Mandibular metastasis from lung adenocarcinoma as the first sign of occult malignancy

Cameron Johnson, DDS, MD^{a,b}, and Andrew Read-Fuller, DDS, MD^{a,b}

^aDepartment of Oral and Maxillofacial Surgery, Baylor University Medical Center, Dallas, Texas; ^bDepartment of Oral and Maxillofacial Surgery, Texas A&M College of Dentistry, Dallas, Texas

ABSTRACT

Metastatic disease to the oral and maxillofacial region is rare, with only about 1% of oral malignancy attributed to metastases. In approximately 20% of these patients, oral metastases are discovered before the detection of the primary tumor. Here we present a case of a 66-year-old man who presented with vague left mandibular pain and new-onset lip numbness as the first sign of occult malignancy from lung adenocarcinoma with multiple metastases.

KEYWORDS Lung adenocarcinoma; mandibular malignancy; mandibular metastasis

The mouth and jaws are uncommon sites for metastatic dissemination, with only about 1% of oral malignancy attributed to metastases.¹ In approximately 20% of patients, oral metastases are discovered before the detection of the primary tumor.² We report a man who presented with vague left mandibular pain and new-onset lip numbness as the first sign of occult lung adenocarcinoma.

CASE DESCRIPTION

A 66-year old man, a former 30 pack-year smoker who had a history of chronic severe generalized periodontitis, underwent extraction of all remaining mandibular teeth. At the time of extractions and at his 1-week postoperative follow-up, he had no complaints, but he returned 3 weeks later with abrupt onset of vague left-sided mandibular pain radiating from the left posterior mandible to the left temporal region. Intraoral exam revealed well-healing gingival tissues without any identifiable bony abnormalities, and a Panorex radiograph showed expected postsurgical osseous changes with no significant abnormalities (*Figure 1a*). The patient returned at postoperative week 8 with ongoing left posterior mandibular pain and new-onset left lower lip numbness. A contrast-enhanced maxillofacial computed tomography (CT) scan revealed a focal area of moth-eaten bony architecture at the left mandibular body just inferior to the recent surgical site, which was highly suspicious for osteomyelitis.

The patient was subsequently admitted to the hospital, with an initial white blood cell count of $8.1 \times 10^9/L$, C-reactive protein of 0.9 mg/dL (normal 0–0.3), and erythrocyte sedimentation rate of 9.0 mm/h (normal 0–20). The surgical team planned for left mandibular surgical debridement with biopsy, initiation of intravenous antibiotics, and head and neck magnetic resonance imaging (MRI) to confirm suspected osteomyelitis. Intraoperatively, extensive necrosis of the left posterior mandible was encountered with multiple specimens collected for biopsy. The MRI showed diffuse supratentorial millimetric brain lesions, multiple C3–C4 osteolytic spinal lesions, and focal left posterior mandibular lesions concerning for diffuse metastases (*Figure 1b*). A contrast-enhanced CT of the neck, chest, abdomen, and pelvis revealed a 2.8-cm speculated lobulated mass within the left lower lung, highly suspicious for the primary tumor, with multiple surrounding subcentimeter satellite nodules, which likely represented metastases (*Figure 1c*). Distant metastases were also seen in the liver, adrenal glands, lumbar spine, and ribs and in the mediastinal, bilateral hilar, mesenteric, and porta hepatis lymph nodes. Cultures of the left mandible were negative, and the biopsy primarily showed necrotic mandibular bone. Biopsies of multiple hepatic lesions demonstrated moderately differentiated adenocarcinoma with immunohistochemical and histologic features most consistent with non-small cell lung cancer. The left mandibular bone sample had nests of variably viable adenocarcinoma with nuclear enlargement, hyperchromasia, and spotty mitotic activity.

Corresponding author: Cameron Johnson, DDS, MD, Department of Oral and Maxillofacial Surgery, Texas A&M College of Dentistry, 3000 Gaston Avenue, Dallas, TX 75246 (e-mail: camjohnson7@tamu.edu)

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Figure 1. Case imaging. (a) Panorax radiograph 3 weeks after mandibular tooth extractions with routine osseous healing of sockets and no bony abnormalities in the mandible. (b) MRI of the head and neck with an extensively abnormal hyperintense T1 STIR signal involving the marrow of the left mandibular body, angle, and ramus. (c) CT of the chest, axial view, with a 2.8-cm spiculated mass in the central left lower lobe with surrounding satellite lesions.

Care was turned over to medical oncology, where the patient underwent brain radiotherapy within a week of diagnosis. He was eventually started on pembrolizumab after genetic testing for the pathological variant of the *NRAS* gene and PD-L1. The patient's treatment is ongoing.

DISCUSSION

Multiple theories exist regarding the metastatic pathway to the head and neck from distant primary tumors. The possible routes of metastasis include the bloodstream and the lymphatic system, although most occur hematogenously.³ The main mechanism of hematogenous metastasis to the oral cavity involves Batson venous plexus, the valveless prevertebral venous network that permits the retrograde path of tumor cells from the lungs to the face.⁴ Metastatic lesions can be found anywhere in the oral cavity, yet 90% are intraosseous and within the mandible and soft tissue localizations are rare.⁵ Metastatic foci in the jaw bones are mainly situated in the red marrow, where there is hematopoietically active bone marrow.⁶ The ascending ramus and angle of the posterior mandible as well as focal osteoporotic bone marrow defects are the most hematopoietically active sites that attract tumor cells, thus accounting for their higher tendency to seed within these sites.⁶ It has also been suggested that the posterior mandible is a common site of metastases due to abrupt angulation of the facial vessels at this site, causing slowing of vascular flow that may promote malignant cell deposition.²

Regardless of the route of travel to the oral cavity, metastases to this area are rare and represent approximately 1% of all oral malignancies.⁷ In an analysis of 673 metastatic tumors to the oral cavity, Hirshberg et al reported that metastases to the oral cavity may occur at any age but are most common during the fifth and sixth decades of life, with the site of the primary tumor differing between sexes. For men, the most common primary site is the lung, followed by prostate, kidney, bones, and adrenal glands, whereas in women it is the breast, followed by female genital organs, kidney, and colorectum.⁸

Because of their rarity and atypical clinical and radiographic appearances, metastatic lesions are a diagnostic challenge.⁹ Over 90% of jawbone malignancies are osteolytic, yet 5% of reported cases to the jawbones lack any radiographic change.⁸ These osteolytic changes, although nonspecific, are usually radiolucent

lesions with ill-defined margins, sometimes with a moth-eaten appearance that can simulate osteomyelitis, as seen with our patient. Clinical manifestations of jawbone metastases can be highly variable, with most patients presenting with pain, toothache, swelling, paresthesia, bleeding, superinfection, dysphagia, interference with mastication, and disfigurement. Furthermore, mandibular metastases sometimes mimic temporomandibular disorders, osteomyelitis, or trigeminal neuralgia.³ Special attention should be given to patients who develop “numb chin syndrome” or mental nerve neuropathy, which should always be alarming for potential metastatic disease.⁸ Interestingly, our patient's only initial complaint was nonspecific left posterior mandibular pain, but it was the new-onset lip numbness that was most concerning and warranted further investigation. It was also noteworthy that he had no other systemic symptoms in the presence of diffuse widespread disease.

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