Taiwan J Oral Maxillofac Surg
27: 211-222, September 2016

Hemangioendothelioma of the Oral Cavity Mimics Cystic Lesion—A Case Report

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Abstract

Hemangioendothelioma is a vascular neoplasm with potential malignant behavior, meaning that the tumor may exhibit local recurrence as well as distant metastasis. It may occur at various anatomic sites, most commonly in the soft tissue, and organs such as liver and lung. The occurrence in the oral cavity is rare, and from literature review, the tumor mostly presented in the gingiva and with occasional adjacent alveolar bone absorption to different extent. Correct diagnosis can be challenging clinically as it may have various clinical manifestation and mimics other pathology from benign entity as pyogenic granuloma to malignancy as sarcoma. Immunohistochemical staining for specific marker is usually needed for definite diagnosis. Surgical removal with safety margin is the first treatment choice. Here, we report a case of hemangioendothelioma in the lower jaw with clinical and radiographic features highly resembling radicular cyst.

Key words: Hemangioendothelioma, Vascular neoplasm.

Introduction

The term hemangioendothelioma was introduced by Borrmann who was the first to propose the concept of vascular tumors with intermediate or low malignant potential[1]. Authentic hemangioendothelioma involved in skin and soft tissue includes papillary intralymphatic angioendothelioma, retiform hemnagioendothelioma, kaposiform hemangioendothelioma, epithelioid hemangioendothelioma, pseudomyogenic hemangioendothelioma[2], and composite hemangioendothelioma[3]. Epithelioid

hemangioendothelioma(HE)[2] was first described by Weiss and Enzinger[4] in 1982 as an angiocentric neoplasm characterized by proliferation of epithelioid or histiocytoid endothelial cell, showing eosinophilic vacuolated cytoplasm and occasionally, fusiform cells. The tumor is primarily found in extremities[4]. Other reported common sites for occurrence of EH include the lung, liver, skin, and bone. EH occurred at in head and neck region is uncommon, even rare in the oral cavity. Up to now, only 29 cases of EH has been reported in the oral cavity. Here, we report a case of hemangioendothelioma with its radiographic feature resembling a cystic lesion at anterior mandible.

Case report

A 19-year-old female without relevant medical history complained painless swelling at left mandibular molar region for years. Recently, toothache developed at left lower premolar region. Clinically, bulging out bony contour was noted at left lower buccal shelf, but without tenderness while palpating. The mucosal surface was smooth and intact at the initial examination without obvious lesion. The panoramic radiograph reveals missing 1st molar on left mandible without bone destruction (fig.1). According to her statement, she then received root canal therapy at dental clinic due to toothache and gingival swelling at lower anterior region. She was later on referred to Endodontic division of KMUH by the local dentist. At that time, clinical exam showed gumboil at lower anterior labial gingiva, no percussion pain at teeth 31~35 (left lower incisors to premolar), and pulp vitality test revealed 32(-), 33(+), 34(+), periapical film (fig.2) shows an ill-defined radiolucent image over apical region of lower left incisor to canine, also, tooth 31 & 35 (left lower central incisor & left lower second premolar) had been initiated endodontic therapy at local clinic.

About one and a half months later, when she came back to the OMFS division for follow-up, an exophytic lobulated mass was grown out from the labial gingiva of left lower anterior teeth. The lesion was about 1.5~2 cm in dimension, and rubbery to firm in consistency (fig.3). And the follow-up radiograph showed a well-defined larger cystic-like radiolucent lesion at anterior mandible. Our pre-operative tentative clinical impression was cystic lesion with inflammatory hyperplasia or pyogenic granuloma (fig.4). Under general anesthesia, surgical excision was done with 1 cm safety margin. During the surgical procedure of soft tissue mass removal, moth-eaten like bony destruction was noted at the peripheral junction between the lesion and intact bone (fig.5). Therefore extraction of those involved teeth was carried out. Due to the suspicious malignant change, some of the tumor mass was sent for frozen section histologic exam. It was reported as a possible sarcoma-like lesion tentatively. However, due to the uncertainty of the nature of the mass, we decided to remove the exophytic mass with extensive bone trimming. We then packed the wound with iodoform gauze for the wound healing. Under pathologic microscopic examination, the lesion manifested with ulcerative and fibrinopurulent membrane, inflammatory cell infiltrated in the stroma, and prominent capillary and lymphatic vessels surrounded by histiocyte and endothelial cells. Mitotic figure was rarely found. Specific Immunohistochemical stain showed that the tumor cell were positive for CD31 and D2-40 and negative for NFP, S-100, CK and CD68. The final diagnosis was

hemangioendothelioma based on histopathological and immunochemical findings that the tumor mass was prominently filled with vessel tissue and the tumor cells were majorly endothelial cells with positive staining for CD31 and D2-40. (fig.6~11)

