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Primary Intraoral Angiosarcoma of Rapid Progression: Case Report and Literature Review

Angiosarcoma Intraoral Primario de Rápida Progresión: Informe de Caso y Revisión de la Literatura

Ivana de Sousa Brandão[1]; Karuza Maria Alves Pereira[2]; Marcelo Bonifácio da Silva Sampieri[1]; Filipe Nobre Chaves[1] & Denise Hélen Imaculada Pereira de Oliveira[1]

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ABSTRACT: Angiosarcoma (AG) is a malignant mesenchymal neoplasm, which generally originates from endothelial cells, and the occurrence of primary lesions in the oral cavity being extremely rare. We report a case of primary intraoral AG manifesting at multiple intraoral sites in a 31-year-old male, with rapid progression resembling Kaposi sarcoma, and discuss the clinical, histological, and immunohistochemical aspects of primary intraoral AG, which led to an accurate diagnosis. Characteristically this tumor has an aggressive nature, metastatic potential and short survival rate, so we highlight the value of an early diagnosis of AG for a better prognosis. This clinical case shows an exceedingly rare primary AG with an unusual presentation involving multiple oral sites, wich was a challenge to definitive diagnosis, so histopathological analysis, combined with histochemistry, was essential to correctly identify the pathological entity of the lesion.

KEY WORDS: angiosarcoma, malignant mesenchymal neoplasm, diagnosis.

INTRODUCTION

Angiosarcoma (AG) is a malignant mesenchymal neoplasm derived mainly from endothelial cells of vascular or lymphatic origin and, although it is most common in subcutaneous blood vessels, it can occur throughout the body (Fujisawa *et al*., 2018). The occurrence of primary lesions in the oral cavity is extremely rare, with its prevalence estimated at 0.14 % of head and neck cancers and 0.0077 % of cancers in general (Chamberland *et al*., 2016).

Clinically, intraoral AG are generally described as expansive masses of blue, red, or purplish color, with or without ulcerations (Patel *et al*., 2017). Because they present variable histopathology, AG can be a difficult neoplasm to diagnose, especially if vasculogenesis is not present as a prominent feature (Fletcher, 1986). Immunohistochemistry and a panel of endothelial markers are often required to confirm the vascular phenotype (Lee *et al*., 2019). The aim of this study is to present a rare case of primary intraoral AG manifesting at multiple intraoral sites with rapid progression and discuss the clinical, histological, and immunohistochemical aspects of the tumor through a literature review.

CASE REPORT

A 31-year-old male patient, farmer, alcoholic, and chronic smoker, sought the stomatology service, complaining of a hemorrhagic lesion that had evolved during approximately one month, according to the patient. Under oroscopy, nodular, granulomatous lesions, purplish-colored, sessile implantation, measuring more than 24 mm were observed in the region of the hard palate and maxillary gingiva (Fig. 1). The lesions presented no apparent cause and were asymptomatic.

The patient reported no important medical history or previous medical treatment. Based on this clinical presentation, the initial diagnostic hypothesis

[1] Post Graduation Program in Health Science, Federal University of Ceará, Sobral, Brazil.
[2] Department of Morphology, School of Medicine, Federal University of Ceará, Fortaleza, Brazil.

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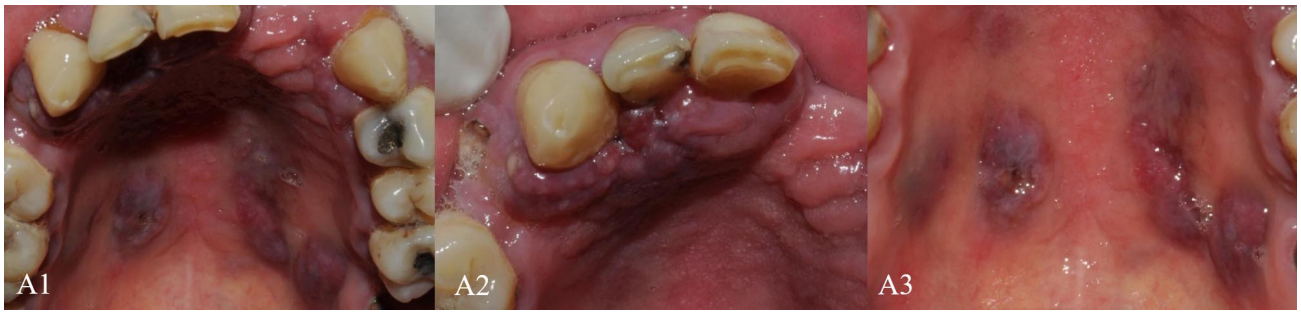

