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Case Report

Case Report

Primary epithelioid angiosarcoma of the mandibular gingiva: diagnostic pitfalls, about an unusual entity

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Abstract

Primary angiosarcoma of the oral cavity is a rare malignant vascular neoplasm variably recapitulating endothelial cells and is generally associated with a worse prognosis. The epithelioid subtype is even uncommon in this localization. To our knowledge, only seven cases of primary oral epithelioid angiosarcoma have been reported until 2021. This histopathological variant is characterized by solid and sheet-like growth patterns that may be misinterpreted as other lesions with epithelioid cells. Herein, we present a new case of primary epithelioid angiosarcoma of the mandibular gingiva to discuss histopathological differential diagnoses and potential diagnostic pitfalls.

Keywords: epithelioid angiosarcoma; gingiva; histopathology; differential diagnosis; case report

Introduction

Angiosarcoma is a malignant vascular neoplasm variably recapitulating endothelial cells [1]. In the oral cavity, it represents ≈1% of all angiosarcomas [1, 2] and occurs preferentially in males with a high incidence in the elderly [1].

Commonly, this sarcoma manifests an aggressive clinical course and a poor prognosis [3]. However, the prognosis is more favorable for lip and tongue primaries but metastasis and recurrences are common [1]. Histologically, this tumor shows a large spectrum of morphological patterns; the epithelioid subtype [epithelioid angiosarcoma (EA)] is even rarer and is characterized by solid and sheet-like growth patterns. Its frequent immunohistochemical expression of epithelial markers can lead to misdiagnosis of carcinoma [4].

Case

We present the case of a 73-year-old man with no significant previous medical history. He experienced purple swelling in the right mandibular gingiva (Fig. 1a). The clinical examination was normal. However, a panoramic radiograph revealed bone resorption around the crowns of the 44 and 46 teeth (Fig. 1b). Further examination, including an extraoral examination and TAP CT scan, did not reveal any other mass or lymphadenopathy.

During the histopathological analysis of the biopsy, it was found that the tumor consisted of solid sheets with incomplete alveolar and vasoformative structures. The tumor cells showed abundant amphophilic cytoplasm, large vesicular nuclei, and prominent nucleoli. Mitotic figures were scattered throughout the tumor (Fig. 2a–c). Immunohistochemical analysis revealed positivity for vascular markers (CD31 and transcriptional regulator ERG) and epithelial markers (CKAE1/AE3, CK7), and negativity for CD34, basaloid markers (P40, CK5/6), and melanic markers (MelanA, HMB45) (Fig. 2d–g). The ki67 index was estimated at 50%. These features pointed to a diagnosis of EA. Initially, the patient underwent a local surgical excision and was recommended for palliative radiochemotherapy. After 2 months, the tumor recurred, with an extension to the mandibular bone. As a result, the patient underwent a segmental mandibulectomy, but he died postoperatively.

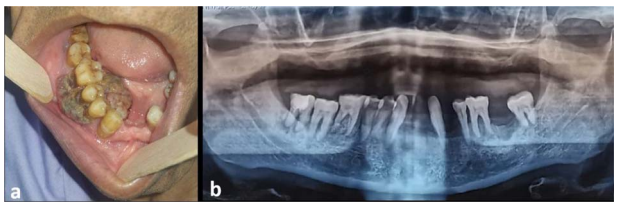

Figure 1. (a) Clinical image of an intraoral EA localized at the mandibular gingiva with extensive red-purple appearance; (b) orthopantomographic image showing resorption of the mandibular bone around the crown of the 44 and 46 teeth.

