Histologic and Immunopathologic Variability in Primary Intraoral Angiosarcoma: A Case Report and Review of the Literature

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Abstract

Primary intraoral angiosarcoma is an exceptionally rare malignancy of vascular origin which can be challenging to diagnose due to microscopic and immunohistochemical variability. A histopathologically challenging case of primary intraoral angiosarcoma, occurring in a pediatric patient is presented. A comprehensive review of the literature reveals that primary intraoral angiosarcomas occur with nearly equal frequency in males and females, affect the gingiva and the tongue most commonly and are treated primarily with surgery. As with angiosarcoma in other sites, primary intraoral angiosarcoma behaves aggressively with the majority of patients succumbing to their disease.

Keywords Angiosarcoma · Oral · Tongue

The histologic details of this case were presented at the AAOMP seminar by the senior author at the 2018 Joint Congress of the American Academy of Oral and Maxillofacial Pathology and the International Association of Oral and Maxillofacial Pathologists, Vancouver, BC June 24, 2018. Some information excerpted from the case handout, written by the senior author, is included in this manuscript.

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Introduction

Angiosarcoma is a rare vascular malignancy, accounting for only 1% of sarcomas [1]. Skin is the most commonly affected site; however, angiosarcomas are known to affect breast, liver, spleen, bone and rarely the deep soft tissue [2]. Amongst head and neck angiosarcomas, oral angiosarcomas are exceedingly uncommon, representing only 2% of all angiosarcomas, and both primary and metastatic oral angiosarcomas are known to occur [3]. Reports of primary oral angiosarcoma are limited, with most cases representing single case reports or small case series. A series of 29 cases, including both primary and metastatic lesions, reported by Fanburg-Smith et al., appears to be the largest collection of oral and salivary gland angiosarcomas reported in the literature to date [4].

By definition, angiosarcomas are vasoformative, but are known to show variable histopathology, including epithelioid, spindled and solid forms [5]. Papillary growth may also be seen [4]. Immunohistochemistry (IHC) is used to confirm the vascular phenotype. Angiosarcomas typically express vascular markers including CD34, CD31, von Willebrand factor (vWF), Fli1, ERG and can express D2–40 [6–8]. Due to variable rates of sensitivity and specificity, a panel of vascular markers is typically advised in the assessment of a potential angiosarcoma [9]. CD 31 is highly sensitive, shows good specificity, and is considered

by many to be the gold standard for diagnosis of angiosarcoma [6, 10, 11]. However, CD31 can be expressed uncommonly in other malignancies, including carcinomas, and is positive most in histiocytic sarcomas [10, 12, 13]. Further, granular positivity in intratumoral macrophages is recognized as a substantial diagnostic pitfall in the diagnosis of vascular neoplasms [14]. Recently, ERG has also been shown to be a sensitive and specific endothelial marker, which is strongly expressed in the majority of angiosarcomas, regardless of differentiation [11].

Morphologically, the spindled type of angiosarcoma is the most common intraoral and salivary gland pattern reported; however, up to 33% of primary oral angiosarcomas in a large case series demonstrated an epithelioid pattern [4]. Given the potential of epithelioid angiosarcomas to express keratins [15] and to mimic poorly differentiated carcinoma, consideration of this entity in the differential diagnosis of a spindled or epithelioid oral malignancy is important, but may fall under the radar of many pathologists.

Angiosarcomas are aggressive neoplasms and are generally associated with a poor prognosis [16–18]. Nevertheless, there is limited evidence from the literature that suggests that primary oral angiosarcomas may have more favourable biologic behaviour when compared to angiosarcomas of other sites [4].

