

## Large Cell Carcinoma of the Lung Metastatic to the Mandibular Gingiva

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**Background:** Although metastases of malignant tumors to the jaws are not unusual, metastases to the gingival soft tissues are relatively rare.

**Methods:** The clinicopathologic features of a metastatic tumor in the mandibular gingiva originating from lung cancer are described. The patient, a 61-year-old man, was admitted to the hospital with complaints of bloody sputum and chest pain while coughing. The patient's chest radiograph showed an abnormal mass in the left upper lobe. After admission, the patient noticed a swelling of the right mandibular gingiva. Histological and immunohistochemical analysis for tumors of the gingiva and the lung were performed.

**Results:** Radiographic examination did not indicate involvement of the underlying bone. The histopathological findings showed that the gingival tumor consisted of a large cell carcinoma, and the mass of the upper lobe displayed the same histology as that found in the gingiva. Immunohistochemical investigation of the gingival tumor revealed similar results to those found in the mass of the lung. Based on the clinicopathologic findings, this case was diagnosed as primary lung cancer with the gingival tumor deemed metastatic. Multiple metastases were found in areas other than the oral cavity; radiation and chemotherapy for the gingival tumor were performed due to persistent bleeding and pain.

**Conclusions:** The resemblance of this gingival mass to an inflammatory lesion demonstrates the need for a detailed examination. This case also emphasizes the need to evaluate positive treatment needed to relieve complications in the mouth, even if the prognosis of the primary tumors remains unfavorable. *J Periodontol* 2002;73:571-574.

### KEY WORDS

Gingival neoplasms; neoplasm metastasis; mandibular neoplasms; lung neoplasms.

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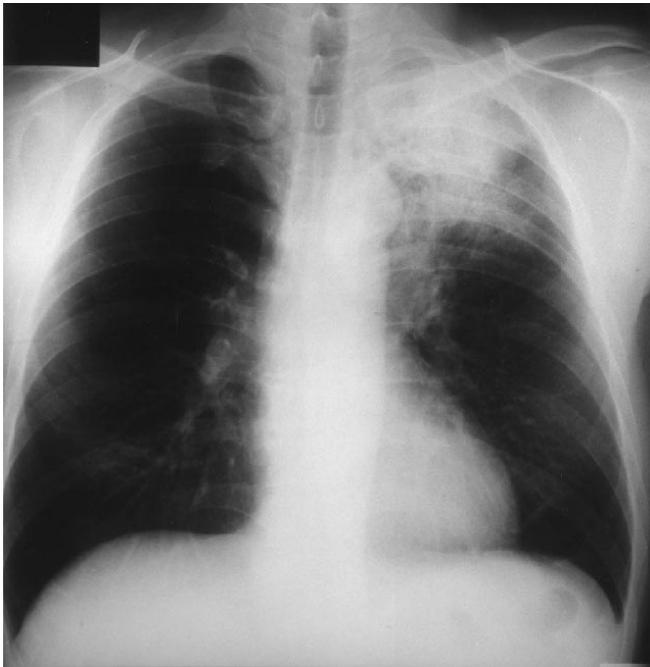
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A survey of the English-language literature referring to malignancies confined to the oral cavity showed that 1% of such malignant tumors are of metastatic origin.<sup>1</sup> There is a general consensus that metastatic neoplasms of oral regions are usually intraosseous, with most of them occurring in the mandible, particularly in premolar-molar regions,<sup>1,2</sup> while oral soft tissue involvement is rare.<sup>1,3</sup> The most common source of oral metastatic tumors for men is the lung, which accounts for approximately 10% to 20% of all oral metastatic tumors.<sup>2,3</sup> The primary tumors in oral metastases most frequently found in the lung are squamous cell carcinomas and adenocarcinomas. Metastasis from large cell carcinoma of the lung to the oral cavity is quite rare.<sup>2,3</sup> Since we have experienced a metastatic large cell carcinoma in the mandibular gingiva from the lung, we report on its occurrence, clinical recognition, and histopathological confirmation.

### CASE REPORT

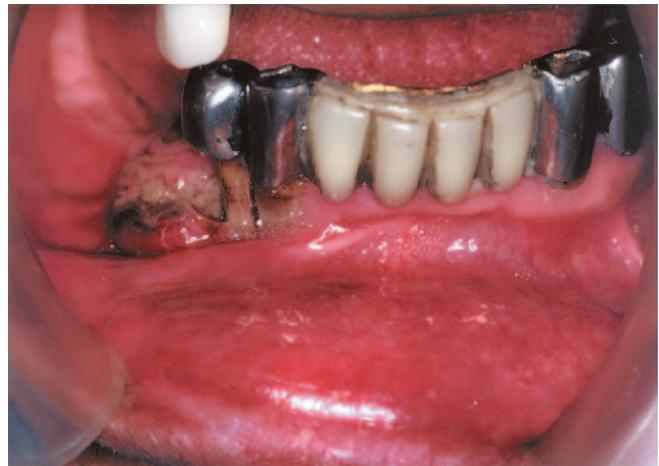
A 61-year-old male patient was admitted to the Department of Internal Medicine of Hyogo Prefectural Awaji Hospital on October 13, 1998 with complaints of bloody sputum, chest pain while coughing, and fever. He had no particular history of disease, but an approximately 40-year history of smoking 40 cigarettes daily. A chest radiograph revealed an irregularly circumscribed opacity in the left upper lobe (Fig. 1). Bronchoscopic biopsy and a cytological smear performed on October 22 revealed no histological malignant findings. However, since tubercle bacilli were detected in bronchoalveolar lavage fluid by polymerase chain reaction, treatment for pulmonary tuberculosis was initiated. In the meantime, the patient noticed a swelling in the right mandibular gingiva and was referred to the Department of Oral Surgery on October 26.

