REVIEW ARTICLE

Gingival Metastasis: A Case Report and Literature Review

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ABSTRACT

Secondary oral cavity neoplasms are rare. We describe a case of an indurated, nonulcerating gingival lesion in a 59-year-old nonsmoking man with no family history of lung cancer. The lesion was the presenting symptom of metastatic lung adenocarcinoma. Reviewing the literature, we find that primary lung cancer among men is one of the most common cancers to metastasize to the oral cavity. Renal and cutaneous neoplasms are the next most common neoplasms to metastasize to the oral cavity. Furthermore, the gingiva, a tissue prone to inflammation, is noted to be a common site for secondary oral cavity neoplasms. This rare case highlights that metastases should influence the clinician's differential of oral mucosal lesions.

INTRODUCTION

Cancer's classic hallmarks—proliferative signaling, evasion of growth suppression, enablement of replicative immortality, induction of angiogenesis, resistance to apoptosis—include the activation of invasion and metastasis.[1] Prevalent sites of metastasis are well documented for common primary neoplasias—for example, the liver for colorectal cancers or the brain parenchyma for melanoma. In contrast, the oral cavity soft tissues and surrounding mandible and maxilla are rare sites of metastatic disease; such lesions account for only approximately 1% of oral neoplasms.[2] However, despite the infrequency of such metastases, the importance of early detection makes knowledge about the demographic characteristics, clinical presentation, appropriate treatment strategies, and typical disease course valuable.[3] We describe a case of a gingival lesion in a nonsmoking man with no family history of lung cancer. The lesion was the first manifestation of his occult metastatic lung adenocarcinoma. A literature review on secondary neoplasms found in the oral cavity and jaw is provided, summarizing demographic patterns, clinical observations, and survival histories, as well as commenting on mechanisms of metastasis.

CASE REPORT

A 59-year-old nonsmoking man with no significant medical history and no family history of lung cancer presented to the Head and Neck Surgery Clinic with a gingival mass. Several years earlier, the patient had started noting sensitivity over his left upper teeth but had no pain or visible lesions. Beginning in January 2014, he noticed a nonulcerating sore on his left maxillary gingiva over tooth 11. He was evaluated at that time by a dentist who diagnosed a bony growth to be managed conservatively. Concerned with interval growth, the patient presented to our clinic for biopsy on March 31, 2014. Review of systems revealed that the patient had had a cough for 3 months. Physical examination showed marked swelling over the left alveolar ridge of tooth 11 (Figure 1). Otherwise a thorough head and neck physical examination, including a direct flexible laryngoscopy, was unremarkable. A biopsy specimen was taken and sent for permanent section in formalin, with the base cauterized with silver nitrate.

Histopathology revealed fibrous connective tissue composed of malignant epithelial cells with enlarged hyperchromatic nuclei and eosinophilic granular cytoplasm (Figure 2). In areas, the cells formed glandular structures. Furthermore, tumor cells were seen infiltrating vital bone trabeculae. Upon immunostaining, the tumor cells were positive for thyroid transcription factor 1 and cytokeratin-7, although negative for cytokeratin-20, thyroglobulin, and prostate-specific antigen. These findings were consistent with a pathologic diagnosis of a metastasis from a primary adenocarcinoma of the lung.

Computed tomography imaging with and without contrast revealed the

Figure 1. Physical examination showing marked indurated swelling over the left alveolar ridge of tooth 11, with bony defect over the lesion. No ulceration is noted.

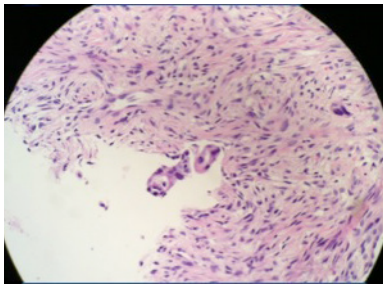

Figure 2. Hematoxylin and eosin stain of the gum lesion revealing islands and cords of malignant epithelial cells with enlarged hyperchromatic nuclei and eosinophilic granular cytoplasm. In areas, cells formed glandular structures.

