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CASE REPORT

Angiosarcoma of the Oral Cavity

Tadashi Terada

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Abstract Angiosarcoma of the oral cavity is extremely rare. A 54-year-old woman consulted to our hospital because of mass of the left cheek next to the mandible. MRI showed a 1 cm tumor. Enucleation of the tumor was performed. Grossly, the tumor was not encapsulated and had a central cavity. Histologically, the tumor consisted of spindle and polygonal cells with hyperchromatic nuclei with nucleoli. Intracytoplasmic vacuoles and mitotic figure were scattered. Vasoformative channels were present in some areas. Lymphoid follicles were scattered in the tumor. The tumor was invasive into the surrounding tissue, and lymphovascular permeation was noted. The surgical margins were positive. Immunohistochemically, the tumor cells were positive for factor VIII-related antigen, CD31, CD34, vimentin, p53 protein, but negative for pancytokeratins, cytokeratin (CK) 7, CK 18, CK19, EMA, S100 protein, α-smooth muscle antigen, desmin, p63, synaptophysin, chromogranin, neuron-specific enolase, CD56, CD10, CD20, CD30, CD45RO, melanosome, myoglobin, KIT, and PDGFRA. The Ki-67 labeling was 46%. The lymphoid tissue in the tumor was positive for CD20, CD45, CD45RO, and CD10. A pathological diagnosis of angiosarcoma was made. No metastatic lesions are found now. Radical operation is planned now.

Keywords Oral cavity · Angiosarcoma · Histopathology

T. Terada (✉)
Department of Pathology, Shizuoka City Shimizu Hospital, Miyakami 1231, Shimizu-Ku, Shizuoka 424-8636, Japan
e-mail: piyo0111jp@yahoo.co.jp

Introduction

Angiosarcoma is a malignant mesenchymal tumor with a differentiation into vascular endothelium. Although angiosarcoma can occur in any *location*, the most common sites are soft tissue and skin [1]. Angiosarcoma of the oral cavity is extremely rare; there are a few case reports [2–4] and case series [5] in the literature. The author herein reports a small angiosarcoma of the left cheek mucosa next to the mandibular gingiva.

Case Report

A 54-year-old Japanese woman was admitted to our hospital because of oral mass located in the left cheek adjacent to the mandibular gingiva. MRI showed a 1 cm tumor at that location (Fig. 1). Excision was performed. Grossly, the tumor was 1 cm in diameter, was not encapsulated, and showed a central cavity (Fig. 2). Histologically, the tumor had small central cavity, but other areas were solid tumor composed of atypical spindle and polygonal cells with hyperchromatic nuclei and nucleoli (Fig. 3a). Mitotic figure were scattered. The tumor cells occasionally showed intracytoplasmic vacuole. In some areas, vasoformative channels containing red blood cells were recognized (Fig. 3b). Lymphoid tissues with follicles were also scattered within the tumor. The tumor was invasive into the surrounding tissue (Fig. 3a) and lymphovascular permeation was recognized in certain areas (Fig. 3c). No papillary lesions were recognized.

An immunohistochemical study was performed with the use of Dako Envision method (Dako, Glostrup, Denmark). The tumor cells were positive for strongly positive for vimentin (Vim 3B4, Dako), factor VIII-related antigen

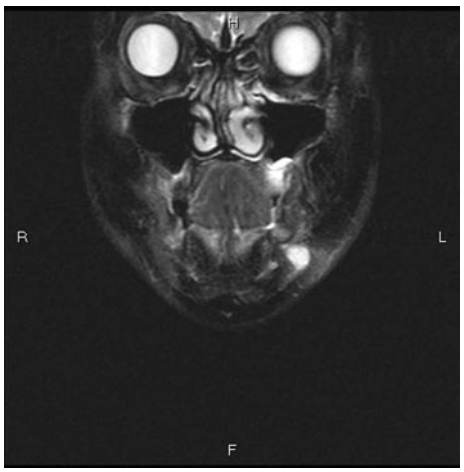

Fig. 1 Coronal section of MRI (not enhanced). A 1 cm tumor is seen in the *left* mandibular oral area

