A Case Report of Angiosarcoma of Maxillary Gingiva: Histopathology Aspects

Firstine Kelsi Hartanto1, Shin Hin Lau2
1 Department of Oral Medicine, Faculty of Dentistry, Trisakti University – Indonesia
2 Institute for Medical Research, Kuala Lumpur – Malaysia

‘Corresponding Author: Firstine Kelsi Hartanto, Faculty of Dentistry, Trisakti University – Indonesia. Email: ine.kelsi@gmail.com

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ABSTRACT

Background: Angiosarcoma is a rare malignant tumor, which most often occurs in the skin and soft tissue. Its occurrence in the head and neck region, and the intraoral region in particular, is uncommon. The aim of this case report is to highlight the importance of histopathological examination and to underscore the characteristic features of angiosarcoma.

Case report: A 52-year-old female presented with a growth in the right maxillary portion of the interdental region of her molar teeth. The growth had been present for approximately one month. A computerized tomography (CT) scan showed metastatic tumors in the lungs, liver, bone, and soft tissue of maxillary gingiva. Intraoral examination found a soft and mobile pedunculated ovoid mass at the right palatal gingiva; the mass was reddish-blue in color. An incisional biopsy was performed to confirm the diagnosis and plan for further treatment. Histopathologic examination revealed malignant endothelial cells in a vasoformative growth pattern, with numerous vascular channels lined with neoplastic endothelium-forming intraluminal buds, projections, and papillae. These projections were interspersed with the tumor cells. Immunohistochemistry analysis showed these endothelial cells demonstrated strong positive immunoreactivity with CD31, factor VIII, and FLi-1. A diagnosis of angiosarcoma was made.

Discussion: Because intraoral angiosarcoma is rare and its clinical presentation can resemble other vascular lesions, it can be a challenging diagnosis for clinicians and pathologists. In the present case, the diagnosis of intraoral angiosarcoma was made based on clinical and histopathology findings. The microscopic features of malignant endothelial cells and the presence of intraluminal projections, supported by positive immunoreactivity with CD31, factor VIII, and FLi-1, confirmed the diagnosis. Conclusion: Angiosarcoma poses a diagnostic challenge to dental practitioners and oral pathologists due to the rarity of occurrence in the oral cavity. Histopathological examination is critical for an accurate diagnosis.

Keywords: angiosarcoma, maxillary gingiva, histopathology
Background

Angiosarcoma is a malignant cancer in which the cells have the morphology and functional features of normal endothelium. Several terms have been used to describe this neoplasm including hemangiosarcoma, lymphangiosarcoma, hemangioblastoma, malignant hemangioendothelioma, and malignant angioendothelioma.\(^1\) Angiosarcoma is an uncommon tumor of the skin and soft tissue.\(^2\) Mark et al. reported that 60% angiosarcoma occurred in the skin and superficial tissue.\(^3\) Its occurrence in the head and neck region is also unusual.\(^4\) When angiosarcoma occurs in the head and neck region, the scalp and facial soft tissue are the most common sites affected; it is rare that the oral cavity is the primary location. When angiosarcoma does occur in the oral cavity, it is typically in the mandible and rarely in the maxilla or maxillary sinus.\(^3\)

The skin lesion of angiosarcoma appears as red plaques and nodules which may be extensive and ulcerated, and in rare cases the lesion is in the form of bruise or a pyoderma, resembled localized skin infection. In the oral cavity, angiosarcomas generally appear as red, blue, or purple nodular tumors.\(^5,6\)

The histological appearance of angiosarcomas can be varied; cells range from spindle to epithelioid in shape.\(^1\) They show irregular anastomosing vascular channels; immature endothelial cells can be arranged in the shape of threads or capillaries in tumor areas. The three main growth patterns of angiosarcomas are angiomatous patterns with epithelioid features, spindle cell patterns, and undifferentiated or solid patterns. Prognosis is generally poor because these tumors often infiltrate substantially beyond their visible borders. Even well-differentiated angiosarcoma can be difficult to control locally and often metastasize widely.\(^7\)

Immunohistochemistry is an important aspect in the diagnosis of angiosarcoma, especially for poorly-differentiated forms. CD31, CD34, factor VIII-related antigen, and lectins have been used as specific markers in immunohistochemistry for angiosarcoma.\(^1,8\)

Case Report

In December 2012, a 52-year-old female was referred to Sibu Hospital in Sarawak, Malaysia with a growth in the right maxillary region of her interdental molar teeth. The growth had become apparent one month earlier. Her medical history included a right breast phyllodes tumor; a right mastectomy was performed in April 2007. She also had degenerative spine disease and an old compression fracture at level T12. CT scans detected metastasis cancer to the lung, liver, bone, multiple lymph nodes at bilateral posterior triangle, and a soft tissue lesion at the right maxillary region. There was no maxillary bony erosion. Intraoral examination showed a soft and mobile pedunculated oval mass, reddish-blue in color, measuring 2.0 cm x 2.0 cm (buccal) and 4.0 cm x 2.0 cm (palatal) at the right palatal gingiva. An incisional biopsy was performed to confirm the diagnosis and plan for further palliative care. She was diagnosed with squamous cell carcinoma, metastatic tumor of breast, and pyogenic granuloma.

