

Lung Cancer with Oral Cavity Metastasis: Two Case Reports

Oral Kavite Metastazı Görülen Akciğer Kanseri: İki Olgu Sunumu

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ÖZ

Malign tümörlerin önemli biyolojik ayırt edici özelliklerinden olan invazyon ve metastaz; kansere bağlı morbidite ve mortalitenin en önemli nedenlerindedir. Oral kavite de görülen metastatik tümörler oral malign karakterli tümörlerin %1-1.5' ini oluşturmaktadır ve bu bölgeye metastaz yapan en yaygın primer odaklar arasında meme, akciğer, böbrek, kemik, prostat ve kolon kanserleri gelmektedir. Çene kemiklerinde en sık tutulum alanı mandibula posterior iken yumuşak doku tutulumları en sık dişetine olmaktadır. 63 yaşında erkek hasta mandibula anterior dişlerin çekimi sonrası gelişen, alveol kemiğe invaze, yüzeyi düzensiz ve ülsere alanlar içeren kitle şikayetiyle başvurmuştur. İnsizyonel biyopsi ile değerlendirilen kitlenin histopatolojik incelemesinde saydam hücrelerden baskın karsinom tanısı almıştır. Primer odağın araştırılması için onkoloji servisine yönlendirilmiş ve PET-CT taraması ile akciğer kanseri teşhisi koyulmuştur. Anamnezinde bir yıl önce akciğer kanseri teşhisi koyulan ve uzun kemik metastazları bulunan 62 yaş erkek hasta sol mandibulada rezidüel diş kökünden kaynaklandığını düşündüğü ağrı şikayetiyle başvurmuştur. Yapılan CBCT incelemesinde sol mandibula ramus bölgesinde inferior alveolar kanalı içine almış, kortikal ve trabekül yapıda güve yeniği tarzında osteolitik alanlar izlenmiştir. Akciğer kanseri ve uzak organ metastazları bulunan hasta onkoloji bölümüne yönlendirilmiş ve palyatif tedavisine devam etmiştir. Her iki hasta da 3 ve 6 ay takip sonunda yaşamını yitirmiştir. Metastazların varlığı kötü prognoza işaret eder ve evrelere göre çeşitli tedaviler uygulanabilir. Oral kavite de meydana gelen değişimler dikkatle takip edilmeli, gerekli durumlarda histopatolojik inceleme ile tanıya gidilmelidir.

Anahtar Kelimeler: Oral kavite, oral kanser, akciğer kanseri, histopatoloji, metastaz

ABSTRACT

Invasion and metastasis, which are important biological hallmarks of malignant tumors, are among the most important causes of cancer-related morbidity and mortality. Metastatic tumors in the oral cavity constitute 1-1.5% of oral malignant tumors and the most common primary foci metastasizing to this region are breast, lung, kidney, bone, prostate and colon cancers. The most common site of involvement in the jaw bones is the mandible posterior, while soft tissue involvement is most common in the gingiva. A 63-year-old male patient presented with a mass invading the alveolar bone with irregular and ulcerated areas after extraction of mandibular anterior teeth. Incisional biopsy was performed and histopathological examination of the mass revealed a diagnosis of carcinoma predominantly composed of clear cells. He was referred to the oncology service for investigation of the primary focus and lung cancer was diagnosed by PET-CT scan. A 62-year-old male patient who was diagnosed with lung cancer one year ago and had long bone metastases in his anamnesis presented with pain in the left mandible, which was thought to be caused by the residual tooth root. CBCT examination revealed moth-eaten osteolytic areas in the cortical and trabecular structure involving the inferior alveolar canal in the ramus region of the left mandible. The patient with lung cancer and distant organ metastases was referred to the oncology department and palliative treatment was continued. Both patients died after 3 and 6 months of follow-up. The presence of metastases indicates a poor prognosis and various treatments can be applied according to the stages. Changes occurring in the oral cavity should be followed carefully and diagnosis should be made by histopathological examination when necessary.

Keywords: Indigo naturalis cell viability, periodontal ligament fibroblast.

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Article History

Submitted 15.12.2023
Revised 23.05.2024
Accepted 23.05.2024
Published 29.08.2024

How to cite this article: Yülek, H, Keser, G, Pekiner, Namdar, F. Lung Cancer with Oral Cavity Metastasis: Two Case Reports. European Journal of Research in Dentistry, 2024;8(2): 72-76. DOI: <http://dx.doi.org/10.29228/erd.74>



INTRODUCTION

Lung cancers and related mortality rates are increasing worldwide. According to GLOBOCAN (Global Cancer Statistics) 2020 data, approximately 2.20 million new cases and 1.79 million deaths were reported in both genders (Sung et al., 2021; Bade et al., 2019). It is more common in men than women and the use of tobacco products is among the most important etiological factors (Nasim et al., 2019; Schabath & Cote, 2019). Significant diversity in lung cancer incidence and demographic distribution is observed among nations, with tobacco smoking rates and economic development stage influencing these trends. Although cancer data in emerging nations are less trustworthy, the recent increase in smoking prevalence in China, Indonesia, Eastern Europe, and Northern and Southern Africa is predicted to increase lung cancer incidence in developing regions (Bray et al., 2018; Torre et al., 2015). Up to 80% of current smokers currently live in low - or middle-income nations, and less developed regions account for more than half of lung cancer fatalities (Torre et al., 2016; Torre et al., 2015).

