Leiomyosarcoma of the Mandible in a 15-year-old Girl: A Case Report and a Brief Literature Review of Mandibular Leiomyosarcomas

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Abstract
Leiomyosarcoma is an uncommon malignant mesenchymal neoplasm that exhibits smooth muscle differentiation. Rare occurrence of this neoplasm in the oral cavity is attributed to the paucity of smooth muscle in this location. Leiomyosarcomas of the oral cavity are associated with aggressive clinical behavior and low survival. To the best of our knowledge, only 69 cases of leiomyosarcoma involving the oral cavity have been reported in the English language literature, with 44 cases manifesting intraosseous in the maxilla and mandible. The purpose of this report is to present an additional case of intraosseous mandibular leiomyosarcoma in a 15-year-old girl and to summarize the data of isolated case reports of primary mandibular leiomyosarcomas that have been published in the English language literature during the past 75 years.

Introduction
Leiomyosarcoma is a malignant neoplasm of smooth muscle (mesenchyme) origin accounting for 7% of all soft tissue sarcomas. These tumors predominantly originate from the uterine wall, gastrointestinal tract, and retroperitoneal region (1). Leiomyosarcomas of the oral cavity are rare and their occurrence in an intraosseous location is even more unusual. The rarity of its occurrence in the oral cavity is probably attributed to the paucity of smooth muscles in this location (2, 3).

Clinical presentations of leiomyosarcomas are usually nonspecific or appear as an enlarging painless mass and hence it is usually misdiagnosed as any other common lesion affecting the oral cavity (3). A definitive clinical and histological examination leads to correct diagnosis of this entity.

To the best of our knowledge, since 1940, only 21 cases of leiomyosarcomas have been reported in the English language literature as single case reports primarily involving the mandible (3–20) and only four of those cases occurred in patients less than 20 years old (3, 4, 15, 20).

Herein, we report an additional case of leiomyosarcoma affecting the mandible in a 15-year-old girl, marking this the 22nd case with mandibular involvement and the fifth case occurring in a patient less than 20 years old. In addition, a brief literature review of mandibular leiomyosarcomas is documented.

Case Report
A 15-year-old girl reported to the Department of Oral Medicine and Radiology in April 2008 with a painful swelling on the left side of her face. No swelling was apparent 6 months earlier; it began in the left lower jaw and was initially asymptomatic, although it grew rapidly and interfered with mastication. Pain developed secondary to ulceration due to mastication and had lasted 45 days.

Physical examination revealed a diffuse left-sided facial swelling and asymmetry with neurosensory deficit on the left side and no apparent lymphadenopathy (Fig. 1a & 1b). An intraoral exami-
the inferior alveolar nerve canal and discontinuity of the inferior border of the mandible were observed (Figs. 3 & 4). Based on the rapid growth and destruction of the bone in a young patient, a malignancy (sarcoma) of bone origin was suspected.

An incisional biopsy was carried out and the histopathological examination revealed highly cellular connective tissue stroma with many mitotic figures. Proliferations of these cells were prominently seen around the blood vessels (smooth muscle) and these cells contained spindle-shaped nuclei. However, some cells contained *cigar-shaped nuclei*, character-
Fig. 5. Photomicrograph showing high cellularity, intense proliferating spindle cells, and variable mitotic figures around the blood vessel (original magnification, H/E, 10×).

Fig. 6. High-power view showing blunt-ended and cigar-shaped nuclei (white arrows) (original magnification, H/E, 40×).

Fig. 7. High-power view showing cigar-shaped nuclei (white arrows) (original magnification, H/E, 100×).

...istically seen in the smooth muscle tumor, leiomyosarcoma (Figs. 5, 6 & 7). Based on the characteristic histological findings, a diagnosis of leiomyosarcoma was made and a hemimandibulectomy was recommended. The patient was unwilling to undergo the surgical procedure; she was referred to a cancer institute for radiotherapy and was lost to follow-up.

Review of Literature

A search of the English language literature for the past 75 years revealed 69 cases of leiomyosarcomas of the oral cavity comprising 44 cases of intraosseous leiomyosarcomas, 8 cases in the tongue, 7 cases in the cheek, and 5 cases each in the floor of the mouth and soft palate (4, 13, 18–22). Of the 44 cases of intraosseous leiomyosarcomas, 23 cases were reported in the maxilla while 21 cases were reported in the mandible (3–20). We report an additional case, now the 70th case of oral leiomyosarcoma and the 22nd case of mandibular leiomyosarcoma.

