Case Report

METACHRONOUS MULTIPLE CARCINOMA OF LIP AFTER SURGERY FOR GINGIVAL CARCINOMA:
A CASE REPORT

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Abstract

A case of multiple carcinoma of the lower lip probably induced by repeated bite trauma due to lack of sensation is reported. A reduction in immunocompetence by carboplatin (CBDCA) might be an additional condition for the carcinogenesis. This case suggests that the reconstruction of the sensory nerve is important after resection of a malignant tumor of the head and neck region.

Key words: Multiple carcinoma—Lip—Lack of sensation—Inferior alveolar nerve injury—Carcinogenesis

CASE REPORT

In November of 1992, a 67-year-old woman visited us with the chief complaint of an ulcer in the right molar gingiva of the mandible. She had a medical history of hypothyroidism. She did not smoke or drink of alcohol.

Clinical examination showed an ulcer on the molar gingiva of the right mandible, 19×20 mm in size. Slight induration was recognized around the ulcer, making the total size 22×22 mm. She had no pain at all. A grossly metastasized lymph node was recognized in the submandibular region.

After a histological diagnosis of squamous cell carcinoma (T2N1M0, stage III) in the molar gingiva of the right mandible and a general preoperative check without major problems, she underwent regional resection of the right mandible (retromolar to first premolar) and right radical neck dissection (Fig. 1). A histopathological diagnosis of the resected specimen was well-differentiated squamous cell carcinoma. The surgical margin was free from the carcinoma. Metastasis was recognized in the right submandibular lymph node. Two cycles of adjuvant chemotherapy consisting of CBDCA and tegafur (UFT) were performed. One month after the surgery a tactile and pain sensational test (1.5 g Frey’s hair and 3 g pin prick test) of the right lower lip revealed that they were absent; there was no recovery at the annual examination. From the beginning of July in 1996, she was biting the right lower lip with her right upper central incisor and right lower lateral incisor teeth after the denture in right molar mandible became worn. She repeatedly suf-
ffered bite wounds and developed ulcers in the mucosa of the lower lip regardless of occlusal adjustment. In March of 1997 when she was 72 years old, an ulcer rapidly increased in size and did not heal, so she returned to our clinic.

She was slightly obese, but had no clear systemic abnormalities. A 21 mm × 19 mm ulcer was accompanied by induration in the mucosa of the right lower lip (Fig. 2). CT-scan and other clinical examination suggested a malignant tumor. At this time, we could not detect any abnormal findings in the regional lymph nodes. The results of clinical laboratory data revealed no abnormalities, but the results of a lymphocyte subset showed abnormal levels of CD3, CD4, CD8 and CD4/CD8 (Table 1). Squamous cell carcinoma was diagnosed through biopsy.

In April of 1997, the patient underwent surgery to remove the carcinoma, and two teeth (the right upper central incisor and right lower incisor teeth) were extracted (Fig. 3). Histopathological findings showed that the tumor was a well-differentiated squamous cell carcinoma accompanied by keratinization and that it infiltrated from the mucosal epithelium to the fascia of the lip in a funnel shape.

After discharge, the patient was monitored on an outpatient basis. In March 1998, left radical neck dissection was performed,
because metastasis to the left submandibular lymph nodes was suggested. No metastasis was detected in the specimens of the left neck, although there was granuloma with foreign body giant cells.

At present, the lack of sensation is still present in the same area of the lower lip, and the patient is doing fine. The denture was not worn any further, and there have been no more bite wounds in the lower lip (Fig. 4).

**DISCUSSION**

This patient had metachronous multiple carcinoma of the lip that was thought to be caused by chronic biting of the lower lip brought about by sensory disturbance. This case suggests the importance of reconstruction of the sensory nerves. However, before we argue this point, we must first consider the fact that this carcinoma was a real multiple carcinoma.

The second tumor appeared away from the site of the first tumor, and continuity between the two tumors was not recognized histologically, this satisfying the definitions of multiple primary carcinoma proposed by Warren, Gates\(^{11}\) and IARC\(^{7}\).

The patient had been suffering from bite wounds in the same location, where the second tumor developed. Histopathological findings suggested that the secondary squamous cell carcinoma appeared on the dermis side of the mucosa where the bite wounds developed (Fig. 5a,b).

In consequence, the secondary tumor was thought to be metachronic double carcinoma originating from the lip, rather than metastatic.

Weaver *et al.*\(^{12}\) reported that mouthwash is one of the risk factors for carcinogenesis, and Thumfart *et al.*\(^{8}\) found that chronic mechanical irritation caused by badly fitting dentures or sharp remaining teeth could cause oro-pharyngeal carcinoma. Uchida *et al.*\(^{10}\) investigated the onset of multiple carcinoma of the oral cavity and reported that the onset is higher in the oral cavity than in other parts of the body and that ectopic irritants are involved. Nomura *et al.*\(^{6}\) suggested that smokers, drinkers, and ALDH 2-deficient patients who consume alcoholic beverages are at a risk for developing oral cavity cancer. However, Morse *et al.*\(^{5}\) found that the use of mouthwash or dentures causes chronic irritation or injury.
of the mucosa of the oral cavity, but does not correlate with dysplasia of the mucosa of the oral cavity. Although the relationship between carcinogenesis and chronic mechanical irritations remains controversial, most studies support the notion that they are correlated.

In addition to the physical stimulation by repeated bite, the two cycles of CBDCA + UFT administration must be considered as a carcinogenetic factor as well. A fairly large number of reports have been made on secondary carcinogenesis caused by CDDP or CBDCA\(^2-4\); many of these cases involved leukemia. There have also been several reports on secondary carcinogenesis of solid cancer\(^3\). Furthermore, a great deal of basic research has been conducted on the mechanism of carcinogenesis induced by chemotherapeutic agents: Turnbull et al.\(^9\) reported that CDDP caused mutations, transformations, and sister chromatoid exchanges. Greene et al.\(^3\) documented that chemotherapeutic agents acted as cancer initiators.

Abnormal levels of CD3, CD4, CD8, and CD4/CD8 were seen in our case before and after surgery. Her immunocompetence seemed to be low, which might be due to the chemotherapy in addition to aging and her own constitution and which might have made her extremely susceptible to carcinogenesis. The sacrifice of sensory nerves such as the inferior alveolar nerve has been considered unavoidable in the performance of such operations, and surgeons have not been active in reconstructing sensory nerves. This case, however, suggests the necessity of the reconstruction of sensory nerves not only to improve the quality of life, but also to prevent a second malignancy, particularly in a patient with possible lowered immunocompetence.

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REFERENCES


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