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Case Report

Epithelioid hemangioendothelioma of the oral cavity: a case report

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Abstract: Epithelioid hemangioendothelioma is a rare vascular neoplasm which exhibits the potential for malignancy and recurrence as well as the ability to metastasize. Although numerous sites of involvement are possible, these tumors most commonly arise in soft tissues, lung, liver, bone, and lymph nodes. In this report, we describe a case of oral epithelioid hemangioendothelioma in a child. This tumor appeared as exophytic ulcerated painless masses in the maxillary and mandibular gingiva. Histologically, the tumor was composed of a proliferation of tumor cells arranged in nests, cords, and short strands. Epithelioid cells exhibited abundant eosinophilic cytoplasm with nuclear and cellular pleomorphism and intra-cytoplasmic vacuoles. (J. Oral Sci. 50, 219-223, 2008)

Keywords: epithelioid hemangioendothelioma; oral cavity; vascular tumor.

Introduction

Epithelioid hemangioendothelioma (EHE), first described by Weiss and Enzinger (1) in 1982, is a vascular tumor characterized by neoplastic proliferation of epithelioid or histiocytoid endothelial cells.

Although this lesion can occur at any age, it is rarely seen in children (1,2). It has a female predilection with a female-to-male ratio of 2.5:1 (3). This neoplasm is usually observed in the extremities; however, it may also occur in bone, lung, brain, liver, and lymph nodes (4,5).

Epithelioid hemangioendothelioma is asymptomatic in most patients; however, patients occasionally present with pain or tenderness. The lesions appear erythematous with a pink or yellowish tan and the maximum diameter ranges from 0.2 to 4.5 cm (3). The most common site of occurrence in the head and neck region is the submandibular area, followed by the soft tissues of the neck (6). This tumor rarely occurs in the oral cavity, and only 26 cases have been reported to date (3,6-19). In the present paper, we report a case of epithelioid hemangioendothelioma of the oral cavity.

Case Report

A 9-year-old boy presented at the Mashhad Faculty of Dentistry on June 10, 2002 with a one-cm-round, pedunculated, ulcerated, painless, red mass in the right buccal gingiva between the maxillary second deciduous molar and first permanent molar. The mass had appeared 6 months ago. His medical history was unremarkable. The lesion was firm and hemorrhagic. No similar lesions were present in other sites of the oral cavity or skin. Moreover, no lymph nodes were palpable. The radiographic appearance of the area was completely normal with no sign of bone resorption. It was provisionally diagnosed as a

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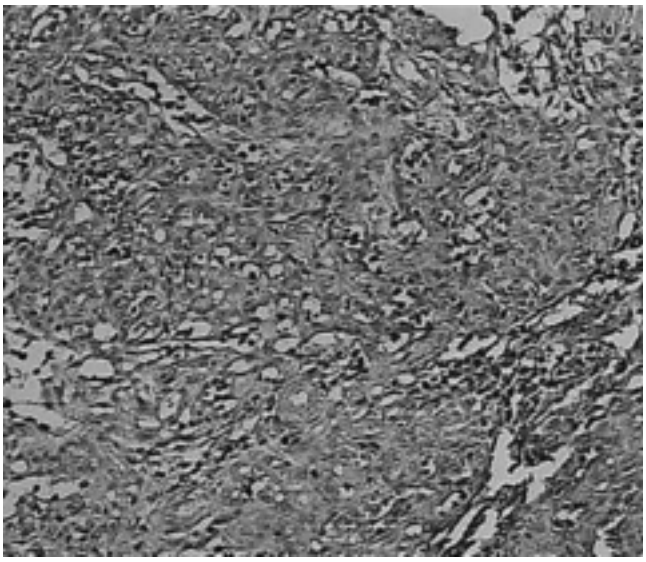

Fig. 1 Proliferation of endothelial cells and infiltration of lymphocytes (×100 magnification, H-E staining).

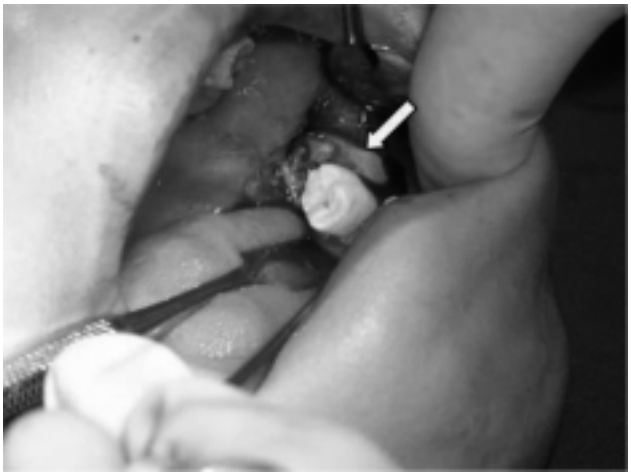

Fig. 2 Clinical view of the exophytic lesion.

pyogenic granuloma.

