

**Case Report**

# Metastasis of Lung Cancer to the Oral and Maxillofacial Region: A Case Report and Review of the Literature

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## Abstract

Lung cancer is the most frequent cause of cancer-related death worldwide. While metastases of lung malignancies to the oral cavity are rare, it is the most common neoplasm to metastasize to this region. Diagnosis of a metastatic lesion in the oral cavity is challenging for clinicians and pathologists, but is critical in improving patient outcomes. This report presents a case of a 75-year-old female with lung adenocarcinoma metastatic to posterior left mandible. A literature review of cases of lung cancer metastasis to the oral and maxillofacial region between 2015 and 2022 was conducted and compared with prior research.

**Keywords:** neoplasm metastasis, differential diagnosis, literature review

## Introduction

Metastatic tumors to the oral region are uncommon (representing 1-2% of oral malignancies) and may occur in the oral soft tissues or in the jawbones.<sup>1</sup> Only 5% of all malignancies involve the oral cavity, and one percent of these malignancies are secondary to neoplasms found below the level of the clavicles.<sup>2</sup> These oral metastases are often a late-stage manifestation found in the presence of widespread disease and are associated with poor long-term prognosis, yet they are sometimes the first sign of an undiagnosed malignancy. The rarity and severity of these metastases make the diagnosis and treatment of these tumors challenging for both the clinician and pathologist.<sup>1</sup> Herein, we present a case of a 75-year-old woman with poorly differentiated lung carcinoma involving the mandible, which was

initially thought to be a lesion of endodontic origin, and a review of literature spanning 2014-2022.

## Case Report

A 75-year-old female in apparent good health was referred to an oral surgeon by her treating endodontist for evaluation of persistent swelling of the lower left mandible. Mandibular left first molar, believed to be the source of swelling, received root canal treatment twice over the 6 months preceding the oral surgery visit (Figure 1). An accompanying computer tomography (CT) scan demonstrated reactive periostitis in the area.

Clinical examination revealed slight fullness of lower left face, with no appreciable lymphadenopathy, redness, or tenderness. Intraorally, marked expansion of posterior left

mandible was noted, although the mucosal surface was intact and did not show ulceration or discoloration.

Based on the clinical presentation, periapical pathology, such as periapical granuloma or radicular cyst, was suspected. Radiographically, periapical granuloma presents with an opacity at the apex of a nonvital tooth, although early lesions may present with no radiographic evidence.<sup>3</sup> Similar to a periapical granuloma, a radicular cyst is associated with an asymptomatic nonvital tooth, with radiographic appearance identical to that of a periapical granuloma. Radicular cysts are more likely to be present in the anterior maxilla rather than the molar region of the mandible seen in this case.<sup>4</sup> A residual radicular cyst was not considered, as this patient's lesion was not at an extraction site or an area where an odontogenic cyst was removed. Residual cysts typically present in areas that are not properly curretted.<sup>5</sup> Although it is not common for the lining of a residual cyst to undergo malignant transformation to squamous cell carcinoma, it should always be included on a differential with a residual radicular cyst when there is history of extraction or surgical removal of a cyst.<sup>6</sup>

A biopsy was obtained apical to the distal root of mandibular left first molar was planned to determine the cause of persistent swelling. A mucoperiosteal flap was created and reflected on posterior left buccal alveolar ridge, and a bony window was created with a low-speed handpiece and abundant sterile saline irrigation. Lesional tissue was obtained through the osseous window and submitted for histologic examination along with the bony window. Histologic examination revealed a proliferation of cells with nuclear hyperchromasia, enlargement, and pleomorphism against a background of extravasated red blood cells (Figure 2). Immunohistochemical staining demonstrated the positivity of the lesional cells for panCK, CK7, TTF-1, and Napsin A. CK20, S100, CD45, HMB45, CDX2, and GATA3 were

negative. This immunohistochemical profile suggested the lung as the primary origin of the present lesion.