Fig. 1. Initial aspect of the intraoral lesions (A1) located in the anterior alveolar ridge (A2) and region of the hard palate (A3).

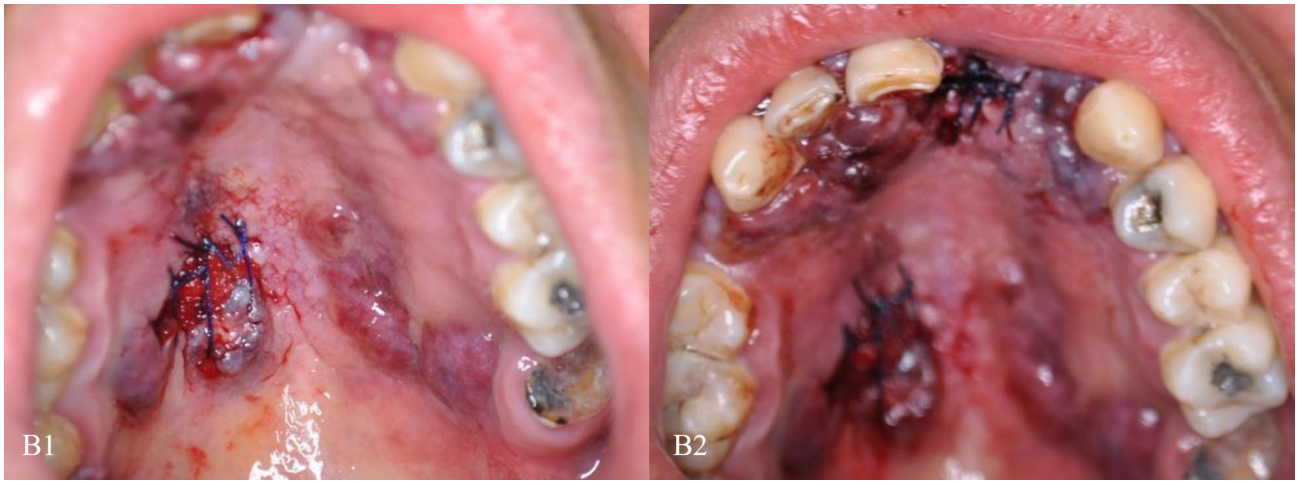

Fig. 2. Incisional biopsy performed in two sites- right posterior region of the hard palate (B1) and anterior alveolar ridge (B2).

was Kaposi sarcoma and serological tests were requested. Serology for HIV and syphilis were negative. So, the patient underwent incisional biopsy in two sites (hard palate and anterior alveolar ridge) (Fig. 2). Less than one month later, the patient returned with rapid progression of the lesions and the tumor covering the entire hard palate region (Fig. 3).

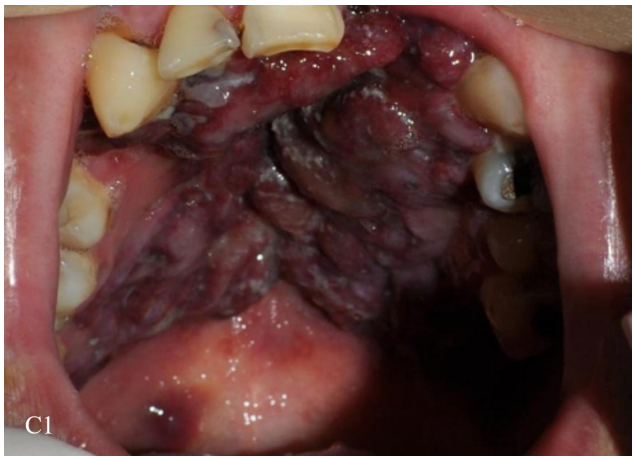

Fig. 3. Clinical appearance after less than 1 month of follow-up evidencing a considerable increase in intraoral lesions.