Invasion and metastasis, which are important biological distinguishing features of malignant tumors, are among the most important causes of cancer-related morbidity and mortality (Kumar et al., 2010). Many cases metastasized to the jaw bones and oral soft tissues have been reported in the literature (Lopes et al., 2023; Kirschnick et al., 2022; Gupta et al., 2022; Hirshberg et al., 2008; D'Silva et al., 2006). The most common primary foci metastasizing to the oral cavity include breast, lung, kidney, bone, prostate and colon cancers (Hirshberg et al., 2014; Bodner et al., 2006; D'Silva et al., 2006). The majority of primary tumors metastasizing to the oral cavity are tumors of epithelial origin and are mostly seen in the 4th and 7th decade. The primary source of metastases to the oral cavity in males is lung cancer, whereas breast cancer has been reported in females (Hirshberg et al., 2014; Hirshberg et al., 2008; Bodner et al., 2006; D'Silva et al., 2006).

Metastatic tumors in the oral cavity constitute 1-1.5% of oral malignant tumors. Approximately 30% of oral cavity metastases are seen as the first sign of malignancy (D'Silva et al., 2006). Lesions can be found in bone, soft tissues or both. The most common site of involvement in the jaw bones is the mandible posterior, while soft tissue involvement is most commonly in the gingiva (Özbayrak, 2020; Pekiner & Özbayrak, 2016; Curien et al., 2007). In the early stages, soft tissue lesions may be confused with reactive lesions such as peripheral giant cell granuloma, pyogenic granuloma and epulis fissuratum (Özbayrak, 2020). Oral cavity metastases can be observed radiographically in many different ways. Sometimes they mimic periodontal diseases with cysts and sometimes they may give radiographic findings like osteolytic areas and moth-eaten appearance (Kumar & Manjunatha, 2013).

Diagnosis of metastases represents a poor prognosis. Surgical excision, radiotherapy and chemotherapy can be applied in oral cavity metastases after treatment of the primary tumor. If the primary lesion recurs or involves

metastases to other sites, symptomatic treatments such as pain reduction and maintenance of function can be performed (Rao et al., 2014; Kumar & Manjunatha, 2013; Hirshberg et al., 2008; D'Silva et al., 2006). In these case reports, two different cases of lung cancer with oral cavity metastasis resulting in loss of patients are presented.

CASE REPORT

Case 1

The complaint of a 63-year-old male patient admitted to our clinic was a painless but bleeding mass in the mandibular anterior region, which gradually grew following tooth extraction about 2 months ago. The patient's anamnesis revealed heavy smoking although he had quit smoking 2 years ago. A radiologically bone-involving mass with irregular and clinically ulcerated areas was observed in the anterior edentulous region of the mandible (Figure 1,2). Incisional biopsy of the lesion was performed under local anesthesia. Histopathological examination revealed a diagnosis of clear cell-dominant carcinoma and the primary focus was requested to be investigated (Figure 3A,B). The patient was referred to the Oncology Department to determine the primary focus and to investigate metastatic spread and PET-CT revealed lung involvement with clavicular and scapular metastases (Figure 4). The diagnosis of lung cancer was made as a result of histopathological and radiological evaluations. The patient who received radiotherapy and chemotherapy for lung cancer and distant organ metastases died after 3 months.



Figure 1: A lesion with irregular and ulcerated areas on the alveolar crest in the anterior edentulous region of the mandible following tooth extraction.

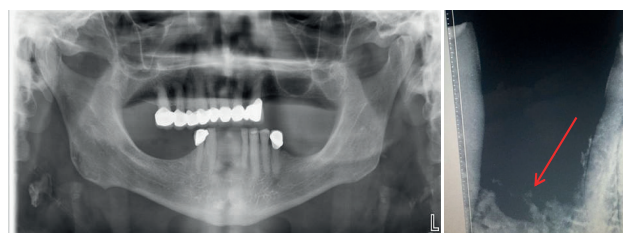


Figure 2 : Invasion of soft tissue lesion to bone on panoramic and periapical radiography.

