Clinicopathological Features of Leiomyosarcoma of the Tongue: an Immunohistochemical Study and Review of the Literature

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ABSTRACT

Leiomyosarcoma (LMS) of the tongue is an extremely rare tumor. We present a case of LMS of the tongue in a 71-year-old man with a one-year history of a painless tongue nodule. Examination of the oral cavity revealed a firm 45-mm mass located on the right lateral border of the tongue. Biopsy and pathological examination showed a malignant muscular neoplasm that required immunohistochemical analysis. The patient underwent surgery with preparation of a cervical flap and unilateral upper neck dissection, during which examination was negative for lymph node metastasis. Definitive histological examination showed LMS of the tongue. After 13 months, a recurrent tumor was detected in the floor of the mouth. The outcome of our patient and review of the literature suggest that these aggressive tumors require wide local excision and prolonged follow up.

INTRODUCTION

Leiomyosarcoma (LMS) is a rare malignant neoplasm that shows smooth muscle differentiation [1]. Primary intra-oral LMS arising in the tongue is extremely rare, accounting for only 3–10% of all such tumors of the head and neck [2]. The most frequent sites of LMS are the uterine myometrium, gastrointestinal tract, and skin [3], while the highest incidence is between the ages of 40 and 49 years.

The prognosis of LMS is poor, with a high rate of recurrence or metastasis. The most common sites of metastasis include the lungs, bone, brain, and lymph nodes. Due to its nonspecific clinical presentation, the diagnosis is made after histological examination [4]. While LMS often shows typical smooth muscle cells of uniform size with no features of malignancy, there may be spindle-shaped cells with elongated, ‘cigar-shaped’ nuclei and eosinophilic cytoplasm that sometimes shows longitudinal striations. Immunohistochemical studies are required for precise diagnosis.

Surgery is the only effective treatment and it is important to perform complete resection to avoid recurrence [5]. Here we report a case of primary intra-oral LMS of the tongue.
CASE PRESENTATION

A 71-year-old man presented with a one-year history of a painless nodule in the tongue (Figure 1). Examination of the oral cavity revealed a firm 45-mm mass on the right lateral border of the tongue. The mass was biopsied, and initial pathological examination identified a malignant muscular neoplasm that required immunohistochemical analysis. Magnetic resonance imaging showed that the mass occupied half of the tongue (Figure 2). There was no regional lymphadenopathy, and general physical examination was unremarkable. Routine laboratory tests yielded normal values and the chest X-ray film was normal. Since laboratory and imaging examinations were within normal limits and there was no evidence of another tumor, the tongue was confirmed as the only site involved.

He underwent subtotal resection of the tongue and reconstruction using a free rectus abdominis muscle flap. After insertion of a central venous line into the right inguinal vein, surgery was performed under general anesthesia, consisting of tracheostomy, raising a cervical flap, and unilateral upper neck dissection (levels 1 to 3) during which examination was negative for lymph node metastasis.

Definitive histological examination of surgical specimens showed LMS of the lateral border of the tongue with no infiltration of the surgical margins.

When the patient was discharged, he was able to feed orally. At 13 months after surgery, a recurrent tumor began to grow rapidly in the floor of the mouth. He was given radiotherapy, but there was a poor response and the patient died of recurrent LMS about 6 months later.

Histopathology and immunohistochemistry findings

Surgical specimens were promptly fixed in 10% neutral buffered formalin for 12–24 hours and then embedded in paraffin. Sections 5 µm thick were cut and stained with hematoxylin and eosin (Figure 3a). Histopathologic examination showed part of a highly malignant neoplasm that was composed of intersecting fascicles of mitotically active eosinophilic spindle cells with pleomorphic nuclei, including atypical forms. Serial sections were employed for immunohistochemistry, which was performed by the standard avidin-biotin/peroxidase technique using antibodies to several antigens (α-smooth-muscle actin, muscle-specific actin, desmin, vimentin, and calponin). The tumor cells displayed consistent immunoreactivity for vimentin (Figure 3b), α-smooth-muscle actin (Figure 3c), calponin (Figure 3d), and muscle-specific actin (not shown).

Review of the literature

Nineteen cases of primary LMS of the tongue have been reported, including the present case, and these are summarized in Table 1 [6–23]. There were 14 male patients and 5 female patients aged from 11 months to 80 years (median age: 52.9 years). Initial treatment was surgical excision alone in 14 patients, radiation alone in 1 patient, palliative chemotherapy in 1 patient, and surgery combined with chemotherapy in 2 patients. One patient refused treatment. Follow up information was available for 16 of the 19 patients and the period ranged from 1 to 72 months (median: 33 months). Four patients died of LMS and 12 patients were alive with no evidence of disease, while information was not available for the other three patients.
Leiomyosarcoma of the Tongue

Figure 3 Photomicrographs of the lesion (hematoxylin and eosin stain). (a) Pleomorphic nuclei (black arrows) and bizarre mitotic figures (white arrows).