Postoperative follow-up shows mucosal healing with shallow vestibule due to loss of supporting bony structure by the surgical removal. (fig.12)

Discussion

Weiss and Enzinger was the first to report 41 cases of EH in 1982 in Armed Forces Institute of Pathology. They described it as a neoplasm occurred in adulthood, with clinical manifestation of a mass with nonspecific symptoms and signs locating either in superficial or deep soft tissue, primarily in extremities[4]. Ellis and Kratochvil in 1986 first introduced 2 cases of EH in the oral cavity. According to Chi et al. in 2005, 12 cases of intraoral EH has been collected and analyzed. It showed the average age of EH was 28 years with a range of 4 to 76 years. There was a female predilection with a female-to-male ratio of 2.5 : 1. The most commonly affected intraoral location was the gingiva or alveolar mucosa[5]. Most intraoral EH was asymptomatic. The clinical differential diagnosis should include benign lesions such as pyogenic granuloma, fibroma, peripheral giant cell granuloma, or inflammatory fibrous hyperplasia. Though most cases are clinically thought as benign lesions, the tumor is however associated with intermediate or low malignant biological behavior. Some cases has been reported displaying multiple recurrence.[2, 6] Gordón-Núñez et al. in 2010 analyzed radiographic and clinical feature of 27 cases, showing that 25% of the cases had tooth mobility and bone resorption to some extent.[7] Some reports suggested that intraosseous EH may display a tendency for multicentricity. Multifocal tumors may arise within a single bone or multiple bones with predilection for bones of the extremities. On the contrary, the reported intraosseous EH in the jaw bones from previous report, 3 in the mandible and 1 in the maxilla, did not show multicentricity[8]. In our reported case, the initial presentation of toothache gumboil appearance with periapical radiolucent lesion on apical region of lower anterior teeth led to the initial clinical impression as a radicular cyst with mucosal inflammatory granulomatous mucosal change. The final diagnosis of hemangioendothelioma mainly depends on the microscopic features of vascular structure that needed to be differentiated from hemangiomas or even well-differentiated angiosarcomas. However, well-formed vascular channels lined by endothelial cells were usually absent. Instead, the vascular structures were small and recapitulated the appearance of vascular channels during early angiogenesis[4]. Up to now, the clinical behavior of EH in the oral region is still elusive for the rarity of the lesion. However, some features such as increasing number of mitotic figure, cellular atypia, and excessive spindle cellular shape are considered as high grade with worse prognosis and prone to develop regional recurrence and/or distant metastasis.[1, 9] In our reported case, the endothelial cell showed little atypia was found under microscopic exam.

As the morphological features were easily to be confused with hemangioma or angiosarcoma,. Therefore, immunohistochemical analysis is important for diagnosis. According to the literature, the majority of intraoral EH were immunoreactive for CD34, CD31, factor