Case Report

An 18-year-old male presented with a 5-month history of a deep, 1.0 × 2.5 cm, painful, non-healing ulcer of the posterior dorsal tongue in the area of the foramen cecum. Previously, he underwent an incisional biopsy at another institution which was reported as granulation tissue. A subsequent incisional biopsy, demonstrated an infiltrative spindled to epithelioid malignancy (Fig. 1). In areas where epithelioid cells were present, abundant eosinophilic cytoplasm and occasional macronucleoli were seen. In many areas, the tumour cells were spindled and demonstrated a fascicular

Fig. 1 Hematoxylin and eosin stained sections depicting the microscopic features of the case presented. **a** Low power image showing an infiltrative, cellular neoplasm (magnification × 1). **b** Cellular pleomorphism was most prominent superficially, and cells in this area were epithelioid. Vascular differentiation was not conspicuous, but primi-

tive vasculature formation can be seen here (magnification × 25). **c** In many areas tumor cells showed a spindled morphology with a myogenic appearance (magnification × 14). A fascicular arrangement was also present in much of the tumor (magnification × 14)

pattern of growth, with a subset of cells showing a myogenic appearance. Cellular pleomorphism was most pronounced in the superficial aspects of the lesion. The vascular nature of the lesion was not prominent; however, slit-like vascular spaces were seen superficially. The malignant cells showed diffuse membranous positivity for CD31 and diffuse nuclear positivity for ERG (Fig. 2). Additionally, AE1–AE3 and vimentin were positive. CD34 and HHV8 were negative. Molecular studies were performed to exclude the possibility of hemangioendothelioma. Interphase fluorescence in situ hybridization (FISH) failed to detect a *TFE3* gene rearrangement, and RT-PCR failed to detect the *WWTR1-CAMTA1* fusion. Subsequent testing was also done to exclude the possibility of pseudomyogenic hemangioendothelioma, with no rearrangements of *FOSB* or *SERPINE1* detected by break-apart FISH. The patient underwent an excision 1 month following diagnosis and was found to have close but negative margins on the surgical specimen. Post-operative radiation treatment was planned; however, follow-up information is not available. The clinicopathologic features of this case are summarized in Table 1.

Review of the Literature

A comprehensive review of the English language literature was conducted, using keyword (oral, angiosarcoma, head and neck) and MeSH terms (hemangiosarcoma, mouth, maxilla and mandible). Cases were excluded from our analysis if they did not report immunohistochemical and/or electron microscopy evidence of vascular differentiation. Due to variability in the sensitivity and specificity of markers used to assess vascular lineage, [9] cases described before CD 31 became commercially available were excluded. A total of 39 cases from 19 reports [4, 17–34] were identified, including the new case reported herein. The clinical, microscopic, treatment and vital status data of the previously reported cases are summarized in Table 2. The median age of affected patients is 63 years, with a wide age range (6–83 years). Five cases occurred in pediatric patients aged 18 years or younger. Of the 39 cases evaluated, 19 cases occurred in females and 20 cases occurred in males. The most common site of involvement of primary intraoral angiosarcoma reported was the

Fig. 2 Immunohistochemical features of the case presented. **a–c** Diffuse immunoreactivity for CD31, ERG and cytokeratin AE1–AE3, respectively (magnification $\times 10$). **d** The tumor was negative for p63 (magnification $\times 8$)

Table 1 Clinicopathologic features of the case presented

Age	Sex	Site	Clinical	Histomorphology and immunohistochemistry	Treatment and vital status
18	M	Dorsal tongue	5-month history of 1.0×2.5 cm deep ulcer	Infiltrative spindled to epithelioid malignancy with areas of fascicular growth Pos: CD31, ERG, CK AE1/AE3, vimentin, SMA (focal), EMA (focal) Neg: CD34, HHV8, desmin, myogenin, S100, p63, HMB45, h-caldesmon INI-1 expression retained	Surgery UK

Pos positive, *UK* unknown, *Neg* negative

gingiva (12), followed by the tongue (11). In order of decreasing frequency, other sites of involvement included: lip (5), soft palate/retromolar trigone (4), hard palate (3) buccal mucosa (2), mandible (1), floor of mouth (1).