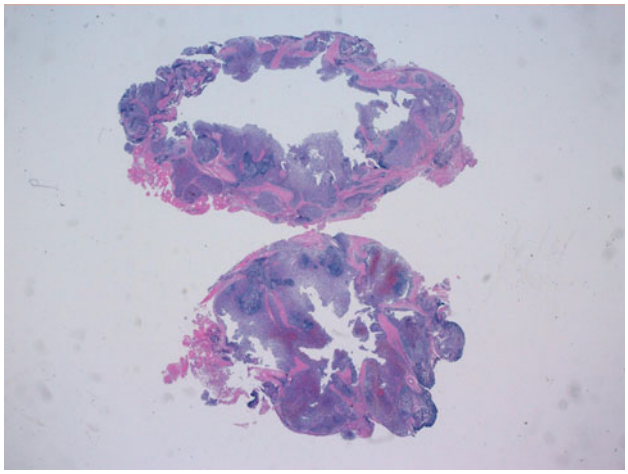

Fig. 2 Very low power view of the tumor. The tumor is cellular solid tumor. Invasion into the surrounding tissue is seen. The tumor had a central cavity. The surgical margins are positive. HE, ×4

(F-VIII-RA) (36B11, Novocastra, Newcastle upon type, UK) (Fig. 4a) and p53 protein (DO-7, Dako). They are weakly positive for CD34 (NU-3A1, Dako) (Fig. 4b), and CD31(1A1, Novocastra) (Fig. 4c). In contrast, they were negative for pancytokeratins (AE1/3, Dako; CAM5.2 Beckton-Dickinson, CA, USA), cytokeratin (CK) 7 (OV-TL, Dako), CK18 (DC10, Dako), CK20 (Ks20.8, Dako), EMA (E29, Dako), S100-protein (polyclonal, Dako), desmin (D33, Dako), α-smooth muscle antigen (1A4, Dako), p63 (4A4, Dako), synaptophysin (SY38, Dako), chromogranin (DAK-A3, Dako), neuron-specific enolase (BBS-/NC/VI-H14), CD56 (MOC-1, Dako), CD45 (LCA, Dako), CD20 (L26, Dako), CD45RO (UCHL-1, Dako), CD30 (Ki-1, Dako), melanosome (HMB45, Dako), myoglobin (polyclonal, Dako), KIT (polyclonal, Dako), and PDGFRA polyclonal, Santa Cruz, CA USA). The Ki-67