Cases of mandibular leiomyosarcomas reported in the literature along with present case have been summarized in Table 1. Patient age when these tumors appeared ranged from 7 to 74 years with a mean age of 34.4 years and peak incidence in third and fourth decades (Fig. 8). The male to female ratio was 1:2. The premolar molar region was the most frequently involved site (20 cases). The left side of the mandible was more commonly involved than the right side (3:1). The sizes of these tumors ranged from 0.5×1 cm to 18×13 cm. Most of the tumors initially presented as a painless enlarging mass associated with tooth mobility and ulcerations, as was noted in the present case, and these tumors rarely crossed the midline.

Radiographic findings of these tumors varied from widening of the periodontal ligament space to periapical radiolucency of the involved tooth to diffuse irregular lytic areas with cortical perforation. Overall metastasis was observed in 8 cases (38%). Metastasis to regional neck nodes was recorded in 6 cases. Other sites of metastasis included lungs (5 cases), spine (2 cases), kidney (1 case), vertebra (1 case), and
<p>| Reference /Year | Sex | Age | Site    | Size cm | Clinical signs &amp; symptoms                                      | Radiographic findings                                                                 | Treatment                        | Metastasis      | Outcome         |
|----------------|-----|-----|---------|---------|---------------------------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------|----------------|----------------|----------------|
| Carmody et al. 1944 (4) | M   | 18  | LPM     | INA     | Large painless swelling                                       | INA                                                                                 | Hemimandibulectomy              | M0             | NED            |
| Miles &amp; Waterhouse 1962 (5) | M   | 34  | LPM     | 2.5     | Swelling, pain, palpable lymph nodes                          | Cortical expansion                                                                  | Excision, neck dissection, RT    | Lungs, neck nodes, and spine | DOD at 34 months |
| Miettinen et al. 1984 (6)   | F   | 62  | Left condyle | 3      | Swelling, pain, limited mouth opening                         | Osteolytic destruction in left condyle                                              | Condylotomy, RT, CHT             | M0             | AWD at 30 months |
| Abdin &amp; Prabhu 1985 (7)     | F   | 29  | RPM     | 18 × 13 × 10 | Large painless swelling, palpable lymph nodes                | Cortical expansion, irregular areas of radiolucenty and radiopacity and pathological fracture | Hemimandibulectomy              | Neck nodes        | ANED at 7 months |
| Bass et al. 1986 (8)        | F   | 62  | LPM     | INA     | Swelling associated with paresthesia, palpable lymph nodes    | Diffuse radiolucenty with erosion of cortical plate                                  | Hemimandibulectomy, radiation therapy | Neck nodes       | ANED at 12 months |
| Poon et al. 1987 (9)        | M   | 23  | Post. mandible | 2 × 1.5 × 0.5 | Painless swelling from gingiva                                | Ill-defined radiolucenty in the molar region                                        | Excisional biopsy, peripheral osteotomy | M0             | ANED at 8 months |
| Krishnan et al. 1991 (10)   | M   | 27  | Ant. mandible | 6      | Painless swelling, tooth mobility                           | Ill-defined expansile radiolucenty with cortical perforation                        | Segmental mandibulectomy, neck dissection, RT | Neck nodes, lung | AWD at 19 months |
| Sozeri et al. 1992 (11)     | F   | 64  | LPM     | 0.5 × 1  | Painless swelling, bleeding, tooth mobility                  | Ill-defined radiolucenty in the first and second molars                            | Wide local excision with mandibular curettage                                      | M0             | ANED at 12 months |
| Freedman et al. 1993 (12)   | F   | 27  | LPM     | 3 × 2   | Painless mass, tooth mobility                                 | Diffuse ill-defined radiolucenty involving molar region with cortical perforation  | Left mandibular resection with radical neck dissection and resection of paraspinal tumor, RT | Neck nodes, vertebra | DOD at 21 months |</p>