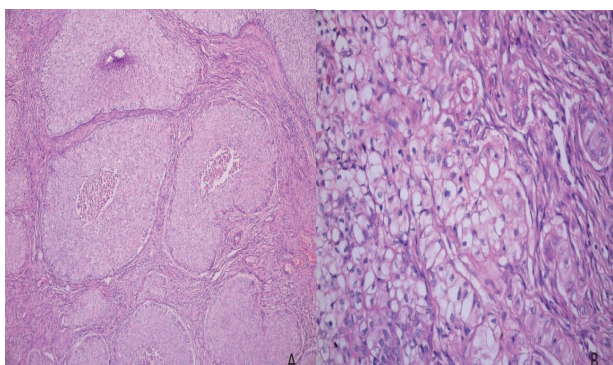


Figure 3: A) Areas of comedo necrosis (HxE, x100) B) Atypical epithelial cells with clear cytoplasm (HxE, x400)

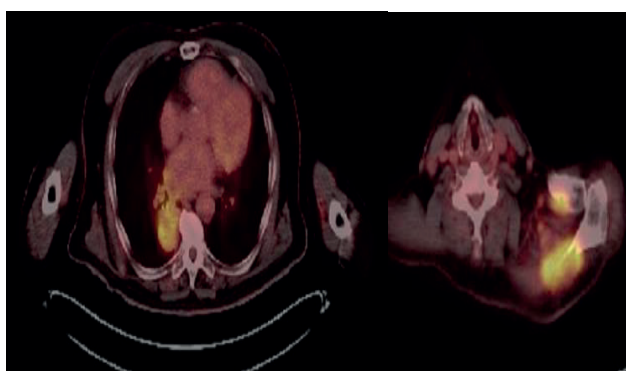


Figure 4: Lung involvement and clavicular and scapular metastases in PET-CT.

Case 2

The patient was admitted to our clinic with the complaint of severe pain in the posterior region of the left mandible, which was thought to be caused by the residual tooth root in the edentulous area (Figure 5) . In the anamnesis of the patient, it was learned that he smoked one packet of cigarettes a day for 30 years and received radiotherapy and chemotherapy for lung cancer one year ago. A history of metastasis to the coccyx bone, femur bone and kidney tissues due to lung cancer was also present. Clinical examination did not reveal any asymmetry or swelling except pain. Panoramic radiography and Cone Beam Computed Tomography (CBCT) examination revealed moth-eaten osteolytic areas in cortical and trabecular structure involving the inferior alveolar canal in the ramus region of the left mandible. The patient with lung cancer and distant organ metastases was referred to the oncology department and palliative treatment was continued. After 6 months of follow-up, the patient died.



Figure 5: Clinical image of the left mandibular posterior edentulous area at the time of the patient’s presentation to the clinic.

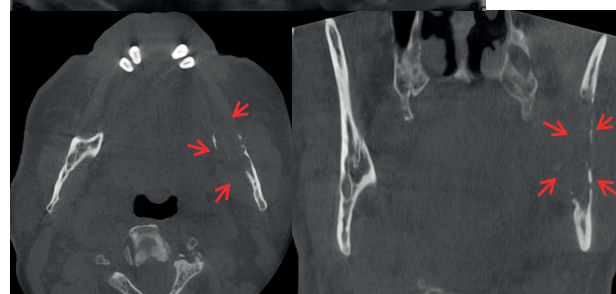


Figure 6: A) On panoramic radiography, irregular areas of cortical bone extending to the ramus in the left posterior edentulous region of the mandible. B) Moth-eaten osteolytic areas in cortical and trabecular structure involving the inferior alveolar canal in the ramus region of the left mandible on CBCT axial and sagittal images.

DISCUSSION

Metastasis to the oral cavity is uncommon, accounting for 1-2% of all oral cancers (Ito et al., 2017; Hirshberg et al., 2014). Oral metastases may be falsely identified as a benign primary oral disease at the time of identification due to its rarity and lack of particular physical features. Some researchers claim that lung, breast, kidney, prostate, thyroid, and stomach cancers are the most common malignancies metastasizing to the oral cavity

(Hirshberg et al., 2014; Tatlidil & Gözübüyük, 2011; Pires et al., 2004), whereas others claim that lung cancer is the most common malignancy metastasizing to the oral cavity, followed by breast, kidney, and liver cancers (Pires et al., 2004). Moreover, lung, breast, kidney, prostate, renal and thyroid carcinomas are the most common primary foci metastasizing to the oral cavity in literature (Lopes et al., 2023; Kirschnick et al., 2022; Gupta et al., 2022; Hirshberg et al., 2014; Hirshberg et al., 2008; D'Silva et al., 2006; Bodner et al., 2006). These lesions, which can be seen at any age, are more common between the ages of 40s and 70s (Hirshberg et al., 2014).