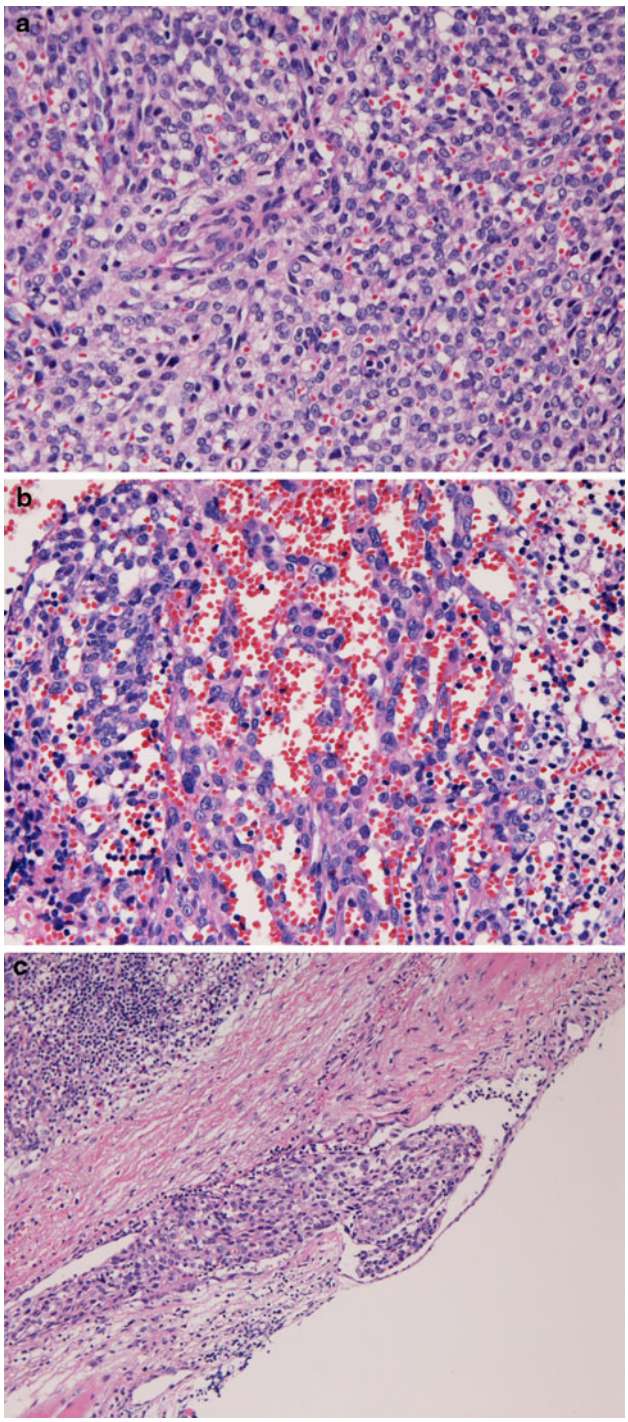

Fig. 3 Histologic features of the tumor. **a** The tumor is composed of atypical polygonal or spindle cells with hyperchromatic nuclei. Nucleoli are present. No apparent differentiation is recognized in this area, but intracytoplasmic vacuoles are seen. HE, ×200. **b** This area shows vasoformative channels containing red blood cells. HE, ×200. **c** This area shows a lymphovascular permeation. HE, ×100

(MIB-1, Dako) labeling was 46% (Fig. 4d). The lymphoid tissue in the tumor was positive for CD20, CD45, CD45RO, and CD10.

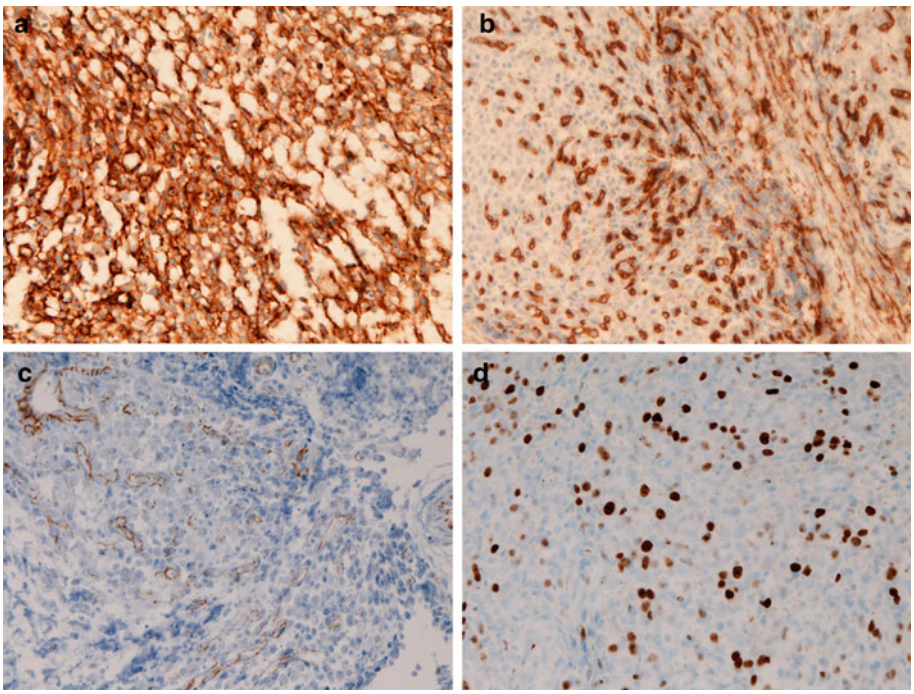

Fig. 4 Immunohistochemical features of the tumor. **a** The tumor cells are strongly positive for factor VIII-related antigen. ×200. **b** The tumor cells were mildly positive for CD34. ×200. **c** The tumor cells were mildly positive for CD31. ×200. **d** The MIB-1 labeling is 46%. ×200

A pathologic diagnosis of poorly differentiated (intermediate or high grade) angiosarcoma of the oral cavity was made. Various imaging modalities including CT and MRI showed no tumors in the body other that the oral cavity tumor; thus no metastatic lesions were found now. The oral cavity tumor (angiosarcoma) was primary. Radical operation was performed, and the patient is now free from tumor 1 month after the operation.