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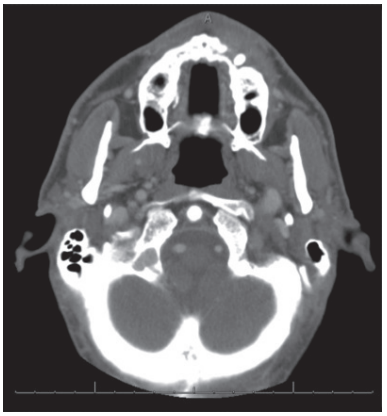

Figure 3. Axial computed tomography image showing gingival lesion as the destructive bone lesion found in left maxilla.

destructive bone lesion in the anterior and inferior aspect of the left maxilla (Figure 3). In the neck, multiple nonspecific small lymph nodes in the jugulodigastric, submandibular, and posterior cervical regions of the neck bilaterally were observed. The largest lymph node highlighted measured 1 cm in diameter.

Furthermore, computed tomography imaging identified the primary lesion as a 4.2-cm mass in the superior segment of the right lower lobe (Figure 4). In the same view, a 1.3-cm lytic lesion in the superior aspect of the T9 vertebral body was found. Right hilar and extensive prevascular, paratracheal, and subcarinal lymphadenopathy was noted. Other imaging views showed multiple lytic lesions involving various other vertebrae and pelvic bones, as well as multiple right hepatic lesions. After counseling and a thorough discussion of options and patient preferences, the patient chose a palliative regimen of radiation to both his primary and secondary sites for the management of his stage IV lung adenocarcinoma.

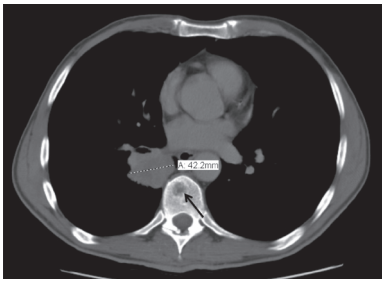

Figure 4. Computed tomography scan showing a 4.2-cm mass in the superior segment of the right lower lobe, identified as the primary lesion. This image also shows a 1.3-cm lytic lesion in a vertebral body (indicated by the black arrow) with extensive neighboring lymphadenopathy.

DISCUSSION

Diagnosis of oral metastatic lesions is challenging, given their rarity.[2-8] Depending on a history of known risk exposures or genetic predispositions, primary tumors of the lesion often can lead the differential. Furthermore, common inflammatory or reactive lesions, such as pyogenic granulomas, peripheral giant cell granulomas, or fibrous epulides, can be commonly mistaken with secondary tumors in the region in sharing similar histories of swelling,

Table 1. Reviewed English-language full-text studies of oral cavity or jaw metastases, with study samples greater than ten and surveying more than one primary site and more than one metastatic site

Study (n)	Male:female ratio	Mean age, years, and SD if included	Top primary tumor types[a]	Top oral cavity or jaw sites for metastases	Survival history
Hirshberg et al,[3] 2008 (673)	Jawbone metastases: 1:1 Oral soft tissue metastases: 2:1	Men: 51.1 Women: 47.1	**Men**: lung, kidney, liver **Women**: breast, genital organs, kidney	1) Mandible 2) Gingiva	Most cases, mean survival time ~7 months
Seoane et al,[4] 2009 (39)	1.2:1	62.3 ± 9.2	**Men:** kidney = lung, prostate, liver **Women:** breast, kidney = thyroid	1) Mandible 2) Upper gingiva 3) Maxilla	Mean survival time since observation of metastasis was 13.5 ± 21.3 months
Shin et al,[5] 2012 (29)	5.8:1	64.8	**Men:** Liver, lung, stomach **Women:** breast, colon = stomach = lung	1) Gingiva 2) Tonsil/pillar 3) Mandible	~86% died within 1 year of developing oral metastases
Maschino et al,[6] 2013 (23)	2.3:1	64.5 ± 13.2	**Men:** lung, kidney **Women:** breast	1) Gingiva/ alveolar mucosa 2) Tongue	Mean survival time was 16.6 months at time of diagnosis
Murillo et al,[7] 2013 (16)	4.3:1	58.8	**Men:** lung, unknown = prostate **Women:** unknown, breast	1) Gingiva 2) Floor of mouth 3) Mandible	Mean survival from diagnosis of an oral metastasis was 8.25 months
McClure et al,[8] 2013 (26)	1.6:1	64	**Men:** lung, colon, prostate **Women:** breast, lung, leg	1) Mandible 2) Gingiva	75% of patients died of their disease within 4 months of the diagnosis of the maxillofacial metastases, irrespective of treatment

