Primary Leiomyosarcoma of the Buccal Mucosa: Report of a Case and Review of the Literature

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Abstract

This clinicopathologic study of primary oral leiomyosarcoma of the buccal mucosa involves a literature review of 15 cases with the addition of our report of a case. The demographic details, tumor size, treatment and outcome are documented for all the cases. In addition, this review examines the histologic features of leiomyosarcoma while noting that differentiation from other spindle cell tumors can be challenging, underscoring the necessity of an immunohistochemical work up for an accurate diagnosis. The unpredictability of the clinical behavior of these aggressive tumors requires, at the very least, wide local surgical excision and prolonged follow up.

Keywords Leiomyosarcoma · Oral cavity · Head and neck

Introduction

Leiomyosarcoma is a malignant tumor with smooth muscle differentiation and accounts for 5–10% of all soft-tissue sarcomas. It occurs most frequently in the retroperitoneum, and is exceedingly rare in the oral cavity [1, 2]. One explanation for the rarity of leiomyosarcomas in the oral cavity is attributed to the relative paucity of smooth muscles in that region [3–5]. Leiomyosarcomas that occur in the jawbones and oral tissues are thought to arise from the tunica media of blood vessels, *erectores pilorum*, circumvallate papillae, or from pluripotential mesenchymal cells [5]. Histopathologically, leiomyosarcomas typically present with interlacing fascicles of spindle cells, and so immunohistochemical discrimination of smooth muscle differentiation is often useful to help distinguish leiomyosarcomas from other tumors with similar light microscopic features. In part because of their rarity, leiomyosarcomas can be easily mistaken for other more common spindle cell lesions in the oral cavity [6].

Case Report

An 86-year old male presented to his oral surgeon with a swelling on his right posterior buccal mucosa, which had been unresponsive to antibiotics. An ulcerated area adjacent to tooth #1 was apparent. Subsequent incisional biopsy revealed an initial histopathologic diagnosis of a traumatic ulceration. However, a month later, the patient returned to the oral surgeon due to an increasing ulceration of the right buccal mucosa, and a re-biopsy was performed. No details regarding the size of the lesion nor radiographic images could be obtained from the oral surgeon. Microscopic examination revealed an infiltrative spindle cell neoplasm predominantly arranged in long fascicles and comprised of cells with abundant eosinophilic fibrillary cytoplasm and oval nuclei (see Figs. 1, 2, 3, 4, 5). Perinuclear vacuoles were present and there were scattered cells with marked cytologic atypia. No necrosis was present but mitotic figures were frequent (5–6 mitotic figures per 10 high-power fields). Immunohistochemical stains confirmed the morphologic impression of leiomyosarcoma as the neoplastic cells were diffusely and strongly positive for cytoplasmic expression of desmin, muscle specific actin, and smooth muscle actin. Unfortunately, attempts to discover information on treatment and follow up with the patient were unsuccessful.

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Fig. 1 At low power (×40), the tumor is comprised of spindle cells arranged in long fascicles. Scattered cells with marked nuclear atypia are present

Fig. 2 At medium power (×100), the spindle cells are arranged in fascicles and contain abundant fibrillary eosinophilic cytoplasm. The nuclei tend to be oval with perinuclear vacuoles. Mitotic figures are common as are scattered cells with marked nuclear atypia

Review of the Literature

In the literature, there have been 16 cases of reported primary leiomyosarcoma of the buccal mucosa, including the present case, summarized in Table 1. A literature search revealed cases involving 6 males and 10 female patients who at presentation ranged in age between 6 and 88 years old (median age was 36.5 years old). Though designation of tumor in some reports included “cheek,” suggesting a dermal location, all tumors occurred in the oral cavity proper. Tumors ranged in dimension from 1.0 to 10.0 cm (median was 2.0 cm; tumor size was not available in our

Fig. 3 Desmin staining (×100) demonstrates diffuse strong staining in the cytoplasm of the neoplastic cells

Fig. 4 Muscle specific actin (×100) demonstrates diffuse moderate staining in the cytoplasm of the neoplastic cells

case, but the grade was moderately differentiated). There was one report of metastasis to regional lymph node. Initial treatment consisted of surgical excision alone in nine cases; a combination of surgery and radiation was reported in one case; a combination of surgery and chemotherapy with radiation was reported in one case; and treatment was refused in one case (treatment information was not available in four cases). Follow up information was available in 11 of the 16 cases, and ranged from 3 to 52 months (with a median of 22 months). Recurrence occurred in three cases. Overall, two patients died of their disease; one patient was alive with disease; and eight patients were alive with no evidence of tumor (follow up information was not available for five cases).