Intraoral findings revealed an elastic, dark red exophytic tumor (13 × 10 mm) with relatively well-defined margins which was distal to the first premolar and covered the second premolar, and partial superficial necrosis in the buccal gingival region between the cuspid and the first premolar on the right mandible, with mild tenderness (Fig. 2). Sub-



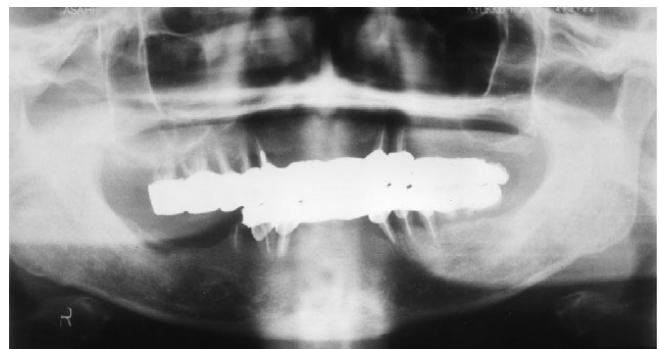
**Figure 1.**

Chest radiograph showing large parenchymal mass in the left upper lobe.



**Figure 2.**

Clinical view showing the exophytic component of the gingival tumor with relatively well-defined margins which is distal to the first premolar and covers the second premolar, and partial superficial necrosis which involves the cuspid and the first premolar on the right mandible.



**Figure 3.**

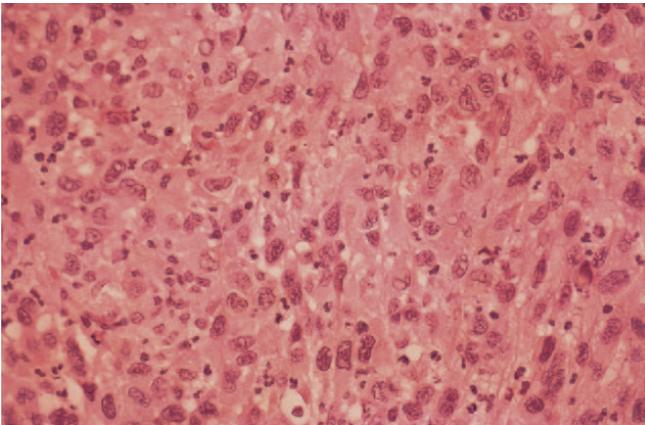
Panoramic radiograph showing no abnormal resorption of the alveolar bone adjacent to the tumor.

mandibular lymph nodes were palpable bilaterally. A panoramic radiograph showed smooth alveolar bone adjacent to the gingival tumor and no obviously abnormal bone resorption (Fig. 3). The most likely differential diagnoses were pyogenic granuloma, periodontal abscess, or malignant tumor. Since antibiotics had failed to reduce the swelling of the gingiva, a biopsy was performed on November 18. Underlying bone could be visibly seen to be intact at biopsy. The biopsy specimen consisted of a solid proliferation of anaplastic large cells without specific structures. A second cytological examination of the lung lesion performed on December 1 was positive for atypical large cell carcinoma. Abdominal computed tomography (CT) also disclosed tumors in the right adrenal gland and multiple enlarged lymph nodes. These clinicopathologic findings indicated that the patient had primary large cell carcinoma of the lung with multiple metastases. The patient had not initially received treatment for the tumors at the request of himself and family. However, he finally accepted radiation for the gingival tumor, since the gingival tumor began to grow rapidly with bleeding and severe spontaneous pain. Chemotherapy with cisplatin and fluorouracil was also administered to make the radi-

ation therapy more effective. While the gingival tumor decreased in size and the symptoms were improved, the patient expired on January 9, 1999. Autopsy was not performed.