Histopathological examination revealed a malignant vascular lesion characterized by a proliferation of spindle-shaped and polygonal cells, some voluminous, with hyperchromatic nuclei exhibiting nucleoli, as well as cellular and nuclear pleomorphism. The cells were organized in a stent-shaped pattern, or formed numerous vascular structures of varying sizes. The stroma was made up of dense fibrous connective tissue presenting a mild mononuclear inflammatory infiltrate. The tumor was invading into the surrounding tissue and lymphovascular permeation was noted. In the immunohistochemical study, being Grocott negative, the tumor cells were positive for CD-34 in vessels and scattered cells, with FLI-1 in spindle cells, and Ki-67 staining greater than 15 % (Fig. 4). This reaffirmed the proliferative potential of the injury.

Based on histopathological and immunohisto chemical analysis, the final diagnosis was AG. However, despite immediate referral to the oncology department, the patient passed away shortly after beginning radiotherapy treatment.

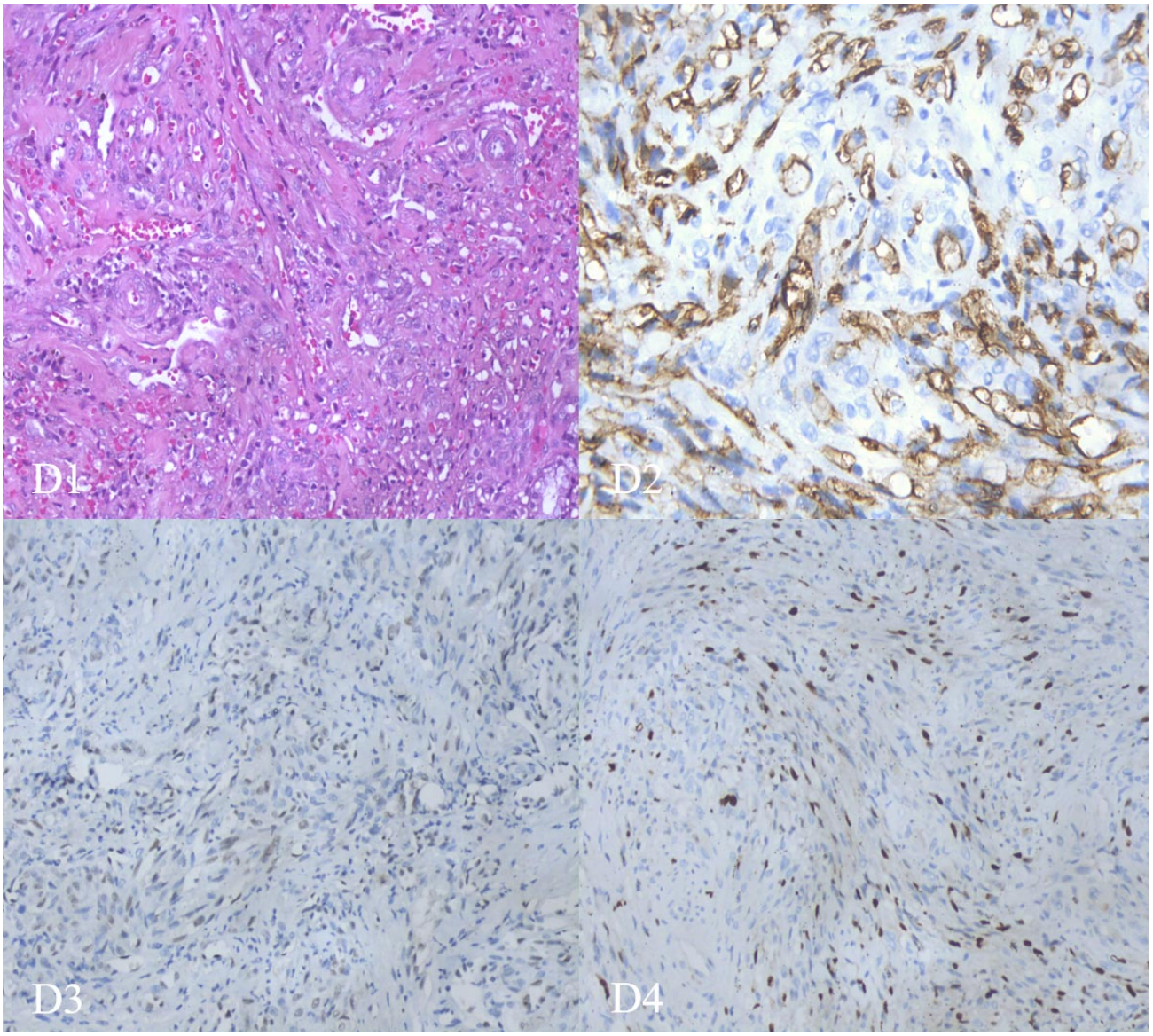

Fig. 4. Histopathological and immunohistochemical analysis revealing the presence of cellular atypia, formation of blood vessels sometimes presenting overlapping endothelial cells giving the impression of cellular projection to the lumen (HE 200 x) (D1). Positive and diffuse expression of CD34 in vessels and dispersed cells (LSAB 400x) (D2). Positive and diffuse expression of FLI-1 in spindle cells (LSAB 200x) (D3). Ki-67 immunoexpression greater than 15 % (LSAB 200x) (D4).

DISCUSSION

AG is one of the rarest soft tissue tumors, characterized by an extremely unfavorable prognosis due to rapid local tumor progression and potential distant metastases (Kusaka *et al*., 2023). The tumor is reported with equal prevalence among the sexes, although some authors suggest a slight male predominance in a ratio of 2:1 (Nagata *et al*., 2014). It affects all ages, with a peak incidence in the 7th decade of life (Chamberland *et al*., 2016), which presents high rates of local recurrence, wide dissemination, and early metastatic potential (Patel *et al*., 2017). In the reported case, the affected individual was male, aged 31 years, presented nodular lesions with ulceration, yet without painful symptoms.