Fig. 5 Smooth muscle actin (×100) demonstrates diffuse strong staining in the cytoplasm of the neoplastic cells

Discussion

The current case reports a primary leiomyosarcoma of the buccal mucosa. However, the vast majority of reported cases of leiomyosarcomas identified in the head and neck have involved the skin and soft tissues, with only a minority of cases involving the oral cavity (5.7%) and even fewer involving the skull and mandible (0.7%) [7]. Prior studies

have also suggested that when leiomyosarcomas do involve the head and neck, there is greater likelihood for the jawbone to be involved with approximately 70% arising in the maxilla or mandible [3, 4, 8, 9].

Clinically, sarcomas of the head and neck present with non-specific signs and symptoms, and in the majority of cases these tumors manifest as a painless mass [3, 4, 10]. Distant metastases can occur in 28% of the patients at diagnosis or during follow-up and are more frequent in high grade sarcomas. The most frequently involved site for distant metastases is lung followed by bone, central nervous system, and liver [3, 10, 11]. In general, because of the low incidence of lymph node metastasis in sarcomas, formal lymph node dissection is often reserved for clinical involvement of regional lymph nodes [10]. However, leiomyosarcomas of the oral cavity, unlike leiomyosarcomas in soft tissue elsewhere, can metastasize to regional lymph nodes [6].

Histologic examination and immunohistochemical staining are essential for the final diagnosis of leiomyosarcomas [12, 13]. Leiomyosarcomas that occur in the oral cavity must be distinguished from other histologically similar, yet clinically benign lesion, such as infantile and adult myofibroma/myofibromatosis and angioleiomyomas [6]. The differential diagnosis of malignant spindle cell tumors in the head and neck includes spindle cell carcinoma and melanoma; sarcomas to be distinguished include malignant nerve sheath tumor and rhabdomyosarcoma [14]. Due to overlap in histologic features, head and neck sarcomas

Table 1 Summary of clinical data of primary buccal mucosal leiomyosarcoma

Authors (year)	Age (years)	Gender	Primary site	Size (cm)	Metastasis	Initial treatment	Follow-up (months)—outcome
Robinson and Whyte (1978) [20]	88	M	Cheek	4.0	n/r	Surgery (recur)	n/a—ANED
Schenberg et al. (1993) [3]	42	M	Buccal mucosa	3.0	n/r	Surgery	32—ANED
Schenberg et al. (1993) [3]	38	M	Buccal mucosa	2.0	n/r	Surgery	15—ANED
Mesquita et al. (1998) [21]	23	F	Buccal mucosa	2.0	n/r	Surgery	24 - ANED
Montgomery et al. (2002) [14]	38	F	Cheek	2.0	n/r	n/a	n/a
Montgomery et al. (2002) [14]	42	M	Buccal	5.0	n/r	n/a	n/a
Yadav and Bharathan (2008) [22]	27	F	Buccal mucosa	1.5 × 1.5	n/r	Surgery	18—ANED
Ethunandan et al. (2007) [23]	51	M	Buccal mucosa	2.0 × 2.0	n/r	Surgery	28—ANED
Yan et al. (2009) [4]	11	F	Cheek	4.0 × 4.0	n/r	Surgery (recur)	20—AWD
Yan et al. (2009) [4]	21	F	Cheek	2.0 × 1.0	n/r	Surgery and chemoradiation	48—ANED
Yan et al. (2009) [4]	16	F	Cheek	4.0 × 4.0	n/r	Surgery	n/a
Yan et al. (2009) [4]	12	F	Cheek	5.0 × 5.0	n/r	Surgery and radiation (recur)	8—DED
Yan et al. (2009) [4]	6	F	Cheek	10.0 × 5.0	Lymph node	Refused treatment	3—DED
Nagpal et al. (2013) [24]	35	F	Buccal mucosa	1.0 × 1.0	n/r	n/a	n/a
Suarez-Alen et al. (2015) [25]	66	F	Buccal mucosa	2.0 × 1.0	n/r	Surgery	52—ANED
Present case (2017)	87	M	Buccal mucosa	NR	n/a	n/a	n/a