The incisional biopsy specimen appeared as a soft tissue mass measuring 2.3 cm x 2.2 cm x 1.6 cm. Histopathology revealed a tumor mass beneath partially-ulcerated oral epithelium. The tumor was comprised of malignant endothelial cells in a vasoformative growth pattern (Fig. 1). The neoplastic cells were large and ovoid-to-spindle shaped, with vesicular nuclei, prominent nucleoli with indistinct cytoplasmic outline, and increased mitotic activity (Fig. 2). Some of the neoplastic cells demonstrated epithelioid cytomorphology. Numerous vascular channels lined with neoplastic endothelium forming intraluminal buds, projections or papillae, were interspersed with the tumor cells. The intervening myxoid stroma was extensively hemorrhagic and diffusely infiltrated by mixed acute and chronic inflammatory cells. Immunohistochemistry studies showed the endothelial-forming vascular channels, with spindle-shaped epithelioid neoplastic cells that were strongly positive for CD31 (Fig. 3), factor VIII (Fig. 4), and Fli-1 (Fig. 5). The patient passed away a short time after the incisional biopsy was performed.
**Figure 1.** The vasoformative growth pattern, characteristic of angiosarcoma (Hematoxylin and eosin stain, 10x).

**Figure 2.** Neoplastic endothelial cells show large, ovoid-to-spindle shapes with vesicular nuclei and prominent nucleoli with indistinct cytoplasmic outline. Intraluminal projection is noted with arrows. (Hematoxylin and eosin stain, 20x).
Figure 3. Cytoplasmic immunoreactivity of the neoplastic cells with CD31 (arrows) (Immunohistochemistry, 20x).

Figure 4. Neoplastic cells were strongly positive for factor VIII (arrows) (Immunohistochemistry, 20x).
Figure 5. Nuclear immunoreactivity of neoplastic cells with FLI-1 (arrows) (Immunohistochemistry, 20x).

Discussion

Angiosarcoma has been described as red to blue in color, with nodular or multi-lobulated growth and a non-ulcerated surface. However, the surface of the lesion can also be ulcerated. The lesion is typically painless, firm on palpation, and associated with spontaneous bleeding. There are three conditions that have been postulated to have a role in the development of angiosarcoma: long-standing lymphedema, prior radiation of benign vascular lesions, and history of trauma to the region. However most cases present without obvious etiology. There was no obvious etiology in the present case.

Clinically, there are a few lesions that can be considered as differential diagnoses of intraoral angiosarcoma, including pyogenic granuloma, hemangioma, Kaposi’s sarcoma, melanoma, and metastatic lesions, which can lead to misdiagnosis. In this case, squamous cell carcinoma, pyogenic granuloma, and metastasis tumor were considered as differential diagnosis. Therefore, a biopsy is required to confirm the diagnosis.

Microscopically, angiosarcoma may show a wide spectrum of histologic differentiation. Well-differentiated angiosarcoma may show anastomosing vascular channels lined with atypical endothelial cells with little mitotic activity, while the poorly-differentiated type may show solid sheets of epithelial-like cells or spindle cells without vasoformative activity. In the poorly-differentiated case, immunohistochemistry studies are needed to distinguish angiosarcoma from other tumors. The well-differentiated and moderately-differentiated angiosarcoma can mimic pyogenic granuloma, hemangioma, hemangio-endothelioma, papillary endothelial hyperplasia, and Kaposi’s sarcoma. Poorly-differentiated angiosarcoma must be distinguished from a large number of conditions including spindle cell carcinoma, mucosal malignant...
melanoma, rhabdomyosarcoma, liposarcoma, synovial sarcoma, malignant fibrous histiocytoma, malignant peripheral nerve sheath tumor, epithelioid sarcoma, malignant myoepithelioma of the salivary gland, and anaplastic non-Hodgkin’s lymphoma with spindle cell features.\textsuperscript{12,7} Since angiosarcoma has a variety of histopathological presentations, a careful microscopic examination and immunohistochemistry are needed to confirm the diagnosis of angiosarcoma. The presence of atypia and nuclear pleomorphism of endothelial cells, endotheial multi-layering, and an infiltrative growth pattern have been proposed as criteria to distinguish angiosarcoma from other neoplasms.\textsuperscript{8,13} Immunohistochemistry studies with von Willebrand factor, CD31 and CD34, and factor VIII-related antigen have been used in diagnosis of angiosarcoma.\textsuperscript{1,4,7} In the present case, a diagnosis of angiosarcoma was confirmed by histopathology of vasoformative growth and anastomosing channels lined with atypical endothelial cells, and positive immunoreactivity with CD31, factor VIII and FLi-1.

There were studies reported that CD31 and factor VIII are commonly considered as positive immunohistochemistry markers of angiosarcoma\textsuperscript{14,15} which was also shown in this case. The reason was immunohistochemistry studies with CD31 and factor VIII often showed technical artifacts positivity in the membranes and cytoplasmic. FLi-1 was also used to confirm the diagnosis of angiosarcoma in this study. This case is in accordance with study by Rossi \textit{et al}. which also used FLi-1 to confirm diagnosis of angiosarcoma.\textsuperscript{16} Therefore, FLi-1 staining was done where it demonstrated more clear nuclear positive immunoreactivity. FLi-1 is typically used in the diagnosis of small round cell carcinoma, particularly Ewing’s sarcoma. FLi-1 protein expression is consistently found in the endothelial cells,\textsuperscript{17} and it has been proposed as a nuclear marker of endothelial differentiation.\textsuperscript{18}

In the present case, it was unclear whether the intraoral growth was a secondary tumor of the previous breast phyllodes tumor.\textsuperscript{19} Another study of 80 cases angiosarcoma revealed local recurrence develops 20\% of patients and 49\% with distant metastasis to lung, lymph node, bone, and soft tissue. This result showed that angiosarcoma is a high-grade sarcoma.\textsuperscript{20}

Conclusion

Angiosarcoma poses a diagnostic challenge to dental practitioners and oral pathologists due to its rare occurrence in the oral cavity and the clinical presentation of this cancer may resemble to squamous cell carcinoma and other localized infections such as pyogenic granuloma. A definitive diagnosis requires histopathology studies, supported by clinical presentation and radiology.

References

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