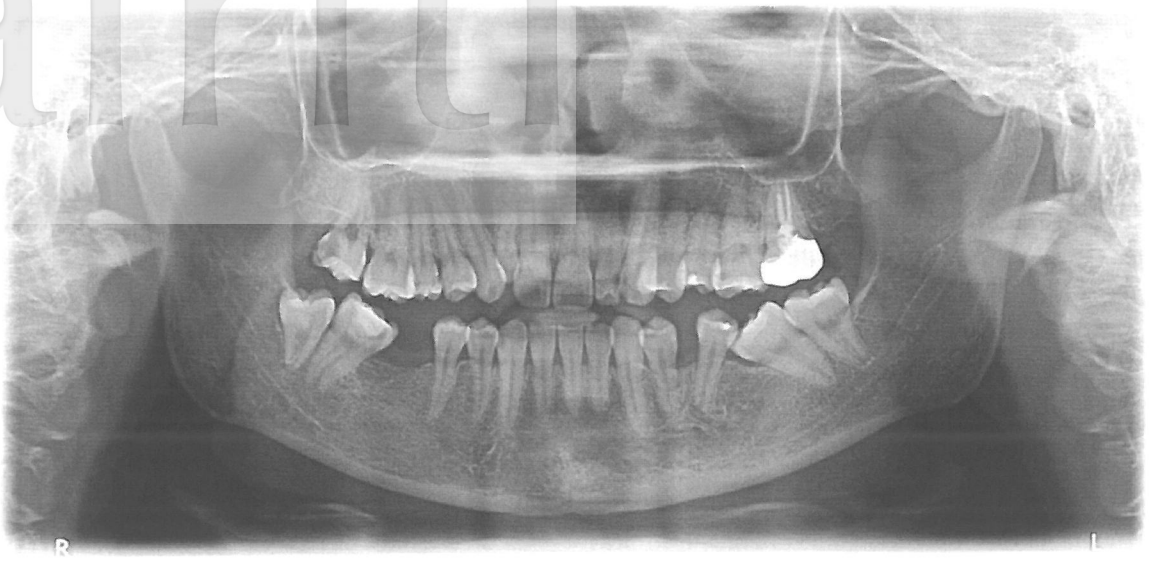

Fig. 1. Initial panoramic radiograph showed missing of left lower 1st molar, no bony destruction or other findings.

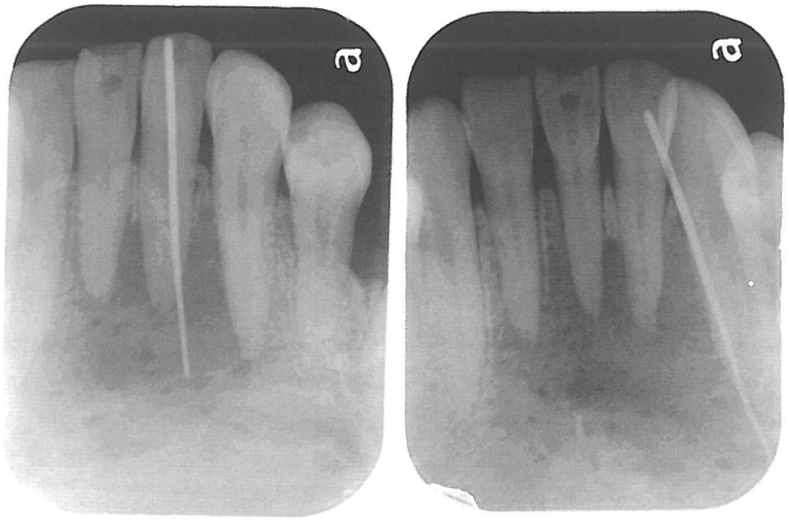

Fig. 2. Periapical film showed mixed diffuse radiopaque-radiolucent lesion at apical region of lower anterior teeth.

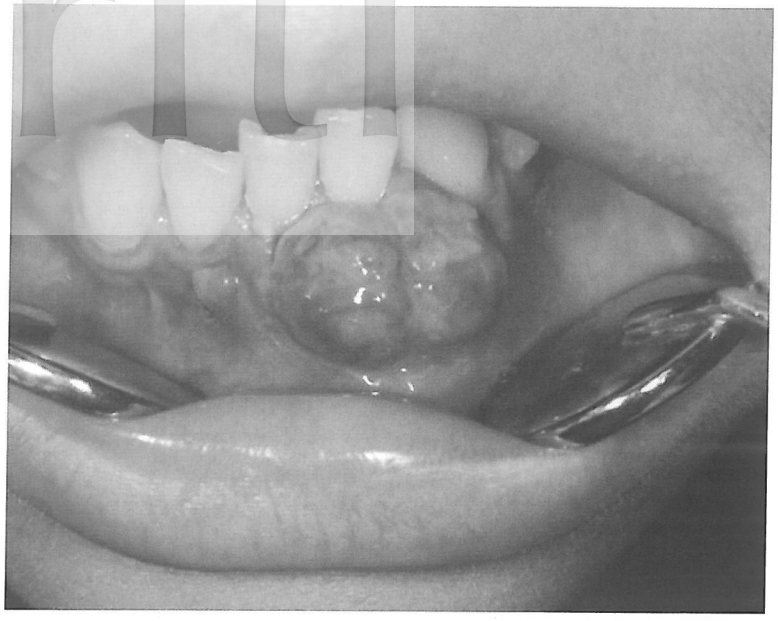

Fig. 3. Exophytic mass lesions at labial gingiva of lower left incisor, with another small gumboil-like lesion aside.