## Materials and Methods

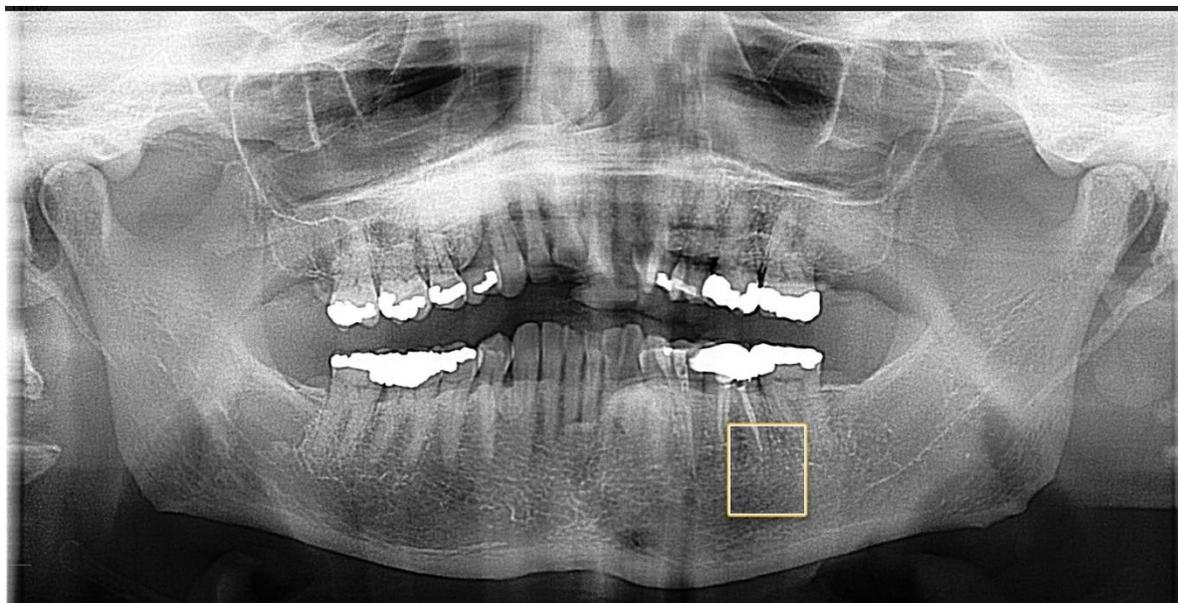
A literature search for metastatic lung cancer cases in the oral and maxillofacial region was performed using references from January 2015 through March 2022 in PubMed, Scopus, Web of Science, and the Columbia University Libraries with combinations of the keywords *metastatic lung cancer*, *metastatic lung carcinoma*, *metastasizing lung cancer*, *metastasizing lung carcinoma*, *jaw metastasis*, *metastasis to oral cavity*, *metastasis to jawbones*, *metastasis to oral and maxillofacial region*, and *metastasis to salivary glands*. The selected publications were analyzed using the following factors: type of lung cancer, site of metastasis, treatment received, and outcome/prognosis. The cases were reported as case reports or reviews of the literature.

We present a review of literature on lung cancer metastases to the oral cavity. To the best of our knowledge, this is the first such literature review since the most recent publication in 2014.<sup>7</sup> Results of the literature review of lung tumors metastatic to the oral and maxillofacial region are presented in Table 1.<sup>7-51</sup>