Despite an uncertain etiology, external stimuli such as trauma, ultraviolet light, and radiation have been associated with its development (Young & Woll, 2017). In cases of younger affected individuals, studies suggest a genetic relationship for tumor development,

and association with congenital diseases, such as neurofibromatosis, bilateral retinoblastoma (Rb1 deletion), Aicardi syndrome, and xeroderma pigmentosum (Goldblum *et al*., 2014). In the present case, no exposure to known risk factors was identified and the primary lesions are in the hard palate and maxillary gingiva.

Primary intraoral AG are reported in the literature since 1956 (Blake & Blake, 1956). However, the occurrence is still considered rare, and only three cases involving more than one site in the oral cavity has been reported until 2024 (Ziegler at al., 1997; Mucke *et al*., 2010; Liu *et al*., 2021). Table I brings together clinical features and clinical outcomes of primary intraoral AG reported in the literature of the last 10 years.

Histopathological findings typically include an increase in irregularly dilated and anastomosed vascular spaces and proliferation of atypical or pleomorphic endothelial cells. However, histomorphology is often variable, ranging from highly differentiated tumors resembling benign or intermediate-grade vascular lesions to anaplastic lesions that are difficult to distinguish from poorly differentiated carcinoma or other high-grade sarcomas (Flucke *et al*., 2020). The histological study of this reported case revealed nuclear atypia, invasion of the surrounding tissue, and lymphovascular permeation, confirming its malignancy. Formation of vascular structures of varying calibers containing red blood cells was also observed, confirming its vascular nature.

Differential diagnoses for AG in the oral cavity include various vascular and pigmented tumors, both benign and malignant, and may include pyogenic granuloma, hemangioma, Kaposi sarcoma, melanoma, squamous cell carcinoma, and metastatic tumors (Nagata *et al*., 2014; Patel *et al*., 2017). Due to the clinical aspects of the lesion in the present case, the principal diagnostic hypothesis was Kaposi sarcoma, a rare angioproliferative malignant tumor that originates

Table I. Review of clinical features and clinical outcomes of primary intraoral AG reported in the literature of the last 10 years, together with our case.