Photomicrographs showing positive immunostaining of spindle cells. Most tumor cells display consistent vimentin immunoreactivity (b), smooth muscle actin immunoreactivity (c), and calponin immunoreactivity (d).

Table 1 Reported cases of primary leiomyosarcoma of the tongue

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Gender</th>
<th>Age</th>
<th>Site</th>
<th>Metastasis</th>
<th>Treatment</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yannopoulos and Stout 1962</td>
<td>1962</td>
<td>M</td>
<td>11mo</td>
<td>Tip of tongue</td>
<td>No</td>
<td>Excision</td>
<td>4-6</td>
</tr>
<tr>
<td>Lack 1986</td>
<td>1986</td>
<td>M</td>
<td>2.5</td>
<td>Base of tongue</td>
<td>No</td>
<td>Excision and chemotherapy</td>
<td>4</td>
</tr>
<tr>
<td>Aydin and Dreyer 1994</td>
<td>1994</td>
<td>M</td>
<td>70</td>
<td>Base and dorsum of tongue</td>
<td>No</td>
<td>Radiotherapy</td>
<td>1.5</td>
</tr>
<tr>
<td>Mayall et al. 1994</td>
<td>1994</td>
<td>M</td>
<td>60</td>
<td>Tip of tongue</td>
<td>No</td>
<td>Excision</td>
<td>1</td>
</tr>
<tr>
<td>Piattelli and Artexa 1995</td>
<td>1995</td>
<td>F</td>
<td>80</td>
<td>Lateral border of tongue</td>
<td>No</td>
<td>Treatment refusal</td>
<td>N/A</td>
</tr>
<tr>
<td>Tandon et al. 1996</td>
<td>1996</td>
<td>M</td>
<td>22</td>
<td>Base of tongue</td>
<td>No</td>
<td>Excision</td>
<td>5</td>
</tr>
<tr>
<td>Gorsky and Epstein 1998</td>
<td>1998</td>
<td>M</td>
<td>57</td>
<td>Lateral border of tongue</td>
<td>Not recorded</td>
<td>Excision and chemotherapy</td>
<td>4 DFD</td>
</tr>
<tr>
<td>Lo Muzio et al. 2000</td>
<td>2000</td>
<td>M</td>
<td>67</td>
<td>Lateral border of tongue</td>
<td>No</td>
<td>Excision</td>
<td>5</td>
</tr>
<tr>
<td>Sakamoto et al. 2005</td>
<td>2005</td>
<td>M</td>
<td>67</td>
<td>Tip of tongue</td>
<td>No</td>
<td>Excision</td>
<td>Not recorded</td>
</tr>
<tr>
<td>Kazemian et al. 2005</td>
<td>2005</td>
<td>M</td>
<td>32</td>
<td>Lateral border of tongue</td>
<td>Yes</td>
<td>Excision and m-RND and chemotherapy</td>
<td>1.5 DFD</td>
</tr>
<tr>
<td>Yang et al. 2006</td>
<td>2006</td>
<td>F</td>
<td>57</td>
<td>Lateral border of tongue</td>
<td>No</td>
<td>Excision and SOHND</td>
<td>3</td>
</tr>
<tr>
<td>Yang et al. 2006</td>
<td>2006</td>
<td>F</td>
<td>54</td>
<td>Tip of tongue</td>
<td>No</td>
<td>Excision</td>
<td>1</td>
</tr>
<tr>
<td>Crossman et al. 2008</td>
<td>2008</td>
<td>F</td>
<td>46</td>
<td>Lateral border of tongue</td>
<td>No</td>
<td>Excision</td>
<td>5</td>
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<tr>
<td>Prins et al. 2010</td>
<td>2010</td>
<td>M</td>
<td>55</td>
<td>Lateral border of tongue</td>
<td>No</td>
<td>Excision</td>
<td>4</td>
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<tr>
<td>Miyoshi 2011</td>
<td>2011</td>
<td>M</td>
<td>63</td>
<td>Lateral border of tongue</td>
<td>No</td>
<td>Excision</td>
<td>Not recorded</td>
</tr>
<tr>
<td>Ahn JH et al 2012</td>
<td>2012</td>
<td>F</td>
<td>54</td>
<td>Lateral border of tongue</td>
<td>Yes</td>
<td>Palliative chemotherapy</td>
<td>1moDFD</td>
</tr>
<tr>
<td>Croce A et al. 2012</td>
<td>2012</td>
<td>M</td>
<td>77</td>
<td>Base of tongue</td>
<td>No</td>
<td>Total laryngectomy extended to the base of tongue</td>
<td>8mo</td>
</tr>
<tr>
<td>Azevedo RS 2012</td>
<td>2012</td>
<td>M</td>
<td>71</td>
<td>Lateral border of tongue</td>
<td>No</td>
<td>Excision</td>
<td>34mo</td>
</tr>
<tr>
<td>Present case</td>
<td>2018</td>
<td>M</td>
<td>71</td>
<td>Lateral border of tongue</td>
<td>No</td>
<td>Excision</td>
<td>19mo DFD</td>
</tr>
</tbody>
</table>