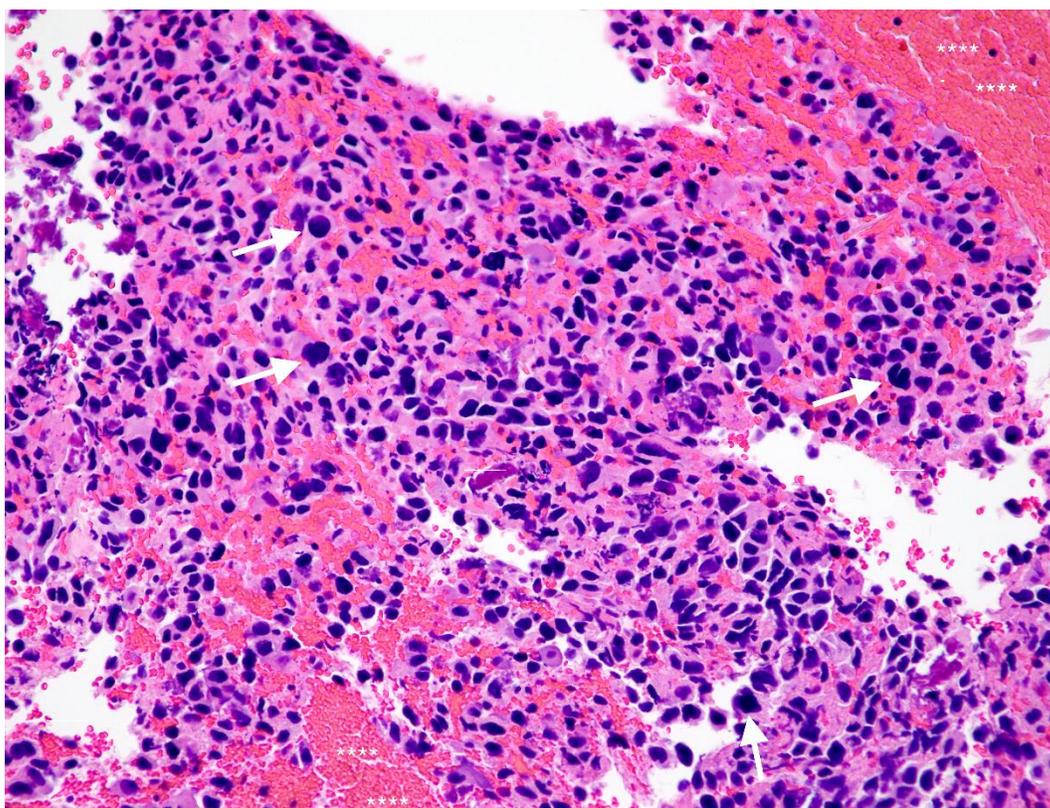
## Results

Forty-five articles were used to identify forty-six cases. All of the publications entered into the final review were case reports (N=46).

Patient age was reported in forty-five of the cases. Most metastatic tumors to the oral and maxillofacial regions were found in patients in their seventh decade (mean age for male was 62.3 years and 67 years for females). This is slightly older than the data from Hirshberg et. al, which reported the most common decades being the fifth and sixth.<sup>1</sup>



**Figure 1:** Preoperative panoramic radiograph with no readily apparent lesion apical to mandibular left first molar.



**Figure 2:** Proliferation of cells demonstrating nuclear hyperchromasia, enlargement, and pleomorphism (arrows) against a background of extravasated red blood cells (asterisks), 100x (hematoxylin-eosin).

**Table 1:** 2015 to 2022. Results of the literature search of lung tumors metastatic to the oral and maxillofacial region from

Reported Case Author, Year of Publication	Age/Sex	Tumor Site	Direction/Extension/Metastasis	Histological Type	Treatment of Lung Primary If Known Prior to Oral Metastasis	Treatment Following Discovery of Oral Lesion	Follow-up	Known lung primary at time of oral diagnosis?	Smoking/Tobacco History
Abe Et al., 2019 <sup>8</sup>	76/M	Hard Palate	Lung	Adenocarcinoma	CTX	CTX	Expired, 4 months after the first admission	Yes	40.5 pack year history, alcohol use unspecified
Arslan et al., 2016 <sup>9</sup>	59/M	Retromolar Trigone (R)	Lung	Mesothelioma	CTX, RTX	None	Expired, 45 days following diagnosis of oral lesion	Yes	Unspecified
Bisht et al., 2017 <sup>10</sup>	32/M	Maxilla (R)	Lung	Adenocarcinoma	---	CTX, RTX	Alive, showed partial response to radiotherapy	No	Smokeless Tobacco, one or two pouches per day. Unspecified alcohol use