Publication	Number of patients	Age/sex	Sites involved	Development time	Clinical outcome
Doeuk *et al*., 2014.	1	46-F	Mandibular gingiva	Unknown	NED 18 months
Nagata *et al*., 2014.	3	55-M	Mandibular gingiva	Unknown	Thoracic vertebrae metastasis
		64-M	Maxillary gingiva	Unknown	Lung metastasis
		78-F	Tonge	Unknown	Lung metastasis
Fomete *et al*., 2015.	1	35-M	Cheeck	4 years	NED were observed at initial presentation or during the follow-up period
Hunasgi *et al*., 2016.	1	30-F	Mandibular gingiva	2 months	NED after a two-year follow-up
Patel *et al*., 2017.	1	57-M	Tongue	Unknown	DOD at 21 months
Haranto *et al*., 2018.	1	52-F	Soft palate	Unknown	DOD short time
Di Battista *et al*., 2020.	1	18-M	Tongue	5 months	Unknown
Komatsu *et al.,* 2020.	1	66-M	Retromolar triangle	Unknown	NED during the 1-year follow-up period.
Lali *et al*., 2021.	1	29-F	left upper alveolus, involving the upper gingivobuccal sulcus and the palate	1 month	The tumor was inoperable. The patient was scheduled for palliative chemotherapy and radiation, but she did not turn up for the treatment.
Bhattacharya *et al*., 2023.	1	48-F	Tongue	4 weeks	Unknown
Kusaka *et al*., 2023.	1	71-M	Tongue	Unknown	NED during the 1-year follow-up.
El Ouazzani *et al*., 2024.	1	73-M	Mandibular gingiva	Unknown	After 2 months, the tumor recurred, with an extension to the mandibular bone and DOD after segmental mandibulectomy.
Present case	1	31-M	Hard palate and maxillary gingiva	Unknown	DOD few days after the diagnosis.

M-male; F- female; DOD - died of disease; NED - no evidence for disease.

in the endothelium, and is seen in immuno compromised patients, such as patients with AIDS (Katsuria *et al*., 2017).

AG typically expresses endothelial markers that include the factor VIII-related antigen (FVIII-Rag), the cytokeratins CD34 and CD31, the fusion product marker FLI-1, the transcriptional regulator ERG, and occasionally the protein podoplanin (D2-40). It has been reported that the high sensitivity and specificity of FLI-1 is equal to or greater than that of other, more established vascular markers (Chamberland *et al*., 2016). Melanoma antigen (HMB45) and S100 protein can be used to distinguish such tumors from malignant melanoma, while myogenic markers (e.g., desmin, actin isoforms, muscle-specific myosin, and myogenin) are employed for differential diagnosis of sarcomas of muscular origin (Nagata *et al*., 2014).

The most common treatment reported in the literature for primary oral AG is surgery, which may be associated with radiotherapy or chemotherapy (Di Battista *et al*., 2020). However, there is a high degree of recurrence and the prognosis is grim, owing to early metastasis and multiple lesions. Up to 32 % of patients have metastatic lesions at the time of diagnosis (Buehler *et al*., 2014), so it is important to rule out any possibility of secondary metastatic disease before making a final diagnosis.

One study reported that over a 40-month follow-up period, only 25.2 % patients diagnosed with AG in the head and neck region remained alive, and the average survival time was only 1.8 years. In multivariate analysis, age ≥ 70 years, tumor size of ≥5 cm, and the presence of metastasis at the time of diagnosis were the independent prognostic factors. Among them, the presence of metastasis is the most important since its presence increases the risk of overall and disease-specific death by 197 % and 399 %, respectively (Lee *et al*., 2019).

A poor prognosis is also associated with Ki67 index > 10 % (Komatsu *et al*., 2020). Our patient also exhibited a high Ki67 index (> 15 %), and died during the initial phase of radiotherapy treatment.