Discussion

The present tumor showed nuclear atypia and mitotic figures. Invasive features and lymphovascular invasion were present. These findings show that present tumor is malignant, though the tumor is very small. The positive expression of p53 protein and high Ki-67 labeling indicates that the tumor is malignant.

The present tumor appeared mesenchymal tumor on HE histology. The positive reaction to vimentin and negative reaction to various cytokeratins and EMA indicate the mesenchymal characters of the present tumor. The present tumor showed vasoformative channels and intracytoplasmic vacuoles on HE sections, suggesting an angiogenic tumor. The positive reaction to F-VIII-RA, CD34 and CD31 endothelial markers, indicates that the present tumor have endothelial characteristics. The presence of red blood cells in the vasoformative channels suggests that the tumor is not a lymphatic tumor but a vascular tumor. Although the CD31 and CD34 immunoreactivities were low and focal, strong and diffuse expression of F-VIII-RA strongly suggests the endothelial origin in the current tumor. Taken together, the present tumor is angiosarcoma histologically and immunohistochemically.

The present tumor showed lymphoid structures within the tumor. This phenomenon has not been described in oral angiosarcoma. The lymphoid tissues showed follicular hyperplasia consisting of B- and T-cells. This tissue may be immune responses to the tumor.

The reason for the central cavitation is unclear in the current tumor. However, it may be an artifact during operation or tissue processing, a remnant of vascular lumen, or central necrosis of the tumor.

Differential diagnosis includes malignant vascular tumors, such as epithelioid hemangioendothelioma, perivascular myoid tumor (malignant Glomus tumor and malignant myopericytoma), perivascular epithelioid tumor (malignant Pecoma), Kaposi's sarcoma, spindle cell carcinoma, malignant melanoma, intravascular endothelial hyperplasia, epithelioid angiosarcoma, and lymphangiosarcoma. The current tumor is different from epithelioid hemanigioendothelioma which shows more little atypia, no vasoformative channels, and collagenization. The present case is different from malignant Glomus tumor and malignant myopericytoma histologically and negative smooth muscle markers. This case is different from Pecoma histologically and absence of melanosome antigen (HMB45), and is different from Kaposi's sarcoma in histological features and absence of multiple lesions and red cell extravazation. This tumor is apparently different from spindle cell carcinoma and malignant melanoma with regards to histology and immunohistochemistry. The tumor

is obviously different from intravascular endothelial hyperplasia in histology and atypical features. The current tumor is different from epithelioid angiosarcoma histologically and absence of CK expression. The current tumor is different from lymphangioma because the vasoformative channels harbored red blood cells.

Generally, angiosarcoma is a very aggressive tumor. Angiosarcoma of the oral cavity may occur in various tissues, such as oral soft tissue, minor salivary glands, and bones [2–5]. The present case occurred in the cheek soft tissue in the oral cavity. Fanburg-Smith et al. [5] reported 22 cases of primary angiosarcoma of the oral and salivary glands. The sites of the 22 cases were tongue in 9, parotid gland in 4, lip in 4, submandibular gland in 3, and palate in 1 [5]. Male and female were equally affected [5]. The symptoms are mass or mass bleeding. The size ranged from 0.8 to 7.0 cm. Histologically, all tumors were vasoformative, 86% had solid areas, and 17% had papillary areas. Immunohistochemically, F-VIII-RA was positive in 19/21, CD31 in 16/19, CD34 in 7/12, and Ulex lectin in 1/1 [5]. The survival differed depending on locations, and ranged from 1 year to 20 years with an average of 7.3 years. The survival is longer in low grade angiosarcoma than high grade angiosarcoma [5].

Conflict of Interest The author has no conflict of interest.

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