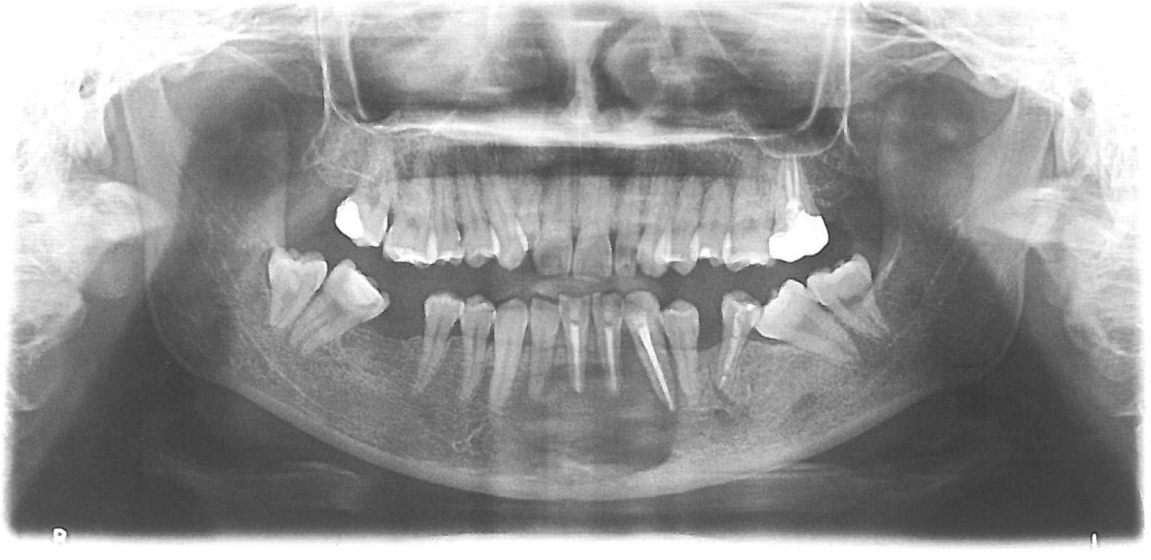

Fig. 4. Well-defined, oval shape radiolucent lesion at the apical region of lower anterior teeth.

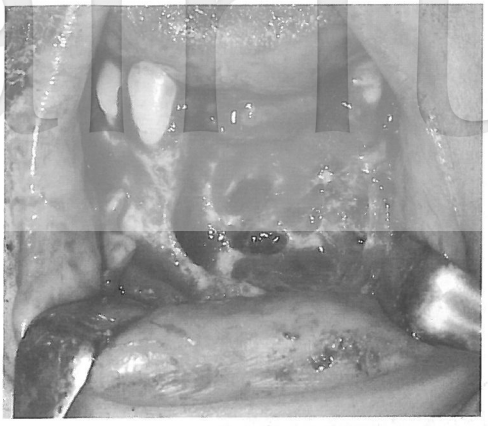

Fig. 5. Before bone trimming, bony destruction with multiple concavity was noted on the bone surface.

