	2 yrs 9 mos Alive
Case 4	BLM 70 mg Linac 15 Gy	Partial	Bilat**	None	1 yr 6 mos Alive

BLM: bleomucin

*: Bilateral total neck dissection

**: Total neck dissection on the affected side and superior neck dissection on the other side

**Fig. 1** Tumor with an ulcer of the tongue (Case 3).

and radiotherapy¹²⁾ were performed preoperatively, resulting in a partial decrease in lesion size. All patients underwent partial resection of the floor of the mouth and tongue, and a mar-

ginal mandibulectomy was concurrently performed in three of them, excluding Case 3. As palpation or CT and ultrasound examination suggested the presence of cervical lymph node metastasis in all four cases, bilateral or unilateral neck dissection was performed but no metastasis were noted histopathologically. The defect of oral cavity was repaired using a cervical island skin flap, as described by Farr et al.⁴⁾, in Case 1, and a pectoralis major myocutaneous flap in the other three cases. Case 1 died after 11 years due to primary lung cancer, but did not show any signs of recurrence of oral cancer. The other three cases are all alive without recurrence.

Histopathologic findings of biopsy specimens: In all four cases, the lesion consisted



Fig. 2 View of the alveolar part invaded by carcinoma that originated in the floor of mouth (Case 1).

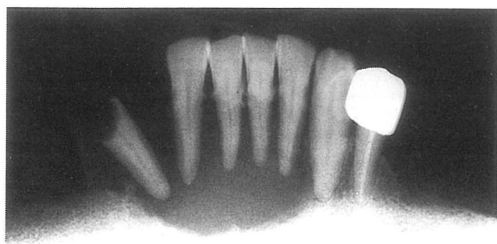


Fig. 3 Roentgenogram showing bone resorption with a well defined boundary (Case 1).

basically of band-like tumor cell nests comparable in width to the thickness of the epithelial layer of the normal oral mucosa. The degree of cancer cell differentiation was moderate or poor, and keratinization was either present or not appreciable. Lesions with broad nests showed a keratinized layer of necrosis in their center (Fig. 4, 5). Examination of transverse sections of these nests revealed a comedo pattern or ductal pattern of nests containing keratinized necrotic debris in their center (Fig. 6). All cases also showed erect spindle cells on the outermost border of the nests in most regions, and there were frequent mitotic figures. At the surface layer or margin of the lesion was seen a pattern of carcinoma in situ with abrupt transition from normal epithelium (Fig. 7). Interstitially, small round cell infiltration was

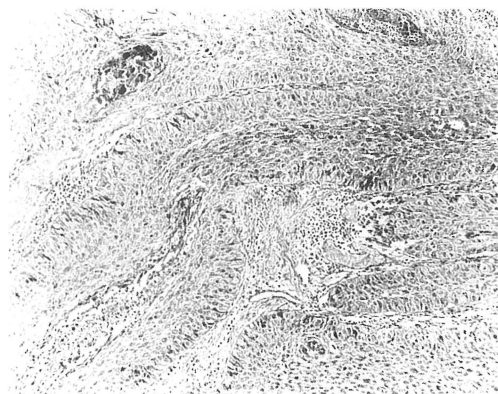


Fig. 4 Carcinoma cell nests showing a band-like pattern (Case 2, H & E, $\times 74$).

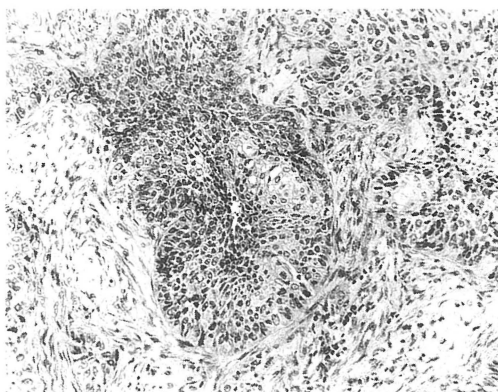


Fig. 5 Carcinoma cell nests showing a band-like pattern (Case 3, H & E, $\times 160$).

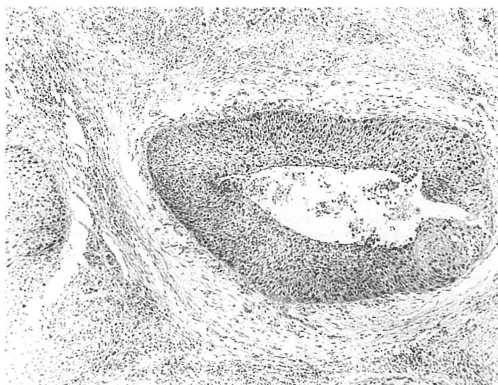


Fig. 6 Carcinoma cell nests showing a ductal pattern (Case 4, H & E, $\times 63$).