Under local anesthesia, an excisional biopsy was performed, and the specimen was submitted for microscopic examination. Grossly, the mass measured 1.5 × 0.5 cm. Histopathologic findings consisted of granulation tissue-like proliferation resembling a pyogenic granuloma. (Fig. 1) Proliferation of endothelial cells with mild atypia and blood vessel formation, proliferation of fibroblasts and collagen formation, infiltration of chronic inflammatory cells, and ulcer formation and fibrinopurulent membrane formation were observed.

After 3 years, another lesion appeared as an exophytic, ulcerated, and painless mass in the buccal gingiva behind the left mandibular first permanent molar. (Fig. 2)

Excisional biopsy was performed again and the specimen was submitted for microscopic examination. Grossly, the mass measured 1 × 1 cm whereas microscopic examination showed a noncapsulated proliferation of epithelioid cells with intra-cytoplasmic lumina in a nest-like arrangement. Moreover, hyperchromatic nuclei were noted and the stroma was collagenized. (Fig. 3)

Immunohistochemical staining revealed CD31 and CD34 positivity, confirming the endothelial nature of the epithelioid cells, and the diagnosis of EHE. (Figs. 4 and 5)

One year postoperatively, there was evidence of recurrence in the buccal gingiva between the right maxillary second premolar and first permanent molar. Excisional biopsy was performed again and the maxillary second premolar and first permanent molar were extracted at the request of the patient's parents; however; this was in contrast with our treatment plan. Grossly, the hemorrhagic mass measured 1.5 × 0.5 cm. After microscopic examination, it was again diagnosed as EHE. Radiographic

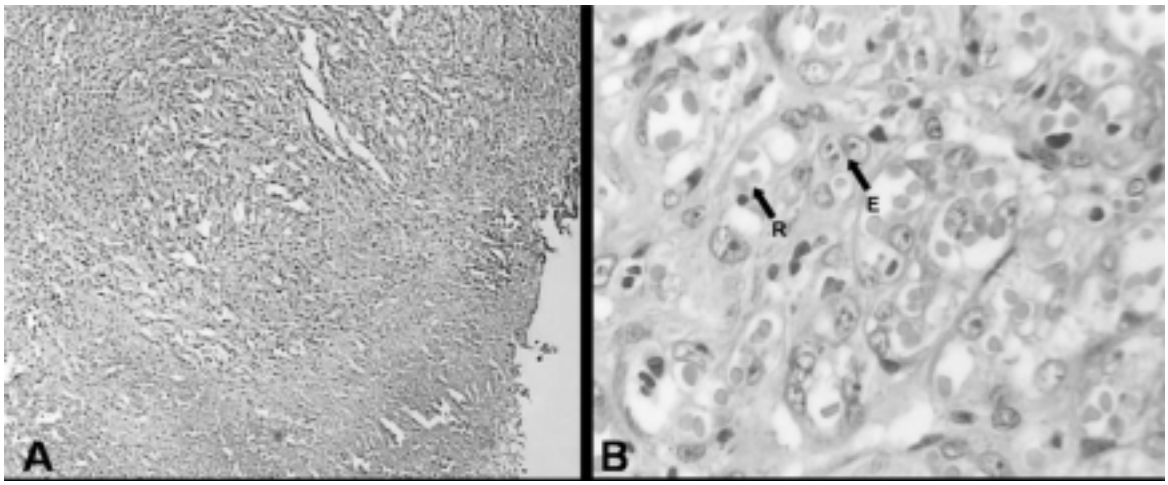

Fig. 3 Proliferation of epithelioid-like endothelial cells (A: ×40 magnification, B: ×100 magnification, H-E staining) (R: Red Blood Cells, E: Epithelioid-like endothelial cells).

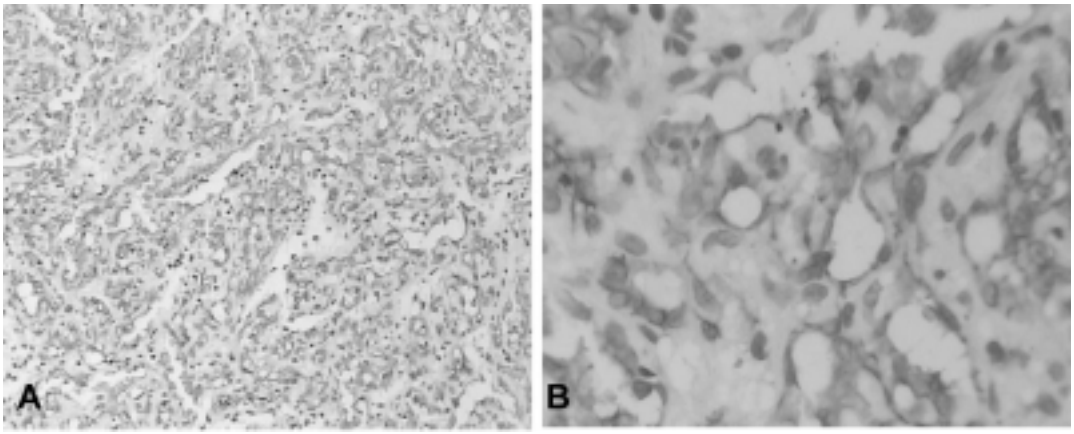

Fig. 4 Positivity of epithelioid-like endothelial cells with CD31 marker in immunohistochemical staining (A: ×100 magnification, B: ×400 magnification).

and sonographic examination revealed that the chest and spleen were intact and normal.