[a] Primary tumor types are ordered by frequency; "=" indicates equivalent frequency in the study.
SD = standard deviation.

pain, and paresthesias. Nonetheless, knowledge of incidence, presentation, common primary sites, common oral cavity metastatic sites, and prognosis indicators may help clinicians in diagnosis and management.[3]

Literature Review Method

To help explore these epidemiologic questions, we searched the English-language literature of MEDLINE between 1992 and 2014 with date of last search on January 2, 2015, for case series of metastatic tumors to the oral cavity and jaw bones. Our inclusion criteria were full-text studies in peer-reviewed journals in which reported data included number of cases, male to female ratio, mean age of cases, primary tumor site types by sex, oral cavity sites for metastasis with histologic confirmation, and survival history. The following article types were excluded from our review: 1) duplicate studies or reviews based on duplicate data; 2) case reports or series with five or fewer oral cavity or jaw metastases because such low-powered studies lacked informative significance; and 3) series that focused on only one primary origin of the tumor or one oral site of metastasis. The reason we excluded the last type of article was that although such studies may be instructive for their given specific focus, they lack the broader potential for implications that could be drawn from studies that included a variety of primary tumor origins or a variety of oral sites of metastases. The following studies found are displayed in Table 1.

Literature Review Findings

Our literature search yielded 6 non-duplicative studies, the largest of which was written by Hirshberg et al[3] in 2008, a case series that spanned from 1916 to 2006. Overall, oral cavity or jaw metastases tended to be male-predominant,[3-8] with the data of Hirshberg et al[3] suggesting that jawbone metastases were more uniform between the sexes. Mean age across the studies hovered between the 40s and 60s, with most studies citing their means in the latter part of the age interval. Top primary tumor types among men included lung, kidney, and liver; in women, top primaries included breast, female genital organs, and lung. Gingiva and mandible dominated as sites for oral cavity and jawbone metastases.[3-8] Our case matches this literature review's demographic sketch. It was not uncommon for these types of metastases to be the presenting symptom; in fact, oral metastases were found to be the first sign of stage IV disease in approximately 25% of cases.[3]

Clinical presentation varied depending on the site of metastasis. Jawbone metastases were described often as rapidly progressive swelling with associated edema and pain. They mostly presented as lytic radiolucent lesions with ill-defined borders on radiograph, or occasionally osteoblastic lesions with varied degrees of radiopacity.[3,8] Oral soft-tissue metastases typically presented also as rapidly progressive hyperplasic growths, with or without ulceration, even within one week's time.[5,7,8] Histologic assessment by way of biopsy becomes essential, though it was noted that severe post-biopsy hemorrhage had been reported in some cases, especially in lesions of metastatic hepatocellular carinoma.[3,7]

Because of the metastatic nature of the disease, treatment strategies in the review focused on "quality of life" measures, including local resection, radiotherapy, or even chemotherapy for global metastases. Prognosis appeared to be dependent on the extent of metastases, and local resection of isolated oral metastatic foci sometimes correlated with overall improved prognosis.[2] Nonetheless, in the above collection of case series, survival was noted to be poor; mean survival among the certain case series that included that parameter ranged from 7 to 16.6 months.[3,4,6,7]

CONCLUSION

This case report highlights a rarely encountered but clinically important finding: that gingival metastases from solid cancers may be a rare but underappreciated diagnosis when presenting as oral mucosal lesions. These tumors often indicate a poor prognosis, yet in certain cases, early identification may render the possibility of improved outcomes. Therefore, such lesions should influence the clinician's differential of oral mucosal lesions. Vigilant recognition of such lesions should prompt steps toward a definitive histologic diagnosis and potential accompanying metastatic evaluation. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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