To conclude, we present an exceedingly rare primary AG with an unusual presentation involving multiple oral sites. Although the overall survival of patients is grim with these aggressive sarcomas, early diagnosis and prompt excision are crucial. Intraoral lesions remains a challenge to definitive diagnosis, so histopathological analysis, combined with histochemistry, was essential to correctly identify the pathological entity of the lesion.

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RESUMEN: El angiosarcoma (AG) es una neoplasia mesenquimal maligna, que generalmente se origina en células endoteliales, y la presentación de lesiones primarias en la cavidad oral es extremadamente rara. Informamos un caso de AG intraoral primario que se manifestó en múltiples sitios intraorales en un hombre de 31 años, con rápida progresión similar al sarcoma de Kaposi, y discutimos los aspectos clínicos, histológicos e inmunohistoquímicos del AG intraoral primario, que llevaron a un diagnóstico preciso. Este tumor se caracteriza por su naturaleza agresiva, potencial metastásico y baja tasa de supervivencia, por lo que destacamos el valor de un diagnóstico precoz del AG para un mejor pronóstico. Este caso clínico muestra un AG primario extremadamente raro con una presentación inusual que involucra múltiples sitios orales, lo que representó un desafío para el diagnóstico definitivo, por lo que el análisis histopatológico, combinado con la histoquímica, fue esencial para identificar de manera precisa la entidad patológica de la lesión.

PALABRAS CLAVE: angiosarcoma, neoplasia mesenquimal maligna, diagnóstico.

REFERENCES

Bhattacharya, S.; Koshy, A.V.; Baldawa, P.; Thakur, S.; Shah, A. & Bhagwat, H. A case report of angiosarcoma of the tongue: A diagnostic dilemma at presentation. *Indian J. Dent. Res., 34(2)*:226-8, 2023.

Blake, H.; Blake, F. S. Angiosarcoma; report of a case. O*ral Surg. Oral Med. Oral Pathol., 19(8)*:821-825., 1956.

Buehler, D.; Rice, S. R.; Moody, J. S.; Rush, P.; Hafez, G. R.; Attia, S.; Longley, B. J.; Kozak, K. R. Angiosarcoma outcomes and prognostic factors: a 25-year single institution experience. *Am. J. Clin. Oncol., 37(5)*:473-9, 2014.

Chamberland, F.; Maurina, T.; Degano-Valmary. S.; Spicarolen, T. & Chaigneau, L. Angiosarcoma: a case report of gingival disease with both palatine tonsils localization. *Rare Tumors, 8(3)*:5907, 2016.

Di Battista, M.; Darling, M. R.; Scrivener, E.; Stapleford, R.; Wehrli, B. & McCord, C. Histologic and immunopathologic variability in primary intraoral angiosarcoma: A case report and review of the literature. *Head Neck Pathol., 14(4)*:1139-48, 2020.

Doeuk, C.; McNamara, Z.; Taheri, T. & Batstone, M. D. Primary angiosarcoma of the mandible: a case report. *J. Oral Maxillofac. Surg.,72(12)*:2499.e1-2499.e24997, 2014.

El Ouazzani, H.; Hamidi, O.; Habimana, A.; Dani, B.; Boulaadas, M.; Zouaidia, F. & Cherradi, N. Primary epithelioid angiosarcoma of the mandibular gingiva: diagnostic pitfalls, about an unusual entity. *J. Surg. Case Rep., 2024(5)*:rjae323, 2024.

Fletcher, C. D. Vascular tumors: an update with emphasis on the diagnosis of angiosarcoma and borderline vascular neoplasms. *Monogr. Pathol., 38*:181-206, 1996.

Flucke, U.; Karanian, M.; Broek, R. W. T. & Thway, K. Soft tissue special issue: perivascular and vascular tumors of the head and neck. *Head Neck Pathol., 14(1)*:21-32, 2020.

Fomete, B.; Samaila, M.; Edaigbini, S.; Agbara, R. & Okeke, U.A. Primary oral soft tissue angiosarcoma of the cheek: a case report and literature review. *J. Korean Assoc. Oral Maxillofac. Surg., 41(5)*:273-7, 2015.