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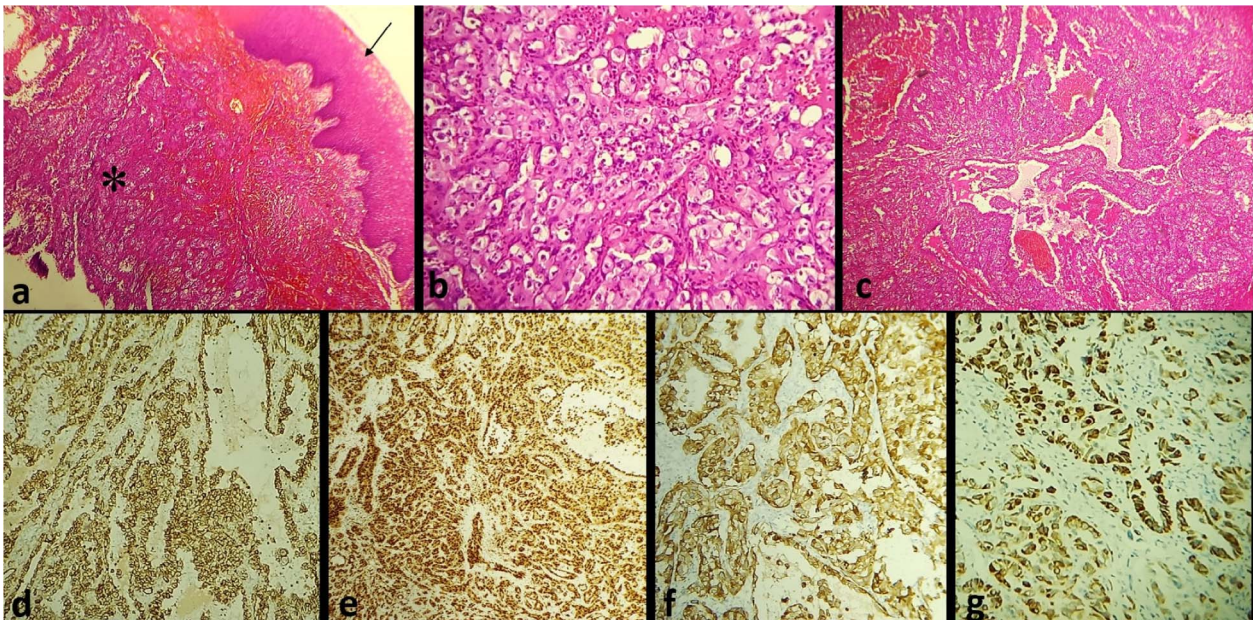

Figure 2. (a) Microphotography of EA showing a solid and sheet-like proliferation (star) under the squamous epithelium covering the gingival mucosa (arrow) (Hematoxylin–Eosin ×10); tumor cells show marked cellular pleomorphism with abundant eosinophilic cytoplasm (Hematoxylin–Eosin ×10); (c) the tumor exhibits a vasoformative architecture; at IHC, tumor cells express CD31 (d), ERG (e), CKAE1/AE3 (f), and CK7 (g).

Table 1. A review of clinical features, treatment, follow-up, and immunophenotype of primary oral EA reported in the literature until 2021, together with our case [3, 4, 6–10].

	Author/year	Age	Sex	Primary site	Treatment	Follow Up	Vascular markers	Epithelial markers
1	Paul D Freedman *et al.*/1992 [7]	32 Y	M	Maxilla (hard palate)	Resection of left side of maxilla	No recurrence No metastasis (For 18 months)	Factor VIII +	NA
2	Masaru Sasaki *et al.*/1996 [4]	69 y	M	Maxilla (hard palate)	Partial maxillectomy + radio-Chemotherapy	Metastasis in stomach, cerebrum, and 12th thoracic vertebra	CD31 + Factor VIII +	Cytokeratin+ EMA-
3	Gianfranco Favia *et al.*/2002 [8]	74 y	F	Maxilla (hard palate)	Partial maxillectomy+ chemotherapy	Died in 3 months	CD34- CD31 + Factor VIII -	CKAE1/AE3+
4	Triantafillidou K *et al.*/2002 [10]	50 y	F	Left maxilla	Left medial maxillectomy	No recurrence No metastasis (for 3 months)	Factor VIII +	NA
5	Abbas Agaimy/ 2012 [9]	71 y	F	Palatine tonsil	Surgical resection	Intra oral and gastro-intestinal metastasis	CD34 + CD31 + Factor VIII + ERG +	CKAE1/AE3+
6	Nagata *et al.*/ 2014 [3]	55 y	M	Mandibular gingiva	Segmental mandibular resection	Thoracic and vertebral metastasis	CD34 +	EMA + CKAE1/AE3 -
7	Yoko Komatsu *et al.*/2020 [6]	66 y	M	Mandibular gingiva	Segmental mandibular resection	No recurrence No metastasis (for 2 years)	CD31 + Factor VIII +	Cytokeratin-
8	Hafsa El Ouazzani *et al.*/2023	73 y	M	Mandibular gingiva	Local surgical excision followed by segmental mandibulectomy	Recurrence and died in 2 months	CD31 + CD34 - ERG +	CKAE1/AE3+ CK7+ EMA -

y: year; M: male; F: female; NA: not available.

