

# Metastatic lung cancer in oral cavity

## A case report and literature review

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### ABSTRACT

Metastatic tumors to the oral cavity are rare and they may be localized in the oral soft tissues or jaw bones. Here we present a very unusual incidence of a metastatic adenocarcinoma in the oral cavity originated from lung as first manifestation. Dentists must be aware and suspect such a diagnosis as it mimics odontogenic infections or other benign disorders especially in high-risk patients such as elderly with history of heavy smoking.

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### INTRODUCTION

Tumors are complex heterogeneous and self-organized biological systems where homeostatic mechanisms are dysregulated leading in rapid proliferation of cells and invasion of surrounding tissues<sup>5</sup>. The uncontrollable proliferation leads in cells to detach from the primary tumor, travel through the blood or lymph system, and form new tumor sites in other organs or tissues of the body<sup>4</sup>. Metastasis is also a complex process regulated by several signaling pathways and requires cell motility, invasion, survival, proliferation, and evasion of the immune system. Metastatic tumors to the oral region may manifest in the soft tissues or in the jawbones however are extremely rare, accounting for approximately 1-2% of malignant oral tumors<sup>10</sup>. Lung cancer represents approximately the 12% of the total cancer incidence burden and the 18% of cancer-related death worldwide placing it at the first place in terms of mortality ranking<sup>1</sup>. Although metastatic tumors in the oral cavity are rare, literature describes that lung cancer as the most common malignancy metastasizing to the oral cavity, followed by breast, kidney, and liver tumors<sup>10</sup>. Metastasis to the oral cavity, although can occur at any age, is most common in elderly individuals aged 60 years and older. Only in a few cases the oral/jaw bones lesions are the first clinical manifestation of primary tumor spread. Here we present a very unusual incidence of a metastatic adenocarcinoma of lung in the oral cavity as first manifestation. Dentist must be conscious and suspicious for such a diagnosis as it mimics odontogenic infections or other benign conditions especially in elderly with history of heavy smoking.

## CASE REPORT

An 86-year-old Caucasian male with heavy smoking history record presented in Dental clinic of General Hospital of Agios Nikolaos in Crete, Greece with a painful swelling in the left upper back teeth region of the jaw in the past 2 months. The patient was referred in the clinic by a private dentist with an initial diagnosis of a periapical abscess caused by residual teeth roots of #24#25 (Left Premolars).

Physical examination revealed a marked swelling on the left posterior maxillary gingival mucosa (left premolar region) (Figure 1, A). Dental periapical x-ray revealed no residual roots but findings of radio lucent area within the lesion (Figure 1, B). A biopsy obtained under local anesthesia without complications and was sent for histology examination. The histological and immunohistochemistry analysis of the specimen revealed a positivity of TTF1 and a metastatic invasion of poorly differentiated lung adenocarcinoma confirming the chest x-ray image of possible non-small cell lung cancer (Figure 1, C). Treatment for the patient was only supportive as his general condition was burdened and his physical performance was extremely poor.

