CASE REPORT

Leiomyosarcoma of the buccal mucosa and review of literature

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ABSTRACT
Leiomyosarcoma (LMS) is an uncommon malignant spindle cell tumor of the head and neck region. The occurrence is particularly rare in the buccal mucosa of the oral cavity. It is a rapidly growing tumor with aggressive behavior and poor prognosis. Method: This article presents a rare case of primary leiomyosarcoma of the buccal mucosa in a 35 year old female and retrospective analysis of primary oral LMS published in the English literature since past 20 years is done. Diagnosis was confirmed by immunohistochemistry profile showing positivity for vimentin, smooth muscle actin (SMA), high proliferative index displayed by Ki-67, focal positivity for pan-CK and negativity for S-100. Conclusion: Based on the presence of malignant spindle cells showing positivity for vimentin and SMA, a diagnosis of leiomyosarcoma was made.

Key words: Ki-67, leiomyosarcoma, smooth muscle actin, spindle cell

INTRODUCTION
Tumors of the smooth muscle are rare in the head and neck region especially the buccal mucosa due to the scarcity of this tissue in this region and thus are frequently seen in the gastrointestinal and female genital tract because of the preponderance of smooth muscle at these sites.[1,2] In the head and neck region, these tumors are believed to arise from the tunica media of the blood vessels. Clinically, they are very aggressive, and the prognosis is poor.[3] In the oral cavity most of the cases are seen in the mandible, maxilla, tongue, cheek, hard and soft palate, floor of the mouth and lip.[4,5] They are less frequently seen on the buccal mucosa. We report a rare case of leiomyosarcoma of the buccal mucosa.

CASE REPORT
A 35-year-old female presented with difficulty in opening the mouth since past 1 month. On clinical examination an ulcerative lesion on the left buccal mucosa adjacent to the maxillary left third molar was observed. The lesion was non-tender and firm in consistency, measuring about 1 x 1 cm in dimension, with inflamed surrounding margins. Lymph nodes were not palpable in the cervical region. An axial computed tomography scan showed an iso-dense mass in the right buccal mucosal region causing the swelling [Figure 1]. Excisional biopsy was done under local anesthesia, and the formalin fixed specimen was processed for histopathological examination. Microscopic examination revealed spindle shaped cells proliferating in various patterns [Figure 2]. The cells showed cellular and nuclear pleomorphism, increased mitotic figures, and prominent nucleoli. Single and multinucleated giant cells containing dark eosinophilic cytoplasm in a myxomatous connective tissue were also observed. Inflammatory cells and hyalinized blood vessels with spindle cells proliferation around them were evident. Immunohistochemical staining showed strong positivity for vimentin [Figure 3], smooth muscle actin (SMA) [Figure 4], and high proliferative index displayed by Ki-67 [Figure 5]. Desmin, S-100, and pancytokeratin were negative. These immunohistochemical findings satisfy the criteria for leiomyosarcoma. Due to loss of follow-up further treatment of the patient could not be completed.

DISCUSSION
The literature review of primary leiomyosarcoma of the oral cavity in past 20 years retrieved is listed in Table 1. Cases of nasopharynx, and metastatic tumors from other organs were excluded. The most frequent site was mandible accounting for 20 cases, followed by maxilla 15 cases, 10 cases in tongue and 9 cases in buccal mucosa, 2 each in lip, floor of the mouth, hard palate, soft palate and maxillary sinus. Out of 63 patients, 33 patients were male (56%) and 30 were female (44%) [Figure 6]. Ages ranged from 6 years to 90 years.

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Prognostically, 28 cases were alive with no disease during the follow-up period which ranged from 6 months to 120 months.

Twenty-one patients died of this disease during the follow-up period which ranged from 1 month to 37 months. Six patients were alive with disease. Information was not available for nine patients who were lost during the follow-up and remaining three cases died of other causes.

Soft tissue sarcomas are relatively rare neoplasms that may arise in any anatomic region. Occurrence in the head and neck accounts for less than 1% of all malignant tumors in this site.\[^5\] Only 3-10% of leiomyosarcoma (LMS) cases arise in the head and neck [Figure 7]. Smooth muscles is sparse in the head and neck region and are mainly found in the walls of blood vessels, erector pili musculature of the skin, circumvallate papillae and myoepithelial cells of the salivary glands. LMS may also be derived from the undifferentiated pluripotential cells.\[^15,19\] Clinically most often LMS presents as a nodular painless, well circumscribed mass, adherent firmly to the surrounding tissues which sometimes may be ulcerated as was in our presented case. There is no age and sex predilection.\[^20\] Histologically LMS typically displays spindle cells with abundant cytoplasm...
Table 1: Data of primary oral LMS from the English literature