Cui et al., 2019 <sup>11</sup>	64/M	Parotid Gland (R)	Lung	Small Cell Carcinoma	---	Sx, CTX	Alive, treatment and follow up are ongoing following three cycles of chemotherapy	No	Unspecified
D'Antonio et al., 2016 <sup>12</sup>	76/M	Palatine Tonsil (R)	Lung	Small Cell Lung Cancer	---	CTX	Expired, 14 months following presentation	No	“Former smoker of 30-40 cigarettes a day” Unspecified Alcohol Use
Forooghi et al., 2019 <sup>13</sup>	57/M	Maxillary Alveolar Ridge (L)	Lung	Squamous Cell carcinoma	CTX, RTX	Symptomat ic treatment	Alive, three months after commencing case evaluation	Yes	“Heavy smoker”, unspecified alcohol use
George et al., 2019 <sup>14</sup>	68/M	Mandible (R)	Lung	Adenocarcinoma	---	Sx, CTX, and RTX	Unspecified	No	“Had a habit of smoking 10-15 cigarettes a day for more the 25 years” ~18 pack years, “occasional alcohol consumption”

Guarda- Nardini et al., 2017 <sup>15</sup>	59/F	Condylar Head (R)	Lung	Carcinoma	---	RTX, CTX, Sx	Expired, 13 months after initial diagnosis	No	“Smoked 10 to 15 cigarettes per day” unspecified how many years, unspecified alcohol use
Gultekin et al., 2016 <sup>7</sup>	72/M	Mandible (R)	Lung	Adenocarcinoma	RTX	Sx,RTX, CTX	Expired, 6 months after initial diagnosis	Yes	40 pack year smoking history, Unspecified alcohol use
Hussain et al., 2020 <sup>16</sup>	66/F	Mandible (R)	Lung	Poorly Differentiated Neuroendocrine Carcinoma	---	Palliative Care	Expired, 4 weeks after initial presentation	No	Never smoker and “low alcohol intake”
Ito et al., 2017 <sup>17</sup>	85/M	Maxillary Buccal Gingiva (L)	Lung	Adenocarcinoma	Supportive Care	RTX	Expired “soon”	Yes	Unspecified
Jeba Et al., 2016 <sup>18</sup>	45/M	Anterior Tongue (L)	Lung	Adenocarcinoma	---	CTX	Lost to follow-up	No	Smoker, unspecified pack years,

									unspecified alcohol use
Johnson and Read-Fuller 2020 <sup>19</sup>	66/M	Mandible (L)	Lung	Adenocarcinoma	---	CTX	Alive, treatment is ongoing as of April 2020	No	30 pack-year smoking history, unspecified alcohol use
Kalaitzidou et al., 2015 <sup>20</sup>	69/M	Anterior Mandible	Lung	“high grade neuroendocrine carcinoma with elements of both small and large cell lung carcinoma”	CTX	None	Expired, prior to surgical excision of oral lesion	Yes	Unspecified
Kaur et al., 2021 <sup>21</sup>	47/M	Mandible (L)	Lung	Adenocarcinoma	---	CTX	Expired, following two cycles of chemotherapy	No	30 pack year history, unspecified alcohol use

Kawahara da et al., 2022 <sup>22</sup>	79/M	Maxilla (L)	Lung	Adenocarcinoma	Sx, RTX	Supportive Care, RTX	Expired, 11 months after initial presentation for oral lesion	Yes	Unspecified
Kitadai et al., 2019 <sup>23</sup>	64/M	Anterior Maxillary Gingiva	Lung	“Non small cell lung cancer favoring adenocarcinoma”	RTX	CTX	Expired due to aspiration pneumonia followed by acute respiratory distress syndrome	Yes	No smoking history, unspecified alcohol use
Lee et al., 2020 <sup>24</sup>	87/F	Submandibul ar Gland (L)	Lung	Small Cell Neuroendocrine Carcinoma	---	Patient Declined	Expired, three months after diagnosis	No	Unspecified
Lee S-Y et al., 2018 <sup>25</sup>	63/M	Tip of Tongue	Lung	Squamous Cell Carcinoma	---	CTX and Sx	Expired, 8 months after presentation for tongue lesion	No	“Heavy alcohol and tobacco use” unspecified pack years