Discussion

Angiosarcoma is a malignant tumor that recapitulates the morphological and functional features of the endothelium to a variable degree [5]. It arises most commonly in the deep muscles of the lower extremities, retroperitoneum, mediastinum, and mesentery [5]. Primary angiosarcomas in the oral cavity represent only 1% of all angiosarcomas [1, 2]; the epithelioid variant is even rarer in this localization [6]. To our knowledge and based on the English-language literature, only seven cases of primary oral EA have been reported. Four of them were described in the review of Yuko Komatsu *et al.* [6]. In this paper, we summarize the clinical features, treatment, follow-up, and immunophenotype of three others, together with our case in Table 1 [3, 4, 6–10]. Upon analysis of these cases, it was observed that EA is more frequently

found in older men, with a preference for maxillary localization. Mandibular origin was observed in two cases. Almost all cases presented recurrence and metastasis.

In our experience as a pathologist, diagnosing oral EA may be a challenge. Grossly, EA shows a bloody cut surface with a red to blush-purple appearance [1], sometimes resembling a pyogenic granuloma. Histologically, it is characterized by sheet-like, atypical multilayered, or solid endothelial proliferation. It displays a greater degree of nuclear pleomorphism and mitotic activity and frequently shows areas of necrosis [6]. Vasoformative architecture with intracytoplasmic vacuoles (neolumen) containing erythrocytes is useful for the diagnosis of EA [1], However, immunohistochemistry (IHC) remains the gold standard for the definitive diagnosis. EA generally shows positivity for CD31, CD34, and ERG. Although CD31 and CD34 can show variable expression [11], ERG has the highest sensitivity (reaching 100%) and specificity for identifying vascular and endothelial differentiation [11].

EA is an exceedingly rare variant and closely mimics spindle or acantholytic cells squamous cell carcinoma [8], causing great diagnosis confusion, particularly if the tumor also expresses the epithelial markers such as cytokeratins and epithelial membrane antigen (EMA) [9]. Miettinen *et al.* [12] found in their study that 50% of EA stained with CK8 and CK18 but less commonly with CK7 and CK19. Interestingly, high-molecular-weight cytokeratins (CK14 and 34βE12) have not been detected in vascular neoplasms [9] unlike squamous cell carcinoma.

On the other hand, EA may be confused with other malignant lesions presenting with epithelioid cells such as epithelioid sarcoma or melanoma [11]. In practice, the negativity of melanic markers (MelanA and HMB45) excludes melanoma, while the positivity of ERG and CD 31 excludes carcinoma and epithelioid sarcoma [11].

EA must also be distinguished from other vascular tumors with epithelioid morphology such as epithelioid hemangioma (EH) and epithelioid hemangioendothelioma (EHE). EH is a benign tumor that lacks pleomorphism and destructive growth [1]. At the same time, EA is a high-grade malignancy characterized by an infiltrative growth pattern. It displays a greater degree of nuclear pleomorphism and mitotic activity than EHE and frequently shows areas of necrosis [10]. It is a very destructive tumor, has a propensity to recur locally, spread extensively, and has an elevated rate of lymph node and systemic metastases, with tumor-related death [13].

Conclusion

To summarize, it is important to consider various possible diagnoses before concluding that a patient has primary oral EA. Furthermore, it is crucial to rule out any possibility of secondary metastatic disease before making a final diagnosis. We recommend that prompt and accurate diagnosis can lead to a better prognosis for this type of tumor.

Conflict of interest statement

The authors declare that they have no competing interests.

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Data availability

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Consent for publication

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient's legally authorized.

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