The most commonly reported treatment modality reported in the literature for primary oral angiosarcoma is surgery. Of the cases included which reported treatment, 81% (17/21) patients were treated with surgery. Of these (excluding the present case, as post-surgical treatment information is not available), 45% (9/20) of cases were treated with surgery alone, 15% (3/20) were treated with surgery and radiation therapy (RT) and 20% (4/20) were treated with surgery and chemotherapy (CMT). A small number of patients (20% or 4/20) were treated with RT and CMT only.

Of the cases with available follow-up information, 50% (15/30) patients died of disease (range 2 months to 9 years; mean 13 months), 1 patient died of other causes and 47% (14/30) were alive with no evidence of disease, with mean follow-up reported as 6 years (range, 1 month to 16 years).

Discussion

Primary intraoral angiosarcomas are rare, and in the head and neck region most commonly involve the scalp. A recent analysis of 1250 angiosarcomas of the head and neck, found the tongue to be the second most common, non-cutaneous site for head and neck angiosarcoma after the facial bones, with 14% (11/80) of cases occurring in this site [35]. The oral cavity can also be affected by metastatic angiosarcoma and a large series of intraoral and salivary gland angiosarcomas reported 7 metastatic lesions, of which 5 arose from a skin primary in the head and neck [4].

Primary intraoral angiosarcoma most commonly affects older individuals, but exceptionally may affect pediatric patients. The peak age incidence for primary intraoral angiosarcoma is similar to that reported for soft tissue angiosarcomas, with most cases occurring in the 7th decade [15], and is slightly younger than the peak incidence from all head and neck subsites [35]. In pediatric patients, angiosarcoma

is exceedingly rare, and most occur in the heart/pericardium [36].

In the deep soft tissue and bone, angiosarcomas more commonly affect males than females [15]. Of the cases reviewed here, an nearly equal distribution between males and females was noted, with a marginally increased frequency in males; however, when only pediatric patients are considered, a stronger male predominance is evident (80%).

The clinical appearance of intraoral angiosarcomas reported in the literature is variable, with many reports describing expansile masses that are blue/red/purple in appearance, with or without ulceration [17, 33]. Some lesions present with bleeding, and most are painless. Ill-defined bony destruction is common in lesions with primary intraosseous presentation, or those invading bone secondarily [19, 33]. The clinical differential diagnosis encompasses several benign and malignant vascular and pigmented lesions, including: pyogenic granuloma, hemangioma, Kaposi's sarcoma, melanoma, carcinoma and metastatic disease [4, 18, 19].

Angiosarcoma can be a histologically challenging neoplasm to diagnose, particularly if vasof ormation is not a prominent feature. In general, angiosarcomas show variable histomorphology, ranging from well-developed anastomosing vascular channels lined by atypical endothelial cells, to solid sheets of epithelioid or spindled cells. Hemorrhage and necrosis are common [37]. With respect to oral lesions, diagnostic difficulty may be further compounded by the relatively common occurrence of the epithelioid subtype in this site [4, 18, 20, 26, 28, 30]. Epithelioid angiosarcomas are more commonly reported in the deep soft tissue and viscera, and occur less frequently in the skin [2, 15, 38]. Epithelioid angiosarcomas can be particularly troublesome as up to 30% may demonstrate cytokeratin reactivity [1, 4] which can lead to potential misdiagnosis as a poorly differentiated carcinoma. Of the cases included in this review, including our case, 13 reported the presence of epithelioid features, whether focal or widespread. However, only 3 cases with epithelioid features also reported the presence of cytokeratin positivity [18, 20]. Fanburg-Smith et al. reported 5 cases in

Table 2 Clinicopathologic features, treatment and vital status of reported cases of primary intraoral angiosarcoma