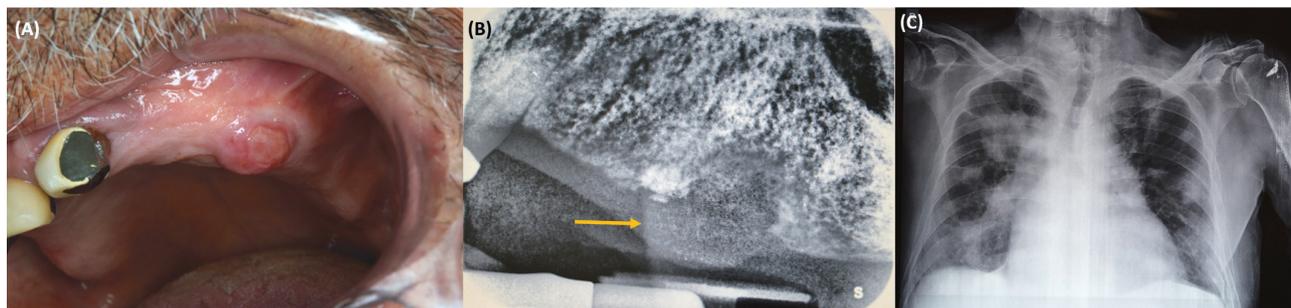
## DISCUSSION

Metastasis is a complex process, often accompanied with dormancy periods prior to any initiation of tumor growth in metastatic organ. Briefly, the metastatic cascade of events involves invasion of the primary tumor lesion to the surrounding extracellular matrix (ECM) from malignant cells that acquire a mesenchymal phenotype with lose cell-cell adhesion, induction of angiogenesis due to hypoxia mechanisms that usually forms immature vessels, inflammation and invasion of ECM with mediation

of matrix metalloproteinases (MMPs). This allows malignant metastatic tumor cells to intravasate into circulation stream, travel, and anchor to endothelial cells of another tissue, extravasate and adapt to the new microenvironment and establish a metastatic colony. The infiltrated cells proceed to overt metastasis reinitiating their proliferative cell cycles at the new tissue, and finally form metastatic colonies that are clinically diagnosed<sup>12,14,17</sup>

Metastatic tumors to the oral cavity are uncommon and available literature is mostly based on sporadic case reports or case series<sup>3,7,15,18</sup>. Possible routes of metastasis to the oral cavity are assumed to be through arterial, venous, and lymphatic circulation where Circulating Tumor Cells (CTCs) circumvent the filtration of the lungs through the valveless vertebral venous plexus or through the arteriovenous shunts in the lungs to move to other organs. Oral lesions can be distinguished in two types, mucosal and jawbone primary tumors or metastatic sites as in this case report. Metastasis in jawbone has been related with remnants of hematopoietic marrow that still exists in some elder in the posterior parts of the mandible and can serve as a favorable niche for metastatic CTCs<sup>7,8,17</sup>. Interestingly, mandible is more often involved than maxilla with molar area to be the most frequent site over premolar and angle-ramus. Regarding mucosal metastasis, gingiva is the most common site in oral soft tissues and chronic inflammation has been associated as a co-factor. A chronically inflamed microenvironment in gingiva with expression of cytokines such as interleukin IL-1 and tumor necrosis factor TNF- $\alpha$ , can facilitate metastasis by stimulate processes that attract CTCs as a promising pre-metastatic niche to engraft and proliferate<sup>9</sup>.

Due to its rarity and lack of specific characteristics, oral metastasis may be mistakenly diagnosed as a periapical abscess or a benign primary oral disease<sup>7,10,13</sup>. Generally,



**FIGURE 1.** The burgeoning periapical tumor lesion. **(A)** Physical examination. **(B)** Dental periapical x-ray. **(C)** chest x-ray shows multiple lesions of the right lung of the finally diagnosed lung adenocarcinoma.

several studies try to assess dentists' awareness, knowledge, attitudes, and practices to recognize or diagnose potential tumor lesions in oral cavity (primary or metastatic)<sup>2,6,11,19</sup>. Most of these studies report a reduced awareness in the diagnosis of possible tumor lesions (metastatic or primary) attributed to several factors mainly the rarity of incidence of oral metastasis or primary tumors and lack of experience as a routine diagnostic procedure for dentists. Visual screening though could potentially reduce mortality in high-risk individuals, hence dentists, as front-line healthcare professionals for oral health, could advance their competencies regarding knowledge and

attitudes to screen high-risk patients for oral tumor lesions<sup>16</sup>. Although the presence of metastatic lesions in the oral cavity usually is sign of extensive metastasis and of very poor prognosis, as was also in this case, palliative care to improve the quality of life and prolong as much as possible is the main goal.

#### CONFLICT OF INTEREST

None.

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### ΠΕΡΙΛΗΨΗ

#### Μεταστατικό καρκίνωμα πνεύμονα στην στοματική κοιλότητα: Ιατρική περίπτωση και σύντομη ανασκόπηση της βιβλιογραφίας

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**Λέξεις - Κλειδιά:** Μεταστατικός καρκίνος, Βλεννογόνος ούλων, Αδενοκαρκίνωμα πνευμόνων

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