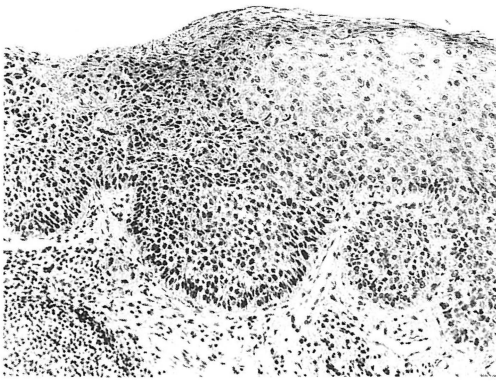


Fig. 7 Marginal epithelium appears as carcinoma in situ (Case 3, H & E, $\times 130$).

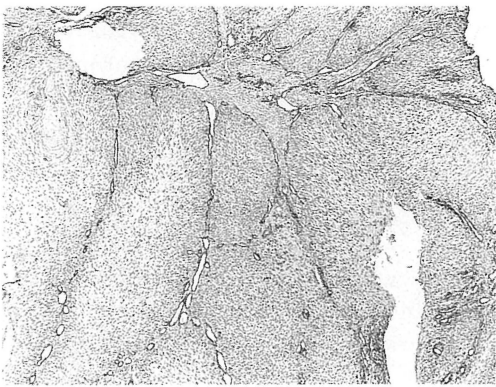


Fig. 8 Laminin staining. A positive reaction to laminin is expressed continuously and linearly around the nests (Case 3, $\times 52$).

remarkable and inflammation was marked in Cases 1 and 3.

The border between the nests and stroma was smooth and distinct. Specimens were stained with silver stain, PAS stain and laminin stain, and in all cases except for Case 1, associated with remarkable signs of inflammation, the basement membrane was attained in a continuous linear pattern with all these staining techniques (Fig. 8). Laminin staining was performed by the ABC method using rabbit anti-mouse laminin polyclonal antibody (E. Y. Laboratories). Mucicarmin staining and Alcian blue staining revealed no positively stained cancer cells in any case.

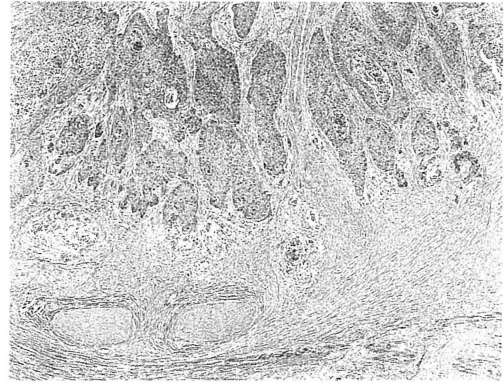


Fig. 9 Peripheral nests are destroyed after preoperative combined treatment with bleomycin chemotherapy and radiotherapy (Caes 3, H & E, $\times 25$).

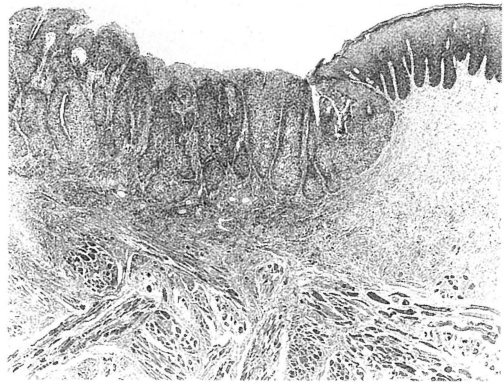


Fig. 10 Recurrent carcinoma of the tongue. Histological figure shows an early stage of downward invasion (H & E, $\times 25$).

Histopathologic findings of resected specimens: In all cases, the nest structure was maintained and most nests were undisturbed by preoperative treatment. The cancer cells were considered to be viable. Some nests, particularly those at the outer margin of the tumor, were destroyed and underwent necrosis (Fig. 9). The contrast between the viable and necrotic nests was remarkable. In all cases, a carcinoma in situ-like structure was retained, without being disturbed, in the surface layer or margin of the tumor. Signs of metastasis were not evident in cervical lymph nodes.

Discussion

Common pathologic and clinical features were noted in all four cases presented in this report: (1) The primary lesion was situated at the floor of the mouth or the lateral under surface of the tongue. (2) The lesions showed endophytic deep proliferation and ulceration. (3) The border with the surrounding tissue was relatively distinct. (4) The border between nests and stroma was smooth and distinct, with the continuity of the basement membrane being well maintained. (5) The nests were band-like, comparable in width to the thickness of the epithelial layer of the oral mucosa. (6) Carcinoma in situ-like features were present at the tumor surface or margin. (7) The response to combined treatment with bleomycin and radiotherapy was relatively poor. This therapy resulted in destruction of peripheral nests but had minimal effect on inner nests. (8) The lesion was locally advanced but was unassociated with cervical lymph nodes metastasis. (9) No recurrence has occurred after the operation.