Hirshberg et al (Hirshberg et al., 2014) emphasized that oral cavity metastases are the first clinical sign of the primary tumor with a rate of 30%. In the first case presented, oral cavity lesion appeared as the first clinical sign and primary source was detected after. In the second case, primary lung cancer was diagnosed one year ago and distant organ metastases were known, but oral cavity metastasis was diagnosed as a result of clinical and radiological examination. Both patients were in their 60s. Metastatic lesions in the oral cavity may manifest with clinical features such as pain, paresthesia, swelling, and the presence of progressively growing soft tissue lesions, but it has also been reported that these lesions may be asymptomatic (Shen et al., 2009). The first case presented with painless swelling that progressed rapidly following tooth extraction, while the second case had only severe pain. Oral cavity metastases are more frequently encountered in the mandible (Özbayrak 2020; Kaplan et al., 2019; Curien et al., 2007). Both cases presented herein were found in the mandible. Metastasis in the oral cavity may be a sign of widespread metastases with a poor prognosis. This may occur in advanced stages of cancer and may result in death in a short time. In both cases, primary lung cancer resulted in death in a short period of time despite the presence of distant organ metastases. The incidence of metastasis formation differs from the occurrence of primary tumors, owing to variances in biologic behavior (Hirshberg et al., 2014). It has been reported that malignancies in the kidney, liver, and lung are more likely to spread to the maxillofacial area. And initial cancers in the lungs tend to metastasize to the jawbones and soft tissue (Shen et al., 2009).

The process of metastatic dissemination is complicated, encompassing both tumor features and host response characteristics. For these reasons, the prevalence of metastasis and the specific location of metastases in distant organs varies greatly between tumor types. However, several patterns in metastasis to the oral soft tissues and bone have been recognized and documented in the past. Metastasis from prostate carcinomas was found to be predisposed to the jawbones, and those from the breast were twice as common in the jawbones as in the soft tissue; in contrast, those from the lung and kidney were more common in the soft tissues (Allon et al., 2014, Hirshberg et al., 2014). Both cases presented in our study had bone involvement.

It is worth noting that the majority of oral metastases occur in the mandible, with maxillary metastases being less prevalent. The circulation and the lymphatic system are two potential pathways for metastasis to the oral cavity. Considering the mandible and maxilla do not have lymphatic capillaries, the only feasible pathway for metastasis to the jaw is through blood vessels (Ito et al., 2017). Metastatic foci in the bones are mostly found in the red marrow (Ito et al., 2017; Yin et al. 2005); however, in adulthood, the mandible includes red marrow primarily in the ascending ramus and angles, whereas the maxilla exclusively contains fatty marrow.

Occasionally, metastatic lesions in the jaw may present with vague pain and be misdiagnosed as pathological entities of dental origin, such as pulpal/periapical disease (Kumar & Manjunatha, 2013). Recently, a case of metastatic breast cancer masquerading as a periodontal abscess in the mandible has been reported (Khalili et al., 2010). In a few cases, tooth extraction preceded the discovery of metastasis. The role of trauma to the oral mucosa, particularly from ill-fitting dentures, sharp teeth or restorations, poor oral hygiene and trauma from tooth extraction, in the causation of oral metastasis needs further investigation (Poulias et al., 2011).

It is crucial to highlight that the majority of jaw bone metastases are most likely to go unnoticed. When an oral metastasis is discovered, it can lead to the detection of a hidden primary tumor elsewhere in the body. The presence of this primary tumor can be detected using advanced imaging methods. Because the majority of patients have micrometastases, the prognosis is poor. End-stage disease leads to loss to follow-up or, in some cases, patient death. For the first case in our study a radiologically bone-invading mass with irregular and ulcerated areas was observed in the anterior edentulous region of the mandible following tooth extraction in the alveolar crest. The lesion was first assumed to be a benign reactive lesion, but an excisional biopsy revealed the presence of a clear cell-dominant carcinoma with a primary tumor on the patient's lung. All things considered, these tumors are of significant clinical importance since they might represent the first hint of a malignancy that has not yet been detected at a distant main site or the first proof that a recognized tumor has spread from its primary location.

CONCLUSION

The detection and supportive treatment of oral cavity metastases following the diagnosis of primary cancer is critical for maintaining patient comfort and function. In circumstances when the underlying malignancy is unknown, clinical, radiological and histological assessments can aid in the early diagnosis of the disease. Dentists should carefully check any changes in the oral cavity, and every alteration in cancer patients should be closely examined.

ACKNOWLEDGEMENT

We thank our colleagues Prof. Faysal Uğurlu and Dr. Burcu Öztürk from Department of Oral and Maxillofacial Surgery for their assistance in surgical operation and Prof. Vakur Olgaç from the Department of Oncologic Cytology and Tumor Pathology, Institute of Oncology, İstanbul University for his assistance with the histopathological examination.

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