Lenouvel et al., 2016 <sup>26</sup>	59/M	Parotid (R)	Lung	Adenocarcinoma	---	Unspecified	Expired due to cardiac arrest	No	30 pack year smoking history, unspecified alcohol use
Matsuda et. Al., 2018 <sup>27</sup>	83/F	Mandible (R)	Lung	Poorly Differentiated Adenocarcinoma	---	CTX	Alive, two years after initial hospital visit for oral lesion	No	Nonsmoker, unspecified alcohol use
McKernon et al., 2017 <sup>28</sup>	61/F	Mandible (L)	Lung	Adenocarcinoma	---	Unspecified	Unspecified	No	40 pack year smoking history, Unspecified alcohol use
Mohamed et al., 2021 <sup>29</sup>	Unspecified age/F	Dorsal Tongue	Lung	Mesothelioma	CTX	Supportive Care	Alive, uninterested in RTX for the tongue lesion at six week F/U	Yes	Unspecified
Moraes et al., 2017 <sup>30</sup>	66/M	Mandible (R)	Lung	Small Cell Lung Cancer	CTX	CTX	Alive at 4 months follow up. Patient was asymptomatic and the x-ray showed	Yes	Unspecified

							signs of new bone formation.		
Nuyen and Tang 2016 <sup>31</sup>	59/M	Maxillary Gingiva (L)	Lung	Adenocarcinoma	---	RTX	Unspecified	No	Nonsmoker, unspecified alcohol use
Oliver et al., 2021 <sup>32</sup>	51/F	Mandibular Condyle (R) and Mandibular Ramus (R)	Lung	Adenocarcinoma	---	Unspecified	Unspecified	No	Unspecified
Pezzuto, et al., 2017 (Case 1) <sup>33</sup>	65/M	Mandible (R)	Lung	Squamous Cell Carcinoma	Sx, CTX	RTX, Hyperthermia Treatment	Expired a few weeks after treatment	Yes	40 pack year history, unspecified alcohol use
Pezzuto, et al., 2017 (Case 2) <sup>33</sup>	65/F	Mandible (R)	Lung	Squamous Cell Carcinoma	CTX	Sx	Expired, 7 days after surgery as a result of bleeding and embolism	Yes	“Pack-years above 40”, unspecified alcohol use

Rajini et al., 2015 <sup>34</sup>	62/M	Mandible (R)	Lung	Poorly Differentiated Adenocarcinoma	---	CTX, RTX	Alive, “response to radiotherapy is good”	No	Unspecified
Rajinikant h et al., 2015 <sup>35</sup>	60/M	Mandible (R)	Lung	Metastatic Malignant Tumor	---	CTX, RTX	Unspecified	No	Unspecified
Rocha et al., 2020 <sup>36</sup>	55/M	Parotid Region (R)	Lung	Adenocarcinoma	RTX, CTX	None	Expired, 1 month following presentation with oral lesion	Yes	“Ex-smoker” pack years unspecified “ex-alcoholic”
Rovira-Wilde et al., 2020 <sup>37</sup>	59/F	Mandible (L)	Lung	Adenocarcinoma	---	Unspecified	Expired, 15 months after initial presentation	No	40 pack year smoking history, Unspecified alcohol use
Schneider et al., 2015 <sup>38</sup>	61/F	Mandible (L)	Lung	Large-Cell Neuroendocrine Carcinoma	RTX and CTX	RTX and palliative care	Expired, 3 months following presentation with oral lesion	Yes	80 pack year smoking history, no history of alcohol use

Soputro et al., 2022 <sup>39</sup>	79/M	Parotid Gland (L)	Lung	Adenocarcinoma	RTX	Sx	Alive, presented to ED 2 months later with left pleural effusion. Long term pleural drainage catheter was placed.	Yes	60 pack year history, prior occupational asbestos exposure, alcohol use unspecified
Souron et al., 2016 <sup>40</sup>	70/M	Posterior Maxillary Gingiva (L)	Lung	Large Cell Neuroendocrine Carcinoma	CTX	Unspecified	Unspecified	Yes	60 pack year smoking history, unspecified alcohol use
Steffen et al., 2020 <sup>41</sup>	50/M	Mandible (L)	Lung	Adenocarcinoma	Sx, RTX	Sx, CTX	Unspecified	Yes	“Former smoker”
Stephen et al., 2020 <sup>42</sup>	65/F	Parotid (L)	Lung	Adenocarcinoma	---	Patient Declined	Unspecified	No	Unspecified
Tamgadge et al., 2020 <sup>43</sup>	41/M	Maxilla	Lung	Adenocarcinoma	Patient never reported back	---	Lost to follow up	No	Gutkha chewer for 20 years, unspecified alcohol use

