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Case report

# Tumor homing to the oral cavity after tooth extraction in a patient with metastatic lung adenocancer: A case report

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ABSTRACT

Angiogenesis plays a major role not only in the growth of the primary tumor, but also in metastasis. Due to the angiogenesis in granulation tissue, the tumor cells easily migrate to and locate in this region, thereby accelerating the pathological angiogenesis process and proliferation via presence of the angiogenesis-stimulating factors in this site.

In this case report, we present tumor homing to granulation tissue following tooth extraction in a 68-year-old male patient with metastatic lung adenocarcinoma. He applied to hospital due to delayed wound healing after tooth extraction for tooth decay approximately 5 months after the diagnosis. A superficially swollen mass of 6 × 6 cm was detected in the tooth extraction site. The histopathological examination suggested that it was a lung carcinoma metastasis. The presence of tooth extraction history together with the pulmonary adenocarcinoma metastasis in the extraction site was explained as "tumoral homing" to granulation tissue following tooth extraction.

This patient is of significance since it is the first case in the literature with "tumor homing" observed in the granulation tissue following tooth extraction.



## 1. Introduction

Approximately 1% of newly diagnosed oral malignancies are secondary to metastatic tumors. The most common histological type is adenocarcinoma.[1] Its differential diagnosis from inflammatory and reactive processes that are common in this site can be difficult. Oral cavity metastasis is not common, and the prognosis is usually poor. Most of the patients die within the first year with a 4-year survival of approximately 10%.[2–5]

In this case, we present "tumor homing" in granulation tissue of a patient who presented with delayed wound healing following tooth extraction.

## 2. Case report

A 68-year-old male patient had presented to the hospital with hemoptysis 16 months ago. The plain chest X ray revealed an apical mass in the right lung. The positron emission tomography/Computerized tomography (PET/CT) detected a mass lesion with a diameter of 65 × 55 × 65 mm extending from the right hilus to the upper lobe apical section and the right para-tracheal margin (Standard Uptake Value [SUVmax]: 32), multiple lymph nodes in right hemi-thorax (SUVmax: 28), and multiple lymph nodes on the right side of the neck (SUVmax: 14). Multiple increased metabolic activity foci, consistent with metastases, were detected in bilateral iliac bones, T7 vertebra and right to the 10th rib. Cranial Magnetic Resonance Imaging (MRI) showed no metastasis. The pathology result of the transthoracic needle biopsy from the mass was reported to be adenocarcinoma. The patient refused to receive chemotherapy, and was administered palliative RT to the right hemi-thorax (3000 cGy in total). He presented to a dentist due to toothache approximately 5 months after the cancer diagnosis. Plain

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X Ray detected decay, but no mass. The tooth was extracted. Upon experiencing complaints of swelling, pain and paresthesia in the right cheek as well as delayed wound healing, the patient presented to the dentist 20 days following tooth extraction. The physical examination revealed palpable right submandibular and cervical lymph nodes and a red–purple, hemorrhagic, swollen mass of approximately 6 × 6-cm size in the tooth extraction site. The patient was referred to the Department of Ear Nose and Throat. The CT of the neck revealed multiple enlarged lymph nodes and a heterogeneous soft tissue mass of 40 × 45 × 35 mm in size. Semi-solid density of the mass was consistent with cystic or necrotic region in the central section, exhibiting regions of contrast uptake within the right mandibular bone structure. The patient underwent PET/CT. In addition to the previous findings, pathologically increased FDG uptake was detected in the C3, C7, T9, T11 and L1 vertebrae. Biopsy was performed from the soft tissue mass in the tooth extraction site.

The patient, who presented to our oncology outpatient clinic, had known to have a coronary artery disease, a history of coronary by-pass, a congestive cardiac failure, an atrial fibrillation, a chronic obstructive lung disorder, an aortic valve replacement and 40 pack year of smoking. The physical examination showed bilateral submandibular and cervical lymphadenopathy, prominent on the right side, and a mass in the right molar tooth extraction site. Pathology preparations obtained from the patient's pulmonary and oral masses were requested and assessed comparatively in our center. The pathology result was reported as adenocarcinoma of acinar pattern from pulmonary mass biopsy. Oral mass revealed a poorly differentiated carcinoma with glandular, cribriform and solid growth patterns showing crushing artefact in most sites, which has obscured the detailed cytologic examination of the tumor cells (Fig. 1a–b). The immunohistochemistry revealed that neoplastic cells were positive for cytokeratin 19, cytokeratin 7, TTF-1, while keratin 14, HMWK, keratin 5/6, keratin 20 were all negative (Fig. 1c). P63 was weakly positive in rare tumor cells. A probable diagnosis of neuroendocrine carcinoma was eliminated by the absence of NSE, chromogranin, synaptophysin, CD56 in neoplastic cells. Surfactant A was negative, however, napsin was weakly cytoplasmic positive in tumor cells. The tumor was not morphologically consistent with any of the malignant odontogenic tumors. The immune–histochemistry profile suggested that the tumor had originated from the lung. The presence of tooth extraction history together with the pulmonary adenocarcinoma and metastasis in the tooth site numbered 48 was explained as “tumoral homing” to granulation tissue following tooth extraction. The patient received palliative radiotherapy to the pelvis and mandibula since he had comorbidities and an ECOG performance score of 3. The patient and his family didn't accept to receive chemotherapy and targeted therapy. Epidermal growth factor mutations were not looked for this patient. He died 7 months after diagnosis.