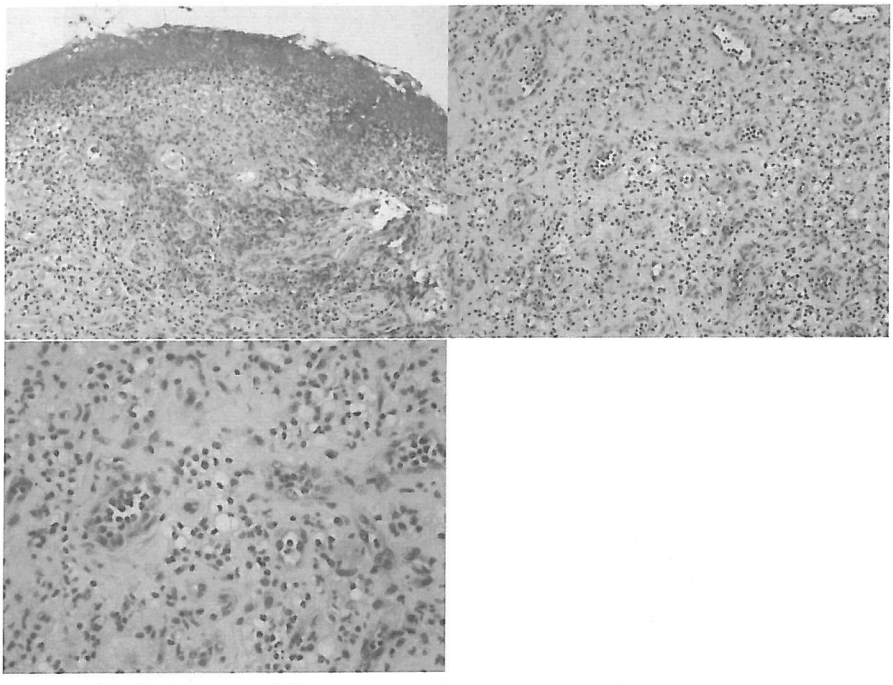

Fig. 6. Upper left: H-E stain 100X

Ulcerated surface was covered by fibrinopurulent membrane with acute and chronic inflammatory cells infiltrating in the underlying stroma. Prominent proliferation of capillary vessels was noted.

Upper right H-E 100X Stroma.

Prominent proliferation of capillary vessels and lymphatic channels was noted with greatly increased vascularity. Plenty of cells had large nuclei and eosinophilic cytoplasm scattering in the stroma with infiltration of acute and chronic inflammatory cells also present.

Lower left H-E 200X Stroma.

Various inflammatory cells including eosinophils, neutrophils, macrophages, histiocytes could been found inside the lumen of capillary vessels and lymphatic channels and in the stroma.

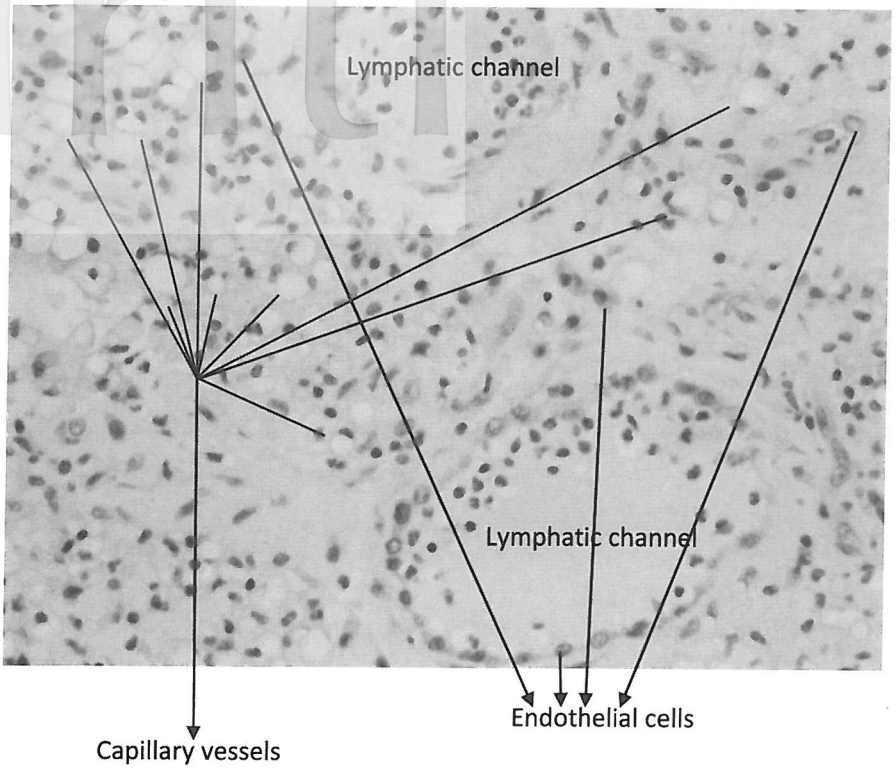

Fig. 7. H-E 200x

Lots of vascular lumen in varied size were surrounded by plump endothelial cells could be found.