| Author | Site | Age/sex | Follow-up | Status |
|--------|------|---------|-----------|--------|
| Mequita et al.[6] | Buccal mucosa | 23/female | 24 | AND |
| Izumi et al.[6,7] | Maxilla | 70/male | 22 | AND |
| Vilos et al.[8] | Gingiva mand premolar | 27/female | 21 | DFD |
| Vilos et al.[8] | Maxilla | 28/female | 7 | AWD |
| Krishnan et al.[9] | Mandible | 27/male | 19 | AWD |
| Sumida et al.[9] | Maxillary sinus with LN metastasis | 77/male | 3 | DFD |
| Yang et al.[10] | Tongue tip | 54/female | 12 | AND |
| Mitsudo K et al.[11] | Maxilla | 35/male | 24 | AND |
| Centeno et al.[12] | Mandible | 13/male | 24 | AND |
| Vilos et al.[13] | Maxillary alveolar ridge | 12/male | 24 | AND |
| Vilos et al.[13] | Mandibular condyle | 56/female | 24 | DFD |
| Vilos et al.[13] | Mandible alveolar process | 64/female | 12 | AND |
| Schenberg et al.[14,15] | Maxilla | 30/male | 6 | AND |
| Schenberg et al.[14,15] | Buccal mucosa | 38/male | 15 | AND |
| Schenberg et al.[14,15] | L maxilla | 26/male | 15 | DFD |
| Schenberg et al.[14,15] | R buccal mucosa | 42/male | 32 | AND |
| Vilos et al.[13] | Tongue | 60/male | 12 | AND |
| Vilos et al.[13] | Upper lip | 90/female | 01 | DFD |
| Vilos et al.[13] | Tongue | 80/female | LOST | INA |
| Vilos et al.[13] | L mand ramus | 26/female | 19 | AND |
| Vilos et al.[13] | R mand angle | 34/male | 26 | AND |
| Vilos et al.[13] | Tongue | 57/male | 48 | DFD |
| Vilos et al.[13] | Mand retromolar region | 63/female | 24 | DFD |
| Vilos et al.[13] | R maxilla | 58/male | 12 | AND |
| Carter et al.[13] | L mand alveolar process | 7/female | 17 | AND |
| Vilos et al.[13] | L mandible | 11/male | 20 | AWD |
| Goldschmidt et al.[18] | L mandible alveolar process | 24/female | 120 | DFD |
| Vilos et al.[18] | Gingiva | -/male | LOST | INA |
| Vilos et al.[18] | L mandible | 27/female | 28 | AND |
| Vilos et al.[18] | Upper lip | 91/female | 46 | DOC |
| Vilos et al.[18] | Hard palate | 34/female | 14 | DFD |
| Vilos et al.[18] | Tongue | 15/female | 50 | AND |
| Vilos et al.[18] | Mandible | 74/female | 2 | DOC |
| Vilos et al.[18] | Maxilla | 28/male | 37 | DFD |
| Vilos et al.[18] | Floor of mouth | 88/female | 1 | DFD |
| Vilos et al.[18] | Maxillary process | 58/male | 55 | AND |
| Vilos et al.[18] | Maxilla | 31/male | 61 | AND |
| Muzio et al.[19] | Tongue | 67/male | 60 | AWD |
| Dias et al.[19] | Soft palate | 67/male | 36 | AND |
| Amarpala and Tilakratne[20] | Tongue | 13/male | 24 | DFD |
| Amarpala and Tilakratne[20] | R mandible | 17/female | LOST | INA |

Table 1: Contd...

| Author | Site | Age/sex | Follow-up | Status |
|--------|------|---------|-----------|--------|
| Amarpala and Tilakratne[20] | Mandible | 23/male | LOST | INA |
| Amarpala and Tilakratne[20] | L maxilla | 24/male | 10 | AWD |
| Amarpala and Tilakratne[20] | Buccal gingival of maxillary canine | 30/female | 48 | DFD |
| Amarpala and Tilakratne[20] | Tongue and epiglottis | 53/female | LOST | INA |
| Amarpala and Tilakratne[20] | R maxillary antrum | 70/male | LOST | INA |
| Ethunandan et al.[21] | Tongue | 79/female | 28 | AND |
| Ethunandan et al.[21] | Tongue | 97/female | 56 | DOC |
| Ethunandan et al.[21] | Maxilla | 50/female | 18 | DFD |
| Ethunandan et al.[21] | Buccal mucosa | 51/male | 28 | AWD |
| Pinheiro JV et al.[22] | Mandible | 40/female | 11 | AND |
| Yadav R and Bharathan S[23] | Buccal mucosa | 27/female | 18 | AND |