## 3. Discussion

Metastases to the oral cavity occur as jawbones and soft tissue metastases. Metastases to the jawbones are approximately 2-fold more common compared to soft tissue metastasis in the oral cavity. Gingival metastasis represents 54% of the soft tissue metastases. While the lungs, kidneys, liver and prostate are the most common primary tumor sites of oral metastasis among males; the breast, genital organs, kidneys and colo-rectum are the most common sites among females. Oral metastasis most frequently occurs between 5th and 7th decades. Gingival metastases may manifest as hyperplastic reactive lesions such as pyogenic granuloma, peripheral giant cell granuloma or fibrous epulis. Metastases to the jawbones usually manifest with the complaints of swelling, pain, and paresthesia.[6,7]

The tumor cells detaching from the primary mass growing by clonal enlargement, heterogeneity and angiogenesis invade the basal membrane. They pass the extracellular matrix and enter the blood vessels. The cells, which successfully survive and remain in the circulation, proliferate by crossing the vascular membranes in the target tissue. Angiogenesis allows adequate perfusion for growth. Metastasis may also occur via lymphatic diffusion and planting into the body cavities as well as hematogenous diffusion. The tumors do not exceed 1–2 mm in thickness or diameter unless there angiogenesis occurs.[4,5,8] The most important angiogenic factors include HIF-1, VEGF, and bFGF (FGF-2). The pathological, fenestrated, weak and new vascular vessels formed via angiogenesis facilitate entry of the tumor cells into circulation and promote the metastatic process. Angiogenesis plays a major role not only in the growth of the tumor, but also in metastasis.[8,9] The granulation tissue has a significant role in wound healing. The histological appearance is characterized by loose extracellular matrix with a basis of new fine–wall capillary net and proliferating fibroblasts. The wound healing is completed by angiogenesis, fibrosis, scar maturation and organization. The factors stimulating angiogenesis in wound healing, namely VEGF and bFGF, are bound to the proteoglycans in basal membrane, and released upon damage to these structures.[8] The mass that occurred in the gingiva of that region following tooth extraction has been explained as a case of “tumor homing”. Due to the angiogenesis that occurs in granulation tissue, the tumor cells easily migrate to and locate in this region, thereby accelerating the pathological angiogenesis process and proliferation via the presence of angiogenesis-stimulating factors at this site.

It is difficult to differentiate the metastases to the oral cavity from the benign processes clinically as they may manifest with similar findings. Therefore, it is mandatory to perform a biopsy, particularly in patients with a known malignancy.[6] Previous cases of oral cavity metastases have been reported in the literature. However, this patient is of significance since it is the first case in the literature with “tumor homing” observed in the granulation tissue following tooth extraction.

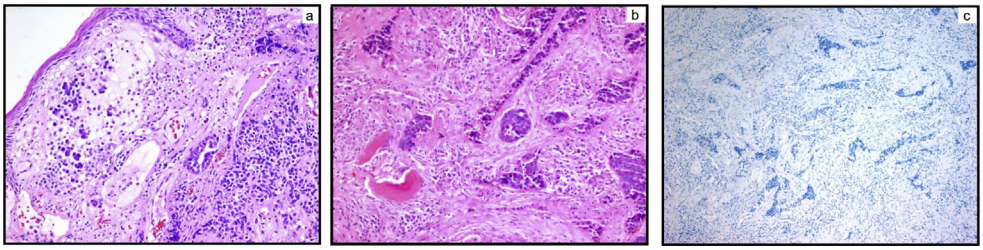


**Fig. 1.** a: Poorly differentiated carcinoma with focal glandular differentiation in the oral mucosa, H&EX100. b: Poorly differentiated pulmonary adenocarcinoma metastasis showing bony destruction, H&EX100. c: The carcinoma was negative for HMWK and diffusely nuclear positive for TTF-1, streptavidine-biotine peroxidase.

## Conflicts of interest

The authors have declared no conflict of interest.

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