Six months after this excisional biopsy, there was evidence of recurrence in the buccal aspect of the gingiva between the left mandibular second premolar and first molar. A wide excisional biopsy was performed again. The patient's parents insisted that the first permanent molar and second premolar be extracted. The microscopic diagnosis was EHE.

Although we had requested that the patient undergo regular follow up, he has not since returned.

Discussion

It is generally believed that malignant hemangioendotheliomas are capable of metastasis and can ultimately lead to death. However, because of the lack of agreement relative to the terminology and criteria for true diagnosis of EHE and because the biologic behavior of these neoplasms differs depending on their anatomic positions and with regard to the age of occurrence, no consistent clinical or histologic criteria for predicting the biologic behavior of this vascular neoplasm in the oral region have yet been identified. However, some features considered suggestive of more aggressive clinical behavior include a mitotic rate more than one per 10 high-power fields, cellular atypia, focal necrosis, and increase in proportion of the spindle cells (3,7,8,20). Fortunately, the present case revealed the appearance of an intermediate lesion rather than a malignant lesion.

Microscopically, EHE is characterized by proliferation of rounded, eosinophilic epithelioid-like endothelial cells with frequent cytoplasmic vacuolization, a growth pattern potentially leading to a misdiagnosis of carcinoma, frequent angiocentricity, and myxohyaline stroma. Spindle cells may also be seen, distinct primitive-appearing vascular channels are formed, with erythrocytes occasionally seen in the lumina (1,7). The epithelioid-like endothelial cells exhibit many features of normal endothelium, including positivity for CD31, CD34, factor VIII-related antigen, and Ulex europaeus antigen (1,3,4,9,21).

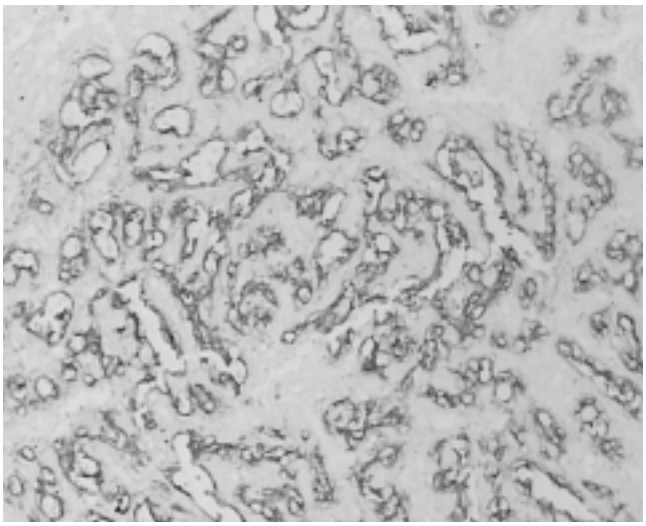

Fig. 5 Positivity of epithelioid-like endothelial cells with CD34 marker in immunohistochemical staining (×400 magnification).

The microscopic differential diagnosis includes carcinoma, melanoma, epithelioid angiosarcoma, and epithelioid sarcoma, whereas, clinically, oral EHE can mimic benign reactive inflammatory conditions such as pyogenic granuloma (2,8).

The biologic behavior of EHE can be categorized as between that of a hemangioma and a conventional angiosarcoma. It recurs in almost 40% of cases and approximately 15% metastasize to distant extracutaneous

locations (3,7,20). It has a mortality rate of 13% for soft tissue lesions (9).

EHE in the oral cavity is rare and only 26 cases have been reported to date (3,6-19). In many of these cases, the clinical impression was that of a benign lesion including pyogenic granuloma. In the present case, the clinical and primary microscopic diagnosis was pyogenic granuloma. Some of the previously reported cases have shown involvement of areas other than gingiva, such as tongue, palatal mucosa or bone, which suggests that these lesions may display a tendency for multi-centricity. Moreover, some cases exhibited local recurrence, whereas in the present case, multiple primary sites and its local recurrence were observed.

Two errors commonly occur while diagnosing this lesion: i) focus on the cord-like arrays of polygonal cells, may lead to misinterpretation of a metastatic carcinoma; and ii) lesions with extensive cytoplasmic vacuolization may erroneously be labeled as adipocytic in nature. Using electron microscopy or immunohistochemical assessment for epithelial and endothelial determinants would be beneficial (20).

Due to the noticeable potential of malignancy in EHE, wide local excision with regular clinical follow up would be an appropriate treatment protocol for cases in the oral cavity (3).

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