n/r none reported, n/a not available, AWD alive with disease, ANED alive with no evidence of disease, DED dead of disease

may be misdiagnosed or misclassified by the pathologist; one review of head and neck soft tissue sarcomas revealed a change in diagnosis by the pathologist in 33–48% of the cases [10]. Given these difficulties, Dry et al. pointed out that some of the previously reported cases that did not perform immunohistochemical studies, may in fact not be of myogenic origin [6]. Leiomyosarcomas are comprised of spindle cells with abundant fibrillary eosinophilic cytoplasm that mimic normal smooth muscle cells. They have oval nuclei that frequently have perinuclear vacuoles, similar to normal smooth muscle cells. The spindle cells of leiomyosarcomas are characteristically arranged in broad sweeping fascicles. Necrosis is common, as are mitotic figures, including atypical mitoses. As they often arise from the smooth muscle of vessel walls, origin from the outer surface of a vessel is commonly seen but not required for the diagnosis.

Cytogenetic studies of leiomyosarcomas have shown complex karyotypes with no consistent aberrations. Though a loss of chromosome 13 is frequent, suggesting involvement of the *RBI* gene in a proportion of leiomyosarcomas [1], a decreased p16 expression has also been detected in 5–33% of leiomyosarcomas [2]. Even Epstein–Barr virus has been associated with leiomyosarcoma, albeit limited to those patients who were immunosuppressed [15]. Most recently, and previously unrecognized in leiomyosarcomas, chromothripsis (unique pattern of clustered rearrangement involving a single chromosome or few chromosomes [16]) and whole genome deletion were noted [17].

Aggressive surgical intervention remains the mainstay of management for patients with localized sarcomas of the head and neck [10, 18]. A retrospective analysis showed that administration of adjuvant/neoadjuvant chemotherapy and/or radiation for head and neck sarcomas did not have a significant impact on disease-free survival and disease-specific survival. Moreover, none of the patients who were treated with chemotherapy and/or radiation without surgery achieved disease-free status [18]. Our own case review showed that surgical intervention with radiation and/or chemotherapy was by far the most frequent treatment option, unless the patient refused or the tumor location was deemed inoperable. The anatomy of the head and neck can limit the ability to obtain wide surgical margins, and thus may be a reason for higher local recurrence rate and a worse disease-specific survival compared to sarcomas arising at other, more accessible, sites [10, 11]. One group found that local recurrence rates for high-grade soft tissue sarcomas after surgical excision was 42%, most arising within 2 years of treatment [11]. For adult soft tissue sarcomas of all anatomic sites, tumor diameter larger than 5 cm, high histologic grade, and positive surgical margins are all correlated with an increased local recurrence rate, distant failure, and a reduced disease-specific survival [7, 10].

It has been suggested that the location of a leiomyosarcoma may be more important than its histologic features, prognostically speaking, as histopathologic examination appears to be limited for predicting the clinical behavior and prognosis of these smooth muscle tumors [3, 13]. At the same time, Eppsteiner et al., found that the 5-year disease-specific survival for well-differentiated leiomyosarcomas was 87.6% compared with 52.7% for poorly differentiated ones [7]. Furthermore, at most locations, mitoses and necrosis do appear to be the best histologic predictors of malignant behavior and presence of these feature should be evidence in favor of malignancy [19].

Conclusion

With only 16 reported cases of oral leiomyosarcoma in the buccal mucosa, it is difficult to draw broad conclusion about its clinical behavior, prognosis, and optimal treatment. Moreover, predicting clinical behavior of these rare but aggressive tumors has remained elusive. Nevertheless, there appears to be some semblance of guidance on appropriate management for disease-free survival, which begins with an astute clinician who suspects that a painless nodule in the cheek may require further investigation via a tissue biopsy; a thorough histologic examination and immunohistochemical work up for a definitive diagnosis; and, if circumstances permit, early surgical excision with tumor-free margins and prolonged follow up.

Compliance with Ethical Standards

Conflict of interest Authors Eugene M. Ko and Jonathan McHugh declares that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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