At the floor of the mouth and margin of the tongue, carcinoma in situ can be often seen as an early carcinoma and features of carcinoma in situ can be frequently noted at the margins of infiltrating carcinomas. The patients reported here likewise showed carcinoma in situ-like features in the surface layers and borders of their carcinomas. Deeply situated band-like nests appeared to be a deep proliferation of tumor tissue which retained the morphologic features of carcinoma in situ. Figure 10 shows the histologic findings of a recurrent carcinoma of the tongue margin in a 50-year-old male. The findings presumably resemble the initial figures of cancer in the four cases presented in this report. As the primary carcinoma of this patient was treated by another clinic, its histologic characteristics could not be examined.

Of paramount clinical importance is the fact that metastasis was not found in any of our cases despite all lesions being advanced and

showing extensive infiltration, normally associated with metastasis. This lack of metastasis may have been due to the well preserved basement membrane rather than the band-like nest structure.

Colorectal, lung and bladder carcinomas with continuous laminin or type IV collagen deposition in the basement membrane have been reported to have a low incidence of metastasis and a good prognosis⁽⁵⁾⁽⁷⁾⁽¹¹⁾⁽¹³⁾. Likewise for oral carcinomas, Noguchi et al.⁽⁹⁾ did not find any lymph node metastasis in a group of patients showing a continuous linear pattern of laminin-positive staining. They also reported that the rate of tumor reduction induced by chemotherapy with cisplatin and bleomycin or pemetumycin was 50.0% in cases showing good continuity of the basement membrane, and, in the presence of an altered basement membrane, 66.5% in cases with T-cell infiltration in cancer nests and 33.2% in cases without such infiltration.

Modes of invasion were classified into 4 grades by Jakobsson⁽⁸⁾ in carcinoma of the larynx. It was reported that cases with grade 1-3 mode of invasion classified by his criteria showed a low frequency of metastasis in carcinomas of the oral cavity, while cases with grade 4 (diffuse growth) showed a high frequency⁽¹⁰⁾⁽¹⁵⁾. The mode of invasion in our presented cases may be grade 2 (cords, less marked borderline) or 3 (groups of cells, no distinct borderline), although it is somewhat difficult to classify them because of their specific mode of invasion.

In the patients presented in this report, combined treatment with bleomycin and radiotherapy only affected nests situated at the outer part of the carcinomas. In this connection, it has been stated that chemotherapy is most effective at the periphery of carcinomas due to contact with host tissue having a good blood supply⁽²⁾⁽⁶⁾.

Crissmann et al.⁽³⁾, performing neck dissection in patients with clinical evidence of N1 staged

carcinomas of the floor of the mouth, reported that 56% of cases were false-positive. They identified two groups of stage II (T2NO) carcinomas. One group consisted of superficial or micro-invasive carcinomas, not associated with metastasis. The other group showed a vertical or nodular growth pattern which had a high incidence of metastasis. Although they also stated that some carcinomas of the floor of the mouth are not associated with metastasis, their viewpoint differed from that of the authors.

As some of the clinical and histologic features of these cases resemble those of mucoepidermoid carcinomas¹⁴⁾, mucicarmin staining and Alcian blue staining were attempted, but these stainings indicated that they were not mucoepidermoid carcinomas.

Although the limited cases that were encountered do not allow for definitive identification of a distinct group, it should be noted that all cases showing histologic evidence of band-like nests shared common clinical characteristics. Histologic findings should therefore be taken into account in forecasting the efficacy of preoperative therapy, diagnosing cervical lymph node metastasis, and evaluating the patient's prognosis.

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(和文抄録)

帯状の胞巣よりなる口腔扁平上皮癌

九州大学歯学部口腔外科学第一講座¹⁾九州大学歯学部口腔外科学第二講座²⁾田代 英雄¹⁾・大村あゆみ¹⁾・大関 悟¹⁾樋口勝規¹⁾・篠原正徳²⁾

11年間に経験された244例の口腔扁平上皮癌のうち、4例で共通の特有な組織学的、臨床的所見がみられた。それらの原発部位はいずれも口底あるいは舌であった。組織所見で癌細胞巢の形態様相は正常上皮層の厚さと同程度幅の帯状を呈していた。基底膜の連続性はよく保たれ、胞巣と間質との境界は平滑で明瞭で

あった。術前放射線化学療法の効果は比較的不良であった。局所的には病巣はかなり進展していたが、頸部転移は認めなかった。術後11年から1年6か月経過しているが再発は起こっておらず、局所進展癌であるにもかかわらず、予後は良いものと思われた。