Author	Age	Sex	Site	Clinical	Histomorphology and immunohistochemistry	Treatment and vital status
Loudon et al. [19]	68	F	Right FOM	Soft tissue mass, bluish, focal ulceration, recent rapid enlargement, ill defined bony involvement	Pos: FVIIIa (patchy/weak), CD31, CK (AE1/AE3, Cam5.2), vimentin	Resection DOD 8 mos
Favia et al. [17]	65	F	Retromolar trigone	Bluish, painful, 5.5×4.4×4 cm	Abortive vessels and spindle cells	RT + CMT
	70	M	Hard palate	Dark red, expanding mass 4×3×3 cm	Pos: FVIIIa, CD31, CD34 Spindle cells, intercellular haemorrhage, slit-like spaces Pos: FVIIIa, CD31, CD34	DOD 3 mos Resection + CMT DOD 3 months
	74	F	Hard palate	Cherry red, expanding mass 5×5×3 cm	Epithelioid angiosarcoma with rare slit-like spaces Pos: CD31 Neg: FVIIIa, CD34	Partial maxillectomy + CMT Died 4 months
	82	F	Alveolar ridge (31–36)	Purplish Red, expanding mass 6×5×3.5 cm	Abortive vessels and pleomorphic spindle cells Pos: CD31, CD34 Neg: FVIIIa	RT + CMT DOD 6 mos
Fanburg-Smith et al. [4]	30	F	Tongue	UK	Epithelioid and solid	UK
	62	M	Tongue	UK	Epithelioid and focal	UK
	24	F	Tongue	UK	Solid	11 years NED UK
	30	F	Tongue	UK	Solid	13 years NED UK
	68	M	Tongue	UK	Solid	DOD 9 years UK
	6	F	Tongue	UK	Solid	UK
	30	M	Tongue	UK	Solid (focal)	4 years NED UK
	65	M	Tongue	UK	Solid	DOD 12 mos UK
	83	F	Tongue	UK	Vasoformative	1 year NED UK
	67	F	Lip	UK	Epithelioid and solid	13 years NED UK
	52	F	Lip	UK	Epithelioid and solid	16 years NED UK
	68	M	Lip	UK	Solid	UK
	18	M	Lip	UK	Papillary	14 years NED UK
	16	M	Soft palate	UK	Very focal, epithelioid papillary, and solid	UK

Table 2 (continued)

Author	Age	Sex	Site	Clinical	Histomorphology and immunohistochemistry	Treatment and vital status
Florescu et al. [20]	82	M	Hard palate	UK	Solid Epithelioid Pos: CD 31, AE1/AE3 (focal) Neg: Vimentin	UK
Driemel et al. [21]	70	M	Alveolar crest of mandible	Poorly defined nodular purple mass, 4 cm	Pos: CD 31, AE1/AE3 (focal) Neg: Vimentin	UK
Arribas-Garcia et al. [22]	63	M	Alveolar ridge	Polypoid, superficially ulcerated mass, 1.5 × 1 × 1 cm with mets to pleura and ileum	Pos: CD31, CD34, FVIIIa, Fli-1, CK (subset)	DOD 2 mos
Yang et al. [23]	15	M	Left paracommissural mucosa of lower lip	Rounded, well-defined tumoral lesion of red-bluish color, 1–1.5 cm diameter	Irregular anastomosing vascular channels with marked cytological atypia Pos: CD34, CD31	Resection NED 2 years
Mücke et al. [24]	81	F	Soft palate	5–10 cm	Pos: CD31, CK	Surgery + RT Recurrence, UK
Terada et al. [25]	76	M	Multifocal (upper right incisor, first molar and lower right second premolar)	Multifocal ulcerative gingival lesions, history of necrotizing gingivitis (HIV neg). Lymph node mets	Atypical cells, hemorrhage and well formed vascular channels lined by endothelium Pos: CD 31 Neg: CD34, CD45, CD68, CK18, HMWK, S100, KP-1, MPO, Factor VIIIa	Resection + RT DOD 6 mos
Suzuki et al. [26]	54	F	Left cheek adjacent to the mandibular gingiva	Oral mass, 1 cm	Solid tumour of atypical spindle and polygonal cells, nuclear hyperchromasia, intracytoplasmic vacuoles and mitoses Pos: Vim, CD34, FVIIIa, CD31 Neg: AE1/AE3, CAM5.2, SMA, EMA, S100, p63	Radical resection NED 1 mos
Sumida et al. [27]	69	F	Right maxillary gingiva	Bleeding, recent enlargement, large, rounded, well-defined mass, purple to red surface, destruction of tuberosity	Epithelioid Pos: FVIIIa, CD31	RT + CMT Lung metastasis 2 mos
Doek et al. [28]	55	F	Anterior mandibular gingiva	Well-defined epulis like lesion, soft, white-red, easy bleeding	Spindled to polygonal Pos: CD31, FVIIIa, SMA, vim Neg: panCK, S100, NSE, CD56	Resection NED 4 years
Nagata et al. [18]	46	F	Left mandible	History of pain in the left jaw for 6 months, infiltrative bony lesion with IAN extension, no paresthesia	High grade epithelioid Pos: CD31, CD34 (weak) Neg: AE1/AE3, pan melanoma, CD68	Resection NED 18 mos
	55	M	Mandibular gingiva	Rapidly expanding bluish mass, hemorrhagic and fragile, 2.5 × 2.0 cm	Epithelioid angiosarcoma with rare slit-like spaces, Grade III Pos: CD34, EMA Neg: AE1/AE3	Resection Thoracic vertebral metastasis DOD 3 mos