<table>
<thead>
<tr>
<th>Authors</th>
<th>Gender</th>
<th>Age</th>
<th>Region</th>
<th>Size</th>
<th>Description</th>
<th>Treatment</th>
<th>Stage</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karlis et al. 1996 (13)</td>
<td>F</td>
<td>26</td>
<td>LPM</td>
<td>6\times3 \times 4</td>
<td>Painful firm swelling in the molar ramus region</td>
<td>Lytic lesion extending posteriorly from the second molar up the ramus to the coronoid process</td>
<td>M0</td>
<td>AWED at 18 months</td>
</tr>
<tr>
<td>Goldschmidt et al. 1999 (14)</td>
<td>F</td>
<td>24</td>
<td>LPM</td>
<td>2\times3</td>
<td>Painful ulcerated swelling distal to the second molar</td>
<td>Ill-defined lytic bone changes distal to the second molar</td>
<td>M0</td>
<td>ANED at 10 years</td>
</tr>
<tr>
<td>Carter et al. 1999 (3)</td>
<td>F</td>
<td>7</td>
<td>LPM</td>
<td>3\times2</td>
<td>Facial asymmetry, asymptomatic mass, tooth mobility</td>
<td>Expansile osteolytic lesion displacement of the inferior alveolar nerve canal, cortical perforation</td>
<td>M0</td>
<td>ANED at 17 months</td>
</tr>
<tr>
<td>Das et al. 1999 (15)</td>
<td>M</td>
<td>11</td>
<td>Left Mandible</td>
<td>8.5 \times 7.6</td>
<td>Painless, firm, and irregular swelling</td>
<td>Recurrent lesion after CHT and RT showed lytic areas in the mandible, right iliac bone, femur, and humerus</td>
<td>CHT, RT</td>
<td></td>
</tr>
<tr>
<td>Dry et al. 2000 (16)</td>
<td>F</td>
<td>27</td>
<td>Left Mandible</td>
<td>2</td>
<td>Pain in the left mandible</td>
<td>INA</td>
<td>Complete surgical excision</td>
<td>M0</td>
</tr>
<tr>
<td>Dry et al. 2000 (16)</td>
<td>F</td>
<td>74</td>
<td>Mandible</td>
<td>3.5</td>
<td>Pain and swelling</td>
<td>INA</td>
<td>Complete surgical excision</td>
<td>M0</td>
</tr>
<tr>
<td>Nikitakis et al. 2002 (17)</td>
<td>M</td>
<td>35</td>
<td>Anterior Mandible</td>
<td>3\times2</td>
<td>Firm swelling in the anterior midline crossing the midline, associated with tooth mobility</td>
<td>Widening of the periodontal ligament and periapical radiolucencies of the involved teeth</td>
<td>Mandibular resection from right angle to left body with right modified RND and left supraomohyoid neck dissection</td>
<td>Neck nodes, spine, lungs</td>
</tr>
<tr>
<td>Name</td>
<td>Gender</td>
<td>Age</td>
<td>Treatment</td>
<td>Findings</td>
<td>Stage</td>
<td>Outcome</td>
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<tr>
<td>Nikitakis et al. 2002</td>
<td>F</td>
<td>51</td>
<td>RPM</td>
<td>Facial swelling, tender to palpation, and limited mouth opening (20 mm)</td>
<td>3x2</td>
<td>Hemimandibulectomy and right supraomohyoid neck dissection</td>
<td>Sternal, lungs</td>
<td>AWD at 19 months</td>
</tr>
<tr>
<td>Vilos et al. 2005</td>
<td>F</td>
<td>26</td>
<td>RPM</td>
<td>Facial asymmetry, limited mouth opening</td>
<td>5x4</td>
<td>Hemimandibulectomy</td>
<td>M0</td>
<td>ANED at 80 months</td>
</tr>
<tr>
<td>Vilos et al. 2005</td>
<td>M</td>
<td>48</td>
<td>LPM</td>
<td>Painless elastic mass, mental nerve hypesthesia</td>
<td>2x1.5</td>
<td>Mandibular segmental resection</td>
<td>M0</td>
<td>ANED at 64 months</td>
</tr>
<tr>
<td>Pinheiro et al. 2007</td>
<td>F</td>
<td>40</td>
<td>LPM</td>
<td>Facial asymmetry, painless swelling</td>
<td>6</td>
<td>Hemimandibulectomy</td>
<td>M0</td>
<td>ANED at 11 months</td>
</tr>
<tr>
<td>Mendonca et al. 2008</td>
<td>F</td>
<td>9</td>
<td>RPM</td>
<td>Pain, spontaneous bleeding from the gums</td>
<td>4</td>
<td>Segmental mandibular resection</td>
<td>M0</td>
<td>ANED at 11 months</td>
</tr>
<tr>
<td>Present case</td>
<td>F</td>
<td>16</td>
<td>LPM</td>
<td>Facial asymmetry, ulcerated mass</td>
<td>3x4</td>
<td>Hemimandibulectomy</td>
<td>M0</td>
<td>Lost to follow-up</td>
</tr>
</tbody>
</table>

Abbreviations
INA: information not available; LPM: left posterior mandible; RPM: right posterior mandible; DOD: died of disease; ANED: alive with no evidence of disease; AWD: alive with disease; RT: radiotherapy; CHT: chemotherapy; M0: no evidence of distant metastasis; RND: radical neck dissection
sternum (1 case).