Fujisawa, Y.; Yoshino, K.; Fujimura, T.; Nakamura, Y.; Okiyama, N.; Ishitsuka, Y.; Watanabe, R. & Fujimoto, M. Cutaneous angiosarcoma: The possibility of new treatment options especially for patients with large primary tumor. *Front. Oncol., 8*:46, 2018.

Goldblum, J. R.; Folpe, A. L. & Weiss, S. W. *Soft tissue tumors.* 6th ed. Philadelphia, Elsevier, 2014.

Haranto, F. K. & Lau, S. H. A case report of angiosarcoma of maxillary gingiva: hisopathology aspects. *Sci. Dent. J., 2(2)*:77-83, 2018.

Hunasgi, S.; Koneru, A.; Vanishree, M. & Manvikar, V. Angiosarcoma of Anterior Mandibular Gingiva Showing Recurrence - A Case Report withImmunohistochemistry. *J. Clin. Diagn. Res., 10(7)*:ZD01-ZD4., 2016.

Kasturia, S. E.; Gunthel, C.; Zeng, C. & Nguyen, M. L. Severe Kaposi Sarcoma in an Urban Public Hospital. *AIDS Res. Hum. Retroviruses, 33(6)*:583-9, 2017.

Komatsu, Y.; Miyamoto, I.; Ohashi, Y.; Katagiri, K.; Saito, D.; Obara, M.; Takeda, Y.; Shiga, K. & Yamada, H. Primary epithelioid angiosarcoma originating from the mandibular gingiva: a case report of an extremely rare oral lesion. *World J. Surg. Oncol., 18(1)*:260, 2020.

Kusaka, I.; Katagiri, K.; Saito, D.; Ohashi, Y.; Oikawa, S. I.; Tsuchida, K.; Miyaguchi, J.; Kusaka, T.; Ikeda, R. & Shiga, K. A case report of angiosarcoma originating from the tongue. *Clin. Case Rep., 11(12)*:e8330, 2023.

Lali, B. S.; Chowdhury, Z.; Gupta, M. & Mishra, A. Primary angiosarcoma of the oral cavity in a young adult. *Autops. Case Rep., 11*:e2020217, 2020.

Lee, K.C.; Chuang, S.K.; Philipone, E.M.; Peters, S.M. Characteristics and prognosis of primary head and neck angiosarcomas: A surveillance, epidemiology, and end results program (SEER) analysis of 1250 cases. *Head Neck Pathol., 13(3)*:378-85, 2019.

Mucke, T.; Deppe, H.; Wolff, K.D. & Kesting, M.R. Gingival angiosarcoma mimicking necrotizing gingivitis. *Int. J. Oral Maxillofac. Surg., 39(8)*:827-30, 2010.

Nagata, M.; Yoshitake, Y.; Nakayama, H.; Yoshida, R.; Kawahara, K.; Nakagawa, Y. & Shinohara, M. Angiosarcoma of the oral cavity: a clinicopathological study and a review of the literature. *Int. J. Oral Maxillofac. Surg., 43(8)*:917-23, 2014.

Patel, P. B.; Kuan, E. C.; Peng, K. A.; Yoo, F.; Nelson, S. D.; Abemayor, E. Angiosarcoma of the tongue: a case series and literature review. *Am. J. Otolaryngol., 38(4)*:475-8, 2017.

Young, R.J.; Woll, P.J. Anti-angiogenic therapies for the treatment of angiosarcoma: A clinical update. *Memo., 10(4)*:190-3, 2017.

Ziegler, C.M.; Hofele, C.; Kübler, A.; Zöller, J.; Born, A. Multilokuläres Angiosarkom der Mundschleimhaut [Multi-local angiosarcoma of the oral mucosa]. *Mund Kiefer Gesichtschir., 1(6)*:356-8., 1997.

Corresponding author:
Ivana de Sousa Brandão
Department of Dentistry
Federal University of Ceara
Campus Sobral, Brazil
Rua Coronel Estanilau Frota, S/N
CEP 62010-560 Sobral CE
BRAZIL

E-mail: ivana.brandao41@gmail.com