Table 2 (continued)

Author	Age	Sex	Site	Clinical	Histomorphology and immunohistochemistry	Treatment and vital status
	64	M	Maxillary gingiva	Dark red, hemorrhagic and fragile expanding mass, 4.2 × 2 cm	Spindle cells, intercellular haemorrhage, slit-like spaces, Grade II Pos: FVIIIa, CD31, CD34, vim Neg: AE1/AE3, S100, SMA	Resection + CMT Lung mets with lobectomy NED 30 mos
	78	F	Tongue	Pink, hemorrhagic, painful expanding mass, 6.0 × 5.0 cm	Abortive vessels and pleomorphic spindle cells, with epithelioid areas Grade III Pos: CD31, vim, AE1/AE3 Neg: FVIIIa, CD34, S100, SMA, desmin	Resection Lung mets DOD 6 mos
Fomete et al. [29]	35	M	Left cheek oral mucosa	Firm, ulcerated mass, protruding intra-orally, 4 year history, 10 × 7 cm	Spindled with sheet like growth, anastomosing dilated vasculature, hemorrhage, necrosis Pos: CD31	Resection NED 3 months NED
Aljadeff et al. [30]	79	M	Between left maxillary lateral incisor and canine	Red and ulcerated exophytic growth, 0.9 × 0.6 × 0.3 cm no pain, no paresthesia, no bone involvement	Large pleomorphic and atypical epithelioid cells Pos: CD31, vim, ERG Neg: CD20, CD30, AE1/AE3, S100, MNF-116	Resection and post op RT DOC, 4 mos
Hunasgi et al. [31]	30	F	Gingiva labial aspect of 31–41	Soft, sessile painless growth arising from the labial gingiva, 3 × 3 cm, 2 month history Alveolar crestal and interproximal bone loss	Spindled to polygonal with anastomosing vascular channels, nucleoli, mitoses, intracytoplasmic vacuoles Pos: FVIIIa, CD31, CD34	Surgery, negative margins NED 2 years
Chamberland et al. [32]	83	M	Gingiva and both palatine tonsils	Painful gingival lesion followed by hematoma of palatine tonsil	Pos: CD31, CD34, SMA (partial) Neg: HHV-8, BNH9, p63, panCK, CK5/6, EMA	CMT + RT DOD 4 months
Patel et al. [33]	57	M	Gingiva and both palatine tonsils	Irritation and fullness in the mouth	Pos: CD31, ERG	Resection + CMT DOD 7 months
Hartanto et al. [34]	52	F	Soft palate	Soft and mobile pedunculated oval mass, reddish-blue in color	Ovoid to spindled Pos: CD31, Factor VIIIa, Fli-1	DOD short time