AND: Alive with no disease, AWD: Alive with disease, DFD: Died of this disease, DOC: Died of other causes, INA: Information not available, LOST: Lost during follow-up, LMS: Leiomyosarcoma

...and centrally placed blunt ended cigar shaped nuclei of varying sizes. Multinucleated giant cells are common. Microscopic criteria for well differentiated LMS include: (i) A pattern of interlacing bundles of smooth muscle cells, (ii) a high mitotic rate, (iii) pleomorphism, and (iv) bizarre cell forms.[21] Immunopositivity for vimentin, SMA, and muscle specific actin MSA has been demonstrated in LMS. Some have also shown immunopositivity for desmin, but this feature is not consistent. The tumor should be immunonegative for S-100 and cytokeratins[22,23]. These histopathological features along with immunohistochemical profiles aids in differentiating LMS from other similar spindle cell malignancies like malignant fibrous histiocytoma, fibrosarcoma, etc., [Table 2].

Oral LMS tend to metastasize to the cervical nodes and lungs, and therefore when LMS is identified, it is necessary to determine whether the lesion is primary or secondary.

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Table 2: Differential diagnosis and immunohistochemical profile of similar spindle cell tumors[22,23]

| Lesions                | Histopathological features                                                                 | IHC markers                                      |
|------------------------|---------------------------------------------------------------------------------------------|--------------------------------------------------|
| Fibrous histiocytoma   | Classic storiform pattern consisting of plump spindle cells in short fascicles around slit like vessels. Shows frequent transition to pleomorphic areas. Characteristically shows large number of multinucleated giant cells with intense eosinophilia | Positive for angiotensin converting enzyme (ACT) and vimentin |
| Fibrosarcoma           | Spindle cells arranged in fascicles with a peculiar herring bone appearance exhibiting low to moderate cellularity. Mild nuclear pleomorphism and rare mitosis, with a collagenous stroma | Only vimentin is positive and negative for all other immunohistochemical markers |
| MPNST                  | Classically the cells recapitulate the features of normal Schwann cells. The cells can range from spindle to fusiform or even round in shape | Positive for S100, CD57, NGF receptor, EMA, claudin-1, Glut-1 |
| Rhabdomyosarcoma (RMS) | Histologically classified into various types such as embryonal, botryoid, alveolar, pleomorphic, small round cell, and intermediate type. The morphologic indicators of skeletal muscle differentiation, e.g. cross-striations; typical rhabdomyoblasts or areas with small round cell differentiation are seen | MyoD1, myogenin, muscle actins, and desmin positive |
| Liposarcomas           | The tumor predominantly consists of mature fat with a variable number of spindled cells with hyperchromatic nucleus and multivacuolated lipoblasts | S-100, MDM2 positive |
| Angiosarcoma           | Small capillary sized vessels composed of infiltrating malignant cells. The lumen may be empty, filled with clear fluid or engorged with red blood cells | Positive expression of CD31, CD34, FLI-1, von Willebrand factor and ulex lectin |
| Spindle cell carcinoma | They are biphasic tumors composed chiefly of fascicles of spindle shaped cells with some cells appearing as epithelial elements. Overall picture is similar to that of anaplastic fibrosarcoma with inconspicuous epithelial element | Spindle cells stain positively for cytokeratin and may also show negativity for vimentin |

IHC: Immunohistochemical, FLI-1: Friend leukemia integration 1 transcription factor, MDM2: Mouse double minute 2 homolog, EMA: Epithelial membrane antigen, NGF: Nerve growth factor, CD: Cluster of differentiation, MPNST's: Malignant peripheral nerve sheath tumor

The likelihood of distant metastasis is related to histologic grade and tumor size; the risk is highest for large, high grade lesions.[24] Because of its similarity to other sarcomas composed of spindle cells like fibrosarcoma, neurogenic sarcoma and malignant fibrous histiocytoma, use of special stains and immunohistochemistry becomes of utmost importance for early diagnosis and prompt management of the cases.[14] Early wide surgical excision with radical neck dissection for lymph node metastasis remains the mainstay of treatment.[25] Palliative radiotherapy and chemotherapy have been tried with variable results. Overall the prognosis of LMS is poor and hence early diagnosis is the key to the management.[26]

CONCLUSION

Oral LMS are rare lesions of the head and neck with aggressive behavior and poor prognosis in most of the cases. Appropriate clinical and histopathological evaluation supplemented with immunohistochemistry is a must. Early and accurate diagnosis followed by radical treatment is of utmost importance for improving the prognosis of these tumors.

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