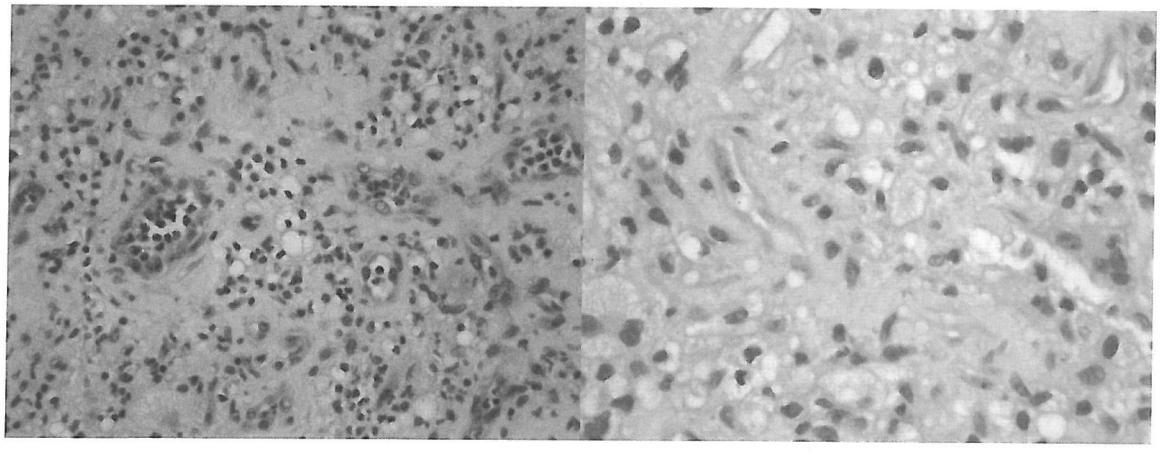

Fig. 8. H-E

Left,200X: Lumens in varied size were surrounded by plump endothelial cells.

Right, 400X: Proliferation of plump immature endothelial cells with little atypia was noted.

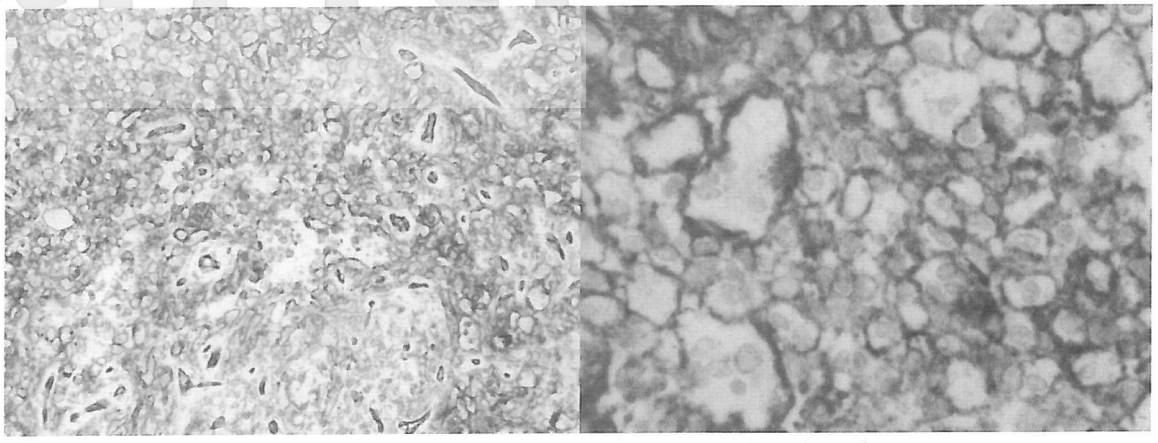

Fig. 9. Immunohistochemical stain CD31
Left, 200X & Right, 400X : diffuse positive for tumor cells.

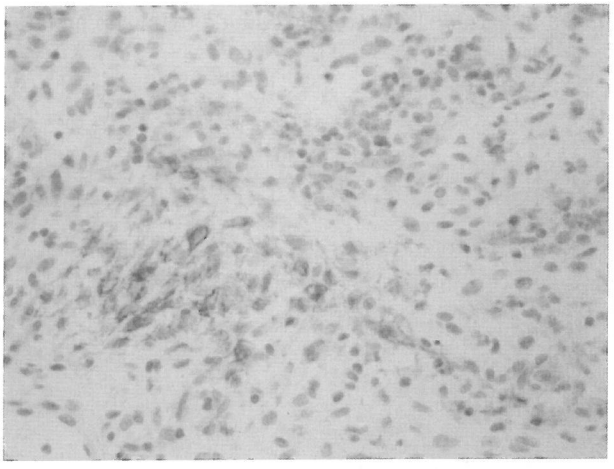

Fig. 10. Immunohistochemical stain CD31
200X Immunohistochemical stain D2-40 : focal positive for tumor cells.