FOM floor of mouth, *Pos* positive, *DOD* died of disease, *RT* radiation therapy, *CMT* chemotherapy, *Neg* negative, *NED* no evidence of disease, *UK* unknown, *DOC* died other cause, *CK* cytokeratin, *Vim* vimentin, *Mets* metastasis

their series with epithelioid features; however, cytokeratin staining was not performed. The case we present was unusual, as this case did not show a predominant epithelioid phenotype, but strongly expressed cytokeratins. It is known that cytokeratin reactivity is not exclusively seen in the epithelioid type of angiosarcoma; however, is thought to occur more frequently when epithelioid features are present [15]. Expression of p63 has also been reported in malignant vascular tumours, including angiosarcoma. Although expression is typically seen in a small subset of nuclei, Kallen et al., reported one case of epithelioid angiosarcoma with p63 positivity in 75% of cells [39].

Of the cases included in this review, 11 reported a predominant or partially spindled morphology [17, 18, 25, 27, 31, 29, 34]. For tumours showing a spindled phenotype, spindle cell carcinoma must be considered in the differential diagnosis. The diagnosis of spindle cell carcinoma depends on confirmation of the epithelial phenotype through demonstration of a typical carcinoma component (in situ or invasive), or immunohistochemical positivity for epithelial markers [40, 41]. In our case, which was strongly positive for cytokeratin, lack of expression of p63 was helpful in excluding spindle cell carcinoma. However, it is known that spindle cell carcinomas may show an absence of epithelial markers [40], or may show only focal or patchy staining, suggesting that tumours that are non-homogeneous and small or poorly oriented biopsies can lead to diagnostic difficulty. To complicate things further, spindle cell carcinomas can also show pseudoangiomatous change, mimicking angiosarcoma [42]. Although angiosarcomas can express both broad spectrum cytokeratin and p63 staining, to the best of our knowledge, no cases exhibiting this phenomenon have been reported to date. EMA staining in angiosarcoma can also occur, but is uncommon [43].

Due to their morphologic diversity, angiosarcomas can also show histologic and immunohistochemical overlap with several other lesions. For epithelioid neoplasms in particular, the primary differential diagnostic considerations may include epithelioid hemangioendothelioma (EHE), pseudomyogenic hemangioendothelioma (PHE, epithelioid sarcoma-like hemangioendothelioma) and epithelioid sarcoma (ES). EHE and PHE are rare malignancies. Distinction between angiosarcoma and these lesions is important as both EHE and PHE demonstrate more indolent behaviour [9, 38]. EHE demonstrates cords and nests of rounded to spindled endothelial cells, with intracellular lumina (blister cells) being characteristic [9, 37]. Tumours are CD31 and CD34 positive and epithelial markers are expressed in 25–40%. The *WWTR1-CAMTA1* fusion is specific for hemangioendothelioma and not found in angiosarcoma [44, 45]. A subset of tumours lacking *WWTR1-CAMTA1* show *YAP1-TFE3* [46]. PHE most commonly presents as a multinodular proliferation affecting the extremities of young males [47]. Similar to EHE, PHEs are known to express vascular and