Wide surgical excision was the most common mode of treatment in this series. Surgery followed by radiotherapy was the treatment modality in four cases. Successful outcome after the surgical treatment was observed in 57% of patients (11 cases, excluding 2 cases that were lost to follow-up) who were followed for a period ranging from 7 months to 10 years. Five patients were reported to be surviving with the disease even after surgical treatment while four patients died of the disease, marking its mortality rate 21%.

Discussion

Enzinger and Weiss (1988) classified leiomyosarcomas into three main groups based on the geographic evidence (1). The first and most common group includes the retroperitoneal and intra-abdominal leiomyosarcomas, which are predominantly seen in women (2 : 1) with a mean age of presentation of 60 years (23, 24). Resection of these tumors is impossible because they are aggressive and large and have frequently metastasized to the lungs and liver by the time of presentation (1).

The second group includes cutaneous and subcutaneous leiomyosarcomas, which typically occur on the extremities and are more common in men than women. These tumors are most commonly seen in the fifth to sixth decades. These tumors metastasize depending upon their depth of penetration and the route of metastasis is hematogenous. Although the tumors of this group grow fast and attain a large size, they are potentially curable by wide surgical excision (1, 25).

The third and rarely occurring group includes leiomyosarcomas of blood vessel origin that originate from medium to large veins with the mean age of presentation of 50 years. These tumors are often surgically unresectable, with a poor prognosis (25).

Leiomyosarcomas are rarely present in the oral cavity owing to the paucity of smooth muscle in the region, except in the walls of blood vessels, erector pili musculature of the skin, circumvallate papillae of the tongue, myoepithelial cells of salivary glands, and primitive mesenchymal tissue (22, 25). The jaw bones are the most frequently involved sites, followed by the tongue, cheek, floor of the mouth, and soft palate (25).

Although intraoral leiomyosarcomas may appear at any age with no predilection for age group (25), mandibular leiomyosarcomas appear in the third and fourth decades with a female-to-male ratio of 2 : 1 compared to 1 : 2 in other sites. In the present case, although the site and sex were in accordance to the reported literature, the age of the patient is unusual, with only four cases reported in the literature occurring in patients younger than 20 years old. Vilos et al. (18) stated that mandibular leiomyosarcomas originate from the neurovascular bundle of the inferior alveolar canal and this statement is in accordance to our finding of leiomyosarcomas manifesting frequently in the posterior mandible.

Because no distinct clinical feature suggests the presence of mandibular leiomyosarcomas, they can manifest as a painless or painful well-circumscribed and frequently ulcerated mass that is firmly adherent to the surrounding tissues.

Roentgenographic manifestations range from widening of the periodontal ligament (17) to superfi- cial bone resorption (20) to diffuse osteolytic changes with cortical bone perforation, as observed in the present case.

Because the clinical signs and symptoms of this entity are varied, delay occurs in the eventual diag-
nosis of the tumor.

Histopathologically, the tumor shows sheets of sweeping, alternating bundles and fascicles of densely packed spindle cells with centrally located and blunt-ended, squared-off, or cigar-shaped nuclei. The presence of mitosis, cellular atypia, and necrosis are often necessary to diagnose a malignant lesion (1, 19) and these tumors must be distinguished histologically from myofibrosarcoma, fibrosarcoma, and malignant peripheral nerve sheath tumor.

Ultrastructurally, myofibrosarcomas differ from leiomyosarcomas in having scanty peripheral myofilaments rather than diffuse cytoplasmic myofilaments, abundant rough endoplasmic reticulum, and tapered rather than blunt-ended nuclei, whereas fibrosarcomas display a sweeping fascicular arrangement and a herring bone pattern with tapered nuclei (26, 27). A malignant peripheral nerve sheath tumor has bullet-shaped nuclei that may be serpentine (27). Although these tumors have many similarities with leiomyosarcomas, subtle histopathological differences provide a basis for the diagnosis of these rare and aggressive neoplasms.

The mortality rate (21%) as summarized by the data is significantly alarming, making an accurate judgment of treatment approach imperative. Successful management of this tumor depends on its early diagnosis, followed by complete surgical excision. The summarized data showed that neither the age nor the sex of the patient was a predictor of prognosis. Surgical management of this tumor seems to be an important prognostic factor with longer survival rate, shown in 57% of the cases. Combining surgery with adjuvant radiation therapy for the leiomyosarcomas did not influence recurrence or survival. Chemotherapy tends to improve the length of survival and quality of life of patients with metastatic disease or inoperable tumors.

To summarize our literature review of mandibular leiomyosarcomas, we emphasize the importance of an early diagnosis of this very rare and aggressive lesion. For the best prognosis, it must be treated surgically, aggressively, and significantly early.

References