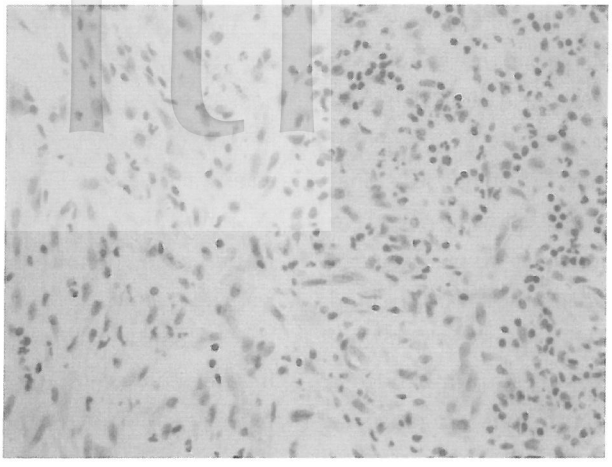

Fig. 11. 200X Immunohistochemical stain S-100 : negative for tumor cells.

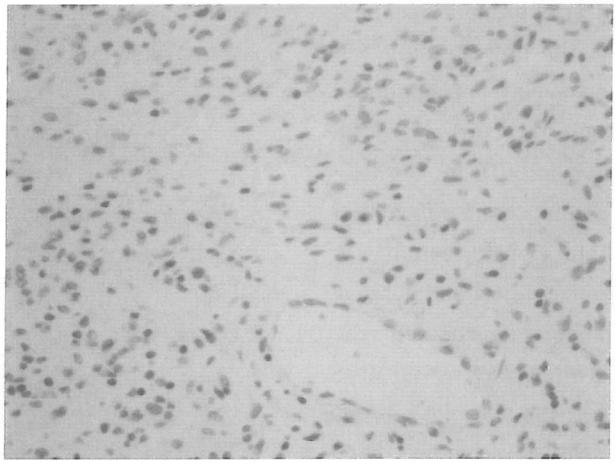

Fig. 12. 200X Immunohistochemical stain CK (epithelial cells) : negative for tumor cells.

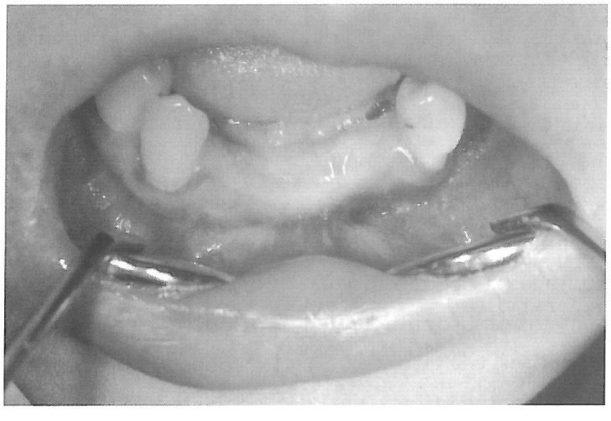

Fig. 13. At the 2months follow-up after surgery, the surgical area showed mucosal healing with scaring and shallow vestibule.

VIII-R Ag and vimentin. These markers are used to characterize cells from the epithelioid endothelial origin[7]. In our case, initial frozen section report during the surgery suggested the possibility of sarcoma. However, the final immunohistochekmical study showing negative for CK and showed little cellular atypia excluded the possibility. CD 31 positive confirmed the endothelial cell origin, though these cell are not typically in spindle or epithelioid morphology. The final pathologic diagnosis is hemangioendothelioma. Considering the reported intermediate malignant potential of the EH, wide local excision was the first therapeutic choice in most cases reported in the literature[5, 8, 9, 10]. It was observed that conservative procedures such as curettage may result in recurrence of the lesions. From data reported in 2010 by Gordón-Núñez et al., 7 cases among 27 intraoral EH developed recurrence within 2 years, and 1 case recurred at 4.8 year. In our case report, surgical excision with bone trimming was done for the patient. No local recurrence was noted at 8 months follow-up. However, the feasibility of this treatment modality in terms of prognosis need more time to follow-up.