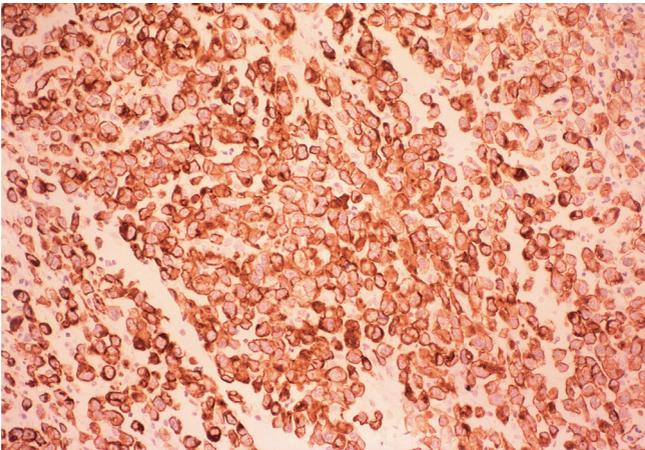
### **Histopathology**

The gingival tumor consisted of a solid proliferation of large polygonal cells with a prominent nucleus. No keratinization or mucus production was observed throughout the lesion (Fig. 4). Immunohistochemistry for low molecular weight cytokeratin, expressed in normal bronchioalveolar epithelium; high molecular weight cytokeratin, observed in normal squa-



**Figure 4.**

*Histopathological features of the gingival tumor, consisting of a solid proliferation of large polygonal cells with prominent nucleus, indicating large cell carcinoma (H & E stain; original magnification  $\times 50$ ).*



**Figure 5.**

*CAM5.2-immunoreactivity is detectable in the cytoplasm of the tumor cells (anti-CAM5.2 immunostain; original magnification  $\times 50$ ).*

mous cell epithelium and basal layer of the bronchial epithelium; and cytokeratin 20 were performed to determine the cytoskeletal profile of the tumor, which may be reminiscent of the original organ or tissue. In addition, for differentiating the tumor from poorly differentiated adenocarcinoma of the lung, amelanotic melanoma and neuroendocrine adenocarcinoma (which may mimic large cell carcinoma of the lung histologically), antibodies against alveolar surfactant

apoprotein; carcinoembryonic antigen; melanocytic antigen; neuron specific enolase; and chromogranin A were employed in the immunohistochemistry. The antibodies were applied with or without enzymatic or microwave pretreatment followed by the labeled streptavidin-biotin method with a kit. While low molecular weight cytokeratin (CAM5.2) showed diffuse and strong reaction in the cytoplasm of the tumor cells (Fig. 5), the other antibodies displayed no reactivity in the tumor. Although a complete autopsy was not permitted, necropsy specimens from the left upper lobe of the lung and the left adrenal gland disclosed similar histological and immunohistochemical findings to the biopsy specimen of the gingival tumor.

## DISCUSSION

The English-language literature from 1964 to 1995 reports only 13 cases of gingival metastases from the lung with a complete histological identification with a primary lung cancer. Of these, 5<sup>4-8</sup> were adenocarcinoma, 3<sup>9,10</sup> squamous cell carcinoma, and 5<sup>11-15</sup> undifferentiated carcinoma. Although there are variances in histological interpretation between pathologists and differences in applied histological classification,<sup>2,3</sup> there have been no reports of gingival metastasis from lung cancer described as a large cell carcinoma other than the case described here. Large cell carcinomas account for 10% to 15% of all cases of lung cancer.<sup>16</sup> They usually occur in the peripheral part of the lung and grow rapidly, so they may often appear as large masses when they are first detected. Their prognosis, therefore, is considered worse than that of other lung carcinomas.<sup>17</sup>

Metastatic oral tumors are uncommon.<sup>1-3</sup> However, the data pertaining to the incidence of oral metastases may be falsely low since a standard x-ray examination does not encompass a detailed study of the jaws, and postmortem examination is not routinely done in the peri-oral region.<sup>2</sup> Periodontists should be aware of oral metastases and determine appropriate management of local and systemic oncologic complications. A biopsy is mandatory to confirm the diagnosis, except in patients with obvious widespread malignancy. In 20.4%<sup>3</sup> to 29.4%<sup>2</sup> of cases, the oral lesion represented the first clinical sign of the malignancy. Frequently, malignant metastatic lesions of the oral soft tissues are confused with benign lesions such as epulis, pyogenic granuloma, peripheral fibroma, or periodontal abscesses.<sup>1,2</sup> An inflammatory lesion was suspected in the present case on the initial examination, but since antibiotic therapy was not effective and the lesion continued to

grow, a biopsy was performed. The result showed the gingival tumor to be a large cell carcinoma, although at the time, the diagnosis of lung cancer had not been confirmed. The diagnosis requires a careful medical and dental history, and complete and accurate physical examination.

Multiple metastases may often have developed systemically when oral metastatic tumors are found, so patients tend to have an extremely unfavorable prognosis.<sup>2</sup> It is therefore difficult to undertake radical procedures in such patients because of their poor general condition and the low probability of complete removal of the primary and metastatic lesions. However, not treating oral metastatic lesions may result in dietary disturbance due to pain and bleeding, so the earlier removal of the oral lesion may be desirable in improving quality of life.<sup>18</sup> For the present case, radio- and chemotherapies were selected to relieve intraoral bleeding and pain, since the patient had generalized metastases and his overall condition was deteriorating. These treatments decreased the tumor size, relieved the patient from unfavorable symptoms, and enabled oral food intake. Thus, palliative treatment such as radiation therapy or chemotherapy, or a combination, should be considered to relieve complications and to preserve the function of the mouth even if the prognosis of the primary tumors remains unfavorable.

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