Tanaka et al., 2020 <sup>44</sup>	66/M	Buccal gingiva of Maxilla (L)	Lung	Malignant Pleural Mesothelioma	CTX	RTX	Expired, 1 month after presentation with gingival tumor	Yes	Unspecified
Thomas and Blake 2021 <sup>45</sup>	40/M	Parotid Region (L)	Lung	Small Cell Carcinoma	---	Unspecified	Unspecified	No	“Chronic Smoking”
Tirkey et al., 2019 <sup>46</sup>	50/M	Attached gingiva of Anterior Maxilla	Lung	Large Cell Carcinoma	RTX, Supportive Care	Unspecified	Unspecified	Yes	Unspecified
Veremis et al., 2020 <sup>47</sup>	81/F	Anterior Maxilla (R)	Lung	Mesothelioma	Sx, CTX, RTX	Sx	Expired, 12 days after discharge	Yes	Unspecified
Xie et al., 2020 <sup>48</sup>	63/M	Root of Tongue	Lung	Malignant Pleural Mesothelioma	Unspecified	---	Unspecified	No	Unspecified

Yanagisa wa et al., 2017 <sup>49</sup>	84/M	Mandible (R)	Lung	Small Cell Lung Cancer	CTX	CTX	Alive, partial remission of symptoms following CTX for oral lesion	Yes	“Heavy smoking history” Unspecified alcohol use
Yang and Xiong 2017 <sup>50</sup>	66/M	Parotid Gland (L)	Lung	Adenocarcinoma	---	Sx, CTX, and RTX	Unspecified	No	“Heavy smoking for 30 years” pack years unspecified, unspecified alcohol use
Zaubitzer et al., 2019 <sup>51</sup>	66/F	Palatine Tonsil (R)	Lung	Poorly Differentiated Adenocarcinoma	---	CTX	Alive, last MRI correlated with stable disease.	No	Former smoker with 40 pack year history, unspecified alcohol use

The sex of the patients was mentioned in all of the publications. Metastatic lung cancer to the oral and maxillofacial region was more prevalent in males (n=33) than in females (n=13; ratio, 2.54:1). This is similar to the 2.5:1 ratio cited for soft tissue metastases.<sup>1</sup>

In line with past research, the jawbones and hard palate were more affected than the oral soft tissues (25:21), and of the bony structures in the oral and maxillofacial region, the mandible was the most frequently affected structure. The mandible was the site of oral metastasis nineteen times (n=19) of the forty-six cases. The posterior mandible or ramus of the mandible was particularly common.

When looking at the oral soft tissues, the attached gingiva of the maxilla was the most commonly affected site (6 cases, 28.5%), followed by the parotid gland (5 cases, 23.8%), and the tongue (4 cases, 19.0%). The remaining soft tissue sites occurred much less frequently.

Patients often presented with several symptoms common to past research, the most common being pain, swelling, and paresthesia. In the event that soft tissue was involved, it was also common that bleeding or ulceration was present.

In twenty-five of the forty-six cases, the patient was unaware of any primary cancer at the time of presentation with oral symptoms. This demonstrates that patients can unknowingly have widespread metastatic cancer and present with symptoms that a dental provider should notice. An occult primary should be considered when a patient presents with symptoms suggestive of metastatic disease or if a lesion persists after dental treatment. No conclusions can be drawn regarding the frequency of distant oral metastases presenting the first symptom of metastatic disease due to bias of reporting unusual cases.

Histological typing was done in forty-four cases. The most common histological type was by far adenocarcinoma (n=24), followed by small cell or neuroendocrine carcinoma (n=9),

mesothelioma (n=5), squamous cell carcinoma (n=5), and non-small cell carcinoma (n=1).