Conclusion

Hemangioendothelioma is uncommon in head and neck region, and even rare in the oral cavity. Most cases are clinically diagnosed as benign lesion. Radiographic exam may show bone destruction to some extent. Definite diagnosis often needs immunohistochemical stain for endothelial cell such as CD34, CD31, Factor VIII-RAg. The treatment methods are mainly surgical excision with safe margin for its clinical biologic behavior showing intermediate to low potential of malignancy. Local recurrence or distant metastasis may occur in some cases. Here, we reported a case of intraoral hemangioendothelioma with radiographic feature mimicking a cystic lesion at anterior lower jaw for its rarity and difficulty in differential diagnosis. In our case, definite histopathologic diagnosis was not confirmed preoperatively owing to lacking biopsy. This reminds us that one should be meticulous about any new arising clinical findings in our daily practice. As in our case, the lobulated mass lesion was somehow different from general cystic lesion, and suspicion should be aroused to make more prudent assessment before final surgical decision was made.

Acknowledgement

We are so grateful to Dr. Ching-Yi Chen & Dr. Yuk-Kwan Chen of oral pathology division in KMUH.

References

1. Marrogi AJ, Boyd D, el-Mofty S,Waldron C. Epithelioid hemangioendothelioma of the oral cavity: report of two cases and review of literature. J Oral Maxillofac Surg 1991; 49: 633-8.
2. Mohtasham N, Kharrazi AA, Jamshidi S, Jafarzadeh H. Epithelioid hemangioendothelioma of the oral cavity: a case report. J Oral Sci 2008; 50: 219-23.
3. Seminars in Diagnostic Pathology, Volume 30, Issue 1, February 2013, Pages 29-44 Superficial Mesenchymal Tumors Involving the Skin.
4. Weiss SW,Enzinger FM. Epithelioid hemangioendothelioma: a vascular tumor

often mistaken for a carcinoma. Cancer 1982; 50: 970-81.
5. Ellis GL, Kratochvil FJ, 3rd. Epithelioid hemangioendothelioma of the head and neck: a clinicopathologic report of twelve cases. Oral Surg Oral Med Oral Pathol 1986; 61: 61-8.
6. Machalka M, Prochazkova L, Husek K. Epithelioid hemangioendothelioma of the mandible. Mund Kiefer Gesichtschir 2003; 7: 180-3.
7. Gordon-Nunez MA, Silva e M, Lopes MF, et al. Intraoral epithelioid hemangioendothelioma: a case report and review of the literature. Med Oral Patol Oral Cir Bucal 2010; 15: e340-6.
8. Chi AC, Weathers DR, Folpe AL, et al. Epithelioid hemangioendothelioma of the oral cavity: report of two cases and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005; 100: 717-24.
9. Orsini G, Fioroni M, Rubini C, Piattelli A. Epithelioid hemangioendothelioma of the oral cavity: report of case. J Oral Maxillofac Surg 2001; 59: 334-7.
10. Molina Palma MI, Cervantes Gongora JA, Garcia de la Torre E, Conde Perez de la Blanca I, Ramirez Tortosa CL. Primary intraoral epithelioid hemangioendothelioma: Case report and review of the literature. Acta Otorrinolaringol Esp 2002; 53: 215-8.

與囊腫病變相似之口內血管內皮瘤一病例報告

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摘 要

血管內皮瘤爲一種血管來源具有潛在惡性表徵的腫瘤，其可能會表現出局部再發或者遠端轉移的現象。此腫瘤可能於不同部位出現，好發於軟組織、肝臟及肺臟。原發於口腔的血管內皮瘤是非常少見的，從文獻回顧發現，口內常好發位置爲牙齦，且常伴隨鄰近齒槽骨不同程度的吸收。臨床上正確診斷出血管內皮瘤是具挑戰性的，因爲其於臨床表徵具有多變性，亦即其可能與良性病灶如發炎性肉芽腫或惡性病灶如惡性肉瘤具有相似的臨床表徵。一般需要配合免疫組織學的分析才能確診血管內皮瘤。基於此腫瘤於生物學上的變化，治療選擇主要爲含安全邊緣的手術切除。我們提出一例下顎血管內皮瘤於臨床與影像學上的特徵近似於根尖囊腫。

關鍵詞：血管內皮瘤，血管腫瘤。

Received: May 04, 2016

Accepted: July 29, 2016

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