epithelial markers. PHE characteristically demonstrates a gene fusion involving *FOSB*. The *SERPINE1-FOSB* fusion was thought to be characteristic of PHE; however, a recent study has also confirmed the presence of *ACTB-FOSB* in a subset of cases lacking the *SERPINE1-FOSB* fusion, which more commonly showed a solitary clinical presentation [48, 49]. The presence of a *FOSB* rearrangement is helpful in distinguishing pseudomyogenic hemangioendothelioma from angiosarcoma, and recent investigations have demonstrated good sensitivity of the *FOSB* antibody in the distinction of PHE from histologic mimics [48, 50, 51]. Classic (distal) epithelioid sarcoma exhibits a multinodular to sheet-like growth pattern. Tumour cells are classically epithelioid, but can also show spindled or rhabdoid morphology. A pseudoangiomatous appearance has been reported due to loss of cellular cohesion and secondary hemorrhage [52]. ES are known to express cytokeratins and EMA, with CD 34 positivity also reported in 50% of cases [53]. Interestingly, ERG positivity has also been demonstrated in ES [11]; however, Stockman and colleagues have helpfully demonstrated that ERG positivity in EHE is significantly more likely when a monoclonal antibody directed at the N-terminus is used [54]. In their study 68% of ES cases tested showed positivity for ERG directed at the N-terminus, while only a single case (3%) showed moderate staining to a C-terminus specific anti-ERG antibody [54]. Furthermore, ES does not express CD31, and most cases of ES will show a loss of INI-1, features which are helpful in distinguishing this lesion from angiosarcoma [53, 54].

A subset of angiosarcomas have shown recurrent alterations involving several genes, including: *KDR/PTPRB/PLCG1*, *MYC/FLT4* and *CIC* [38, 55]. *MYC/FLT4* coamplification is primarily reported in angiosarcomas secondary to radiation or chronic lymphedema [38, 56, 57]. *CIC* rearrangements have been reported in a small subset of cases demonstrating epithelioid morphology, and have been primarily associated with young adults and cases occurring outside of the breast [55]. The molecular alterations reported are thought to characterize approximately 50% of angiosarcomas [38, 55].

Surgical excision is the most common treatment modality for all angiosarcomas, including those arising intraorally [4, 58], with some patients also receiving radiation treatment or chemotherapy. In general, as a stand-alone treatment, radiation is reported to be less effective than surgery, and chemotherapy is recommended for local disease not amenable to surgery, or metastatic disease [35, 59, 60].

Angiosarcoma is an aggressive neoplasm that is generally associated with a poor prognosis [9]. Head and neck cases of angiosarcoma are no exception, and recently, Lee et al. reported the 5-year overall survival for head and neck angiosarcomas to be 26.5% [35]. Fanburg-Smith et al., suggested that primary oral angiosarcomas may behave more

favorably when compared to angiosarcomas of other sites. In their series, only 22% (2/9) patients with a primary oral angiosarcoma died of disease [4]. However, when these results are combined with all of the other reported cases, the majority of patients with primary oral angiosarcoma (50%) succumb to their disease. Interestingly, when site of occurrence is considered, 43% (3/7) of patients with angiosarcoma in the tongue died of disease (DOD) [4, 18], 64% (7/11) cases from the gingiva DOD [17, 18, 21, 24, 26, 32, 33], and no cases from the buccal mucosa or lip died of disease [4, 22, 25, 29]. It should be noted; however, in two cases involving the cheek/buccal mucosa area, the duration of follow-up was extremely short [25, 29]. Due to the limited number of cases published, definitive conclusions about the biological behaviour of primary oral angiosarcomas cannot be made, particularly with respect to how behavior may differ from cutaneous angiosarcomas. Nevertheless, there do appear to be some differences in biologic behaviour based on intraoral site affected, with lesions occurring in the buccal mucosa or lip behaving considerably better than those occurring elsewhere in the oral cavity. Complete data on treatment is not available in all cases with follow-up information, but practically speaking, lesions of the buccal mucosa and lip may be more amenable to complete excision, which may explain why these lesions behave better.

Conclusion

This paper reports a histopathologically challenging case of primary intraoral angiosarcoma. Our case demonstrates some of the potential pitfalls that may arise in the diagnosis of rare intraoral malignancies. Analysis of the literature suggests that the gingiva and tongue are the most common sites of occurrence for primary intraoral angiosarcoma, and just as in other anatomic subsites, primary intraoral angiosarcoma behaves aggressively, with the majority of patients succumbing to their disease.

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