In twenty-six cases there was some form of tobacco use reported in the patient history (56.5% of cases). Twenty-four of these cases reported that the patient was either a current or former smoker and in two of the cases the patient used a form of smokeless tobacco. It should be noted that tobacco could have been used in a greater number of the cases, but tobacco use was not specified in sixteen of the cases.

In the reported cases chemotherapy was by far the most common treatment modality. Chemotherapy was used in thirty-one (67.4%) of the cases. This is to be expected as it is known that oral metastases are often a late-stage manifestation found in the presence of widespread disease.<sup>1</sup> Radiation therapy was used in twenty-one cases (45.7%), and surgical excision was used in twelve of the cases (26.0%). Treatment was not specified in six of the cases, the patient declined any treatment in two of the cases, and one patient was lost to follow up.

Metastasis of a distant primary malignancy to the oral cavity is associated with poor long-term prognosis.<sup>1</sup> Of the reported cases, twenty-two of the patients (47.9%) had died prior to publication of an associated case report. The overwhelming majority of the patients who died did so within weeks to months of diagnosis of their oral lesion. At the time of publication ten cases (21.7%) reported that the patient was still living. No follow-up information was provided on the patient in fourteen of the cases.

## Discussion

Metastasis to the oral cavity may occur at any age, but is most common during the fifth and sixth decades of life. There is an almost equal sex distribution in jawbone metastases, whereas in the oral soft tissues there is a 2:1 male to female ratio. 70% of oral metastases manifest after the primary tumor becomes evident, while the remaining 30% are the first clinical manifestation

of tumor spread.<sup>1</sup> The most common location for these metastases to the oral cavity is the mandible. This predilection is likely due to sites of bone metastasis concentrating in red marrow, as opposed to the primarily fatty marrow composition of the maxilla.<sup>52</sup>

Lung cancer is one of the most malignant solid tumors. Almost 1,608,823 cases of lung cancer and 1,378,415 cancer deaths occur worldwide each year.<sup>53</sup> Lung cancer is also the most common neoplasm to metastasize to the oral cavity,<sup>2</sup> usually via blood vessels.<sup>1</sup> The average survival rate for metastatic lung cancer is 4 months to 1 year, with a maximum survival rate of five years.<sup>54</sup>

Lung cancer may also metastasize to the soft tissues. These metastases can appear as dental or periodontal infections and resemble reactive lesions like pyogenic granuloma, epulis, and peripheral giant cell granuloma, or odontogenic infection.<sup>55</sup> For gingival metastases, fast growth, a tendency for bleeding, mechanical disorders due to tumor development, ulceration, and a patient's clinical condition can all suggest a lesion of malignant nature.<sup>56</sup> Common symptoms of oral metastases to the oral cavity include a rapidly progressing lesion with potential pain and paresthesia, a bony swelling with tenderness over the affected area, dysphagia, disfigurement, and bleeding.<sup>57,58</sup>

Gnathic metastases can be initially misdiagnosed as endodontic lesions, as was the case with our patient. According to recent literature, about 0.65%–4.22% of clinically diagnosed endodontic periapical pathoses receive a nonendodontic histopathologic diagnosis, emphasizing the difficulty and importance of identifying and classifying these lesions, particularly the malignant nonendodontic lesions (MNPLs).<sup>59</sup> MNPLs are common in the posterior mandible and are usually radiolucent and unilocular, with tooth mobility or bone resorption. On physical examination, metastatic jaw lesions can develop a bony swelling with

tenderness over the affected area, pain, and paresthesia. Jaw metastases do not possess a pathognomonic radiographic appearance, most often presenting as lytic radiolucencies with ill-defined margins.<sup>2</sup> Our case featured swelling of the posterior mandible as the major symptom, with no apparent radiolucency.

## Conclusion

The ages, sex, most common locations and symptoms of lung cancer metastases to the mandible in this literature review were all similar to previous research done by Hirshberg et al.<sup>1</sup> and others. 54% of the cases in the literature review were unaware of the primary cancer prior to the discovery of the oral lesion, compared to only 30% reported in past research. Malignant nonendodontic lesions can present similarly to many benign lesions in the oral cavity, and early detection and biopsy of these lesions are critical to improving the prognosis of these cases.

## Conflict of Interest:

The authors declare no conflict of interest.

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