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DISCUSSION

LMS is a malignant smooth muscle tumor. Soft tissue sarcomas account for less than 1% of all cancers, with LMS comprising approximately 10% to 20% of these tumors [24]. Generally, LMS arises in the gastrointestinal tract, retroperitoneum, and uterus, which are all sites with abundant smooth muscle. These tumors rarely occur in the head and neck region, probably because of the paucity of smooth muscle [25]. Primary LMS of the tongue has been suggested to arise from the ductus lingualis, the smooth muscle in blood vessel walls, or of the circumvallate papillae [26].

Although a careful history and clinical examination may be helpful, histologic examination and immunohistochemical staining are essential for diagnosis of LMS [8, 17, 27–30]. Microscopically, primary oral LMS shows proliferation of neoplastic spindle cells arranged in an interlacing fascicular pattern with oval to elongated, blunt-ended (cigar-shaped) nuclei. The nuclei may be hyperchromatic with varying degrees of atypia and pleomorphism.

The spindle cells comprising the tumor react with antibodies targeting smooth muscle antigenic epitopes of mesenchymal origin, such as smooth muscle actin, muscle-specific actin (HHF 35), and vimentin.

Histopathologically, the present tumor had a prominent spindle cell component, arranged in intersecting fascicles and the tumor cells showed characteristic ‘cigar-shaped’ nuclei. These features are typical for LMS, but similar findings may occur in a wide number of different neoplasms, such as fibrosarcoma, myofibrosarcoma, synovial sarcoma, solitary fibrous tumor, spindle cell liposarcoma, spindle cell carcinoma and other spindle cell neoplasms. In most instances, immunohistochemistry provided useful clues to the diagnosis of LMS, with immunostaining for vimentin, α-smooth muscle actin, and muscle-specific actin being detected most frequently. A negative reaction is expected for antibodies against epithelial antigenic epitopes, such as cytokeratins and epithelial membrane antigen (EMA). A negative reaction should also be seen for antibodies against S-100 protein (melanoma and neurogenic sarcoma). Immunohistochemistry and/or electron microscopy has become an indispensable diagnostic tool to differentiate various types of spindle cell neoplasms from each other.

LMS has a low metastatic potential and haematogenous metastasis occurs infrequently, while lymph node metastasis is very rare. Optimum treatment for LMS of the tongue is wide local excision. Adjuvant radiotherapy can be given postoperatively [8,25]. Review of the literature showed that initial surgical management seems to be an important prognostic factor since complete excision is associated with a low local recurrence rate and longer survival. It is evident that resection with microscopically tumor-free margins is of paramount importance for achieving long-term survival in patients who have primary oral LMS. Adjuvant radiotherapy can be performed, but some authors have questioned its utility and have reported no improvement of disease-free or overall survival [31]. Cervical lymph node dissection is usually not necessary, unless there is clinical evidence of regional lymph node metastasis. In the absence of cervical lymphadenopathy, we performed supra-omohyoid neck dissection in our patient while accessing the blood vessels for free flap reconstruction.

According to the literature, radiation therapy and chemotherapy was performed in a few patients, but efficacy seemed to be limited. Adjuvant radiation therapy or chemotherapy appears to be ineffective for achieving local control when there is residual tumor postoperatively. Chemotherapy is generally reserved for palliative use.

After complete tumor removal, local recurrences and regional or widespread metastases are rare, but the tumor may reappear, even several years after primary treatment. Long-term follow-up of all patients is therefore necessary, with regular and careful examinations conducted at short intervals.

In conclusion, we reported a rare case of LMS of the tongue, with recurrence at 13 months after resection. Very few cases of primary LMS of the tongue have been reported, but some patients have had late recurrence or metastasis, suggesting that prolonged or indefinite follow-up is needed [31].

The prognosis of LMS is usually poor and the tumor recurred in the present patient despite pathologically negative resection margins. Given the limitations of surgical treatment for LMS, wide excision with histological confirmation of tumor-free margins seems to be necessary, as well as long-term follow-up.

Conflict of Interest

The authors have no funding, financial relationships, or conflict of interests to disclose.

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Leiomyosarcoma of the Tongue

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