Case Report

Report of a Rare Case of Epitheliod Hemangioendothelioma in Tongue

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ABSTRACT

Epitheloid hemangioendothelioma (EHE) is a rare vascular neoplasm of intermediate malignant potential. EHE commonly involves lungs, liver soft tissue, and bone. EHE is extremely rare in tongue and up to our best knowledge only nine cases of EHE of tongue reported in the literature. Clinicallyو EHE usually presents as an asymptomatic mass. Microscopically, EHE exhibits proliferation of epitheloid cells and spindle shaped endothelial cells. Epitheloid cells show cytoplasmic vacuoles with few cells containing RBCs. A 34-year-old male presented to our institution with the chief complain of swelling on the base of the tongue from eight months. Surgical excision was done. An extensive work up of immunohistochemistry was done using different markers including CD 31, CD 34, Ki 67, Factor VIII, and BCL2. Correlation of histopathology and immunohistochemistry confirmed the diagnosis of EHE. The follow up period of 2 years was uneventful.

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Introduction

Epitheloid hemangioendothelioma (EHE), a rare subtype of hemangioendothelioma was first reported in 1982 by Weiss and Enzinger. [1] EHE is a vascular tumor considered and intermediate neoplasm between hemangioma (benign) and angiosarcoma (malignant). [2] Occurrence of EHE is exceedingly rare in oral cavity; an exhaustive literature review could reveal only 31 cases. Tongue is considered a rare site in oral cavity with only nine reported cases so far. [3] EHE tends to show local recurrence. [4] EHE is characterized microscopically by neoplastic proliferation of epitheloid and histiocytoid endothelial cells. [2] Microscopical differential diagnoses of EHE include carcinoma, hemangiopericytoma, angiosarcoma angiofibroma, and angioleiomyoma. [4-6] An immunohistochemical work up using different panels of tumor markers is required to arrive at a final diagnosis. [2] The clinical course of EHE is usually benign with a painless mass. Intra- orally, it imitates different benign tumors including pyogenic granuloma, lipoma, fibroma, peripheral giant cell granuloma, and so on. [7] We report a case of EHE presented as a painless swelling on the base of the tongue which was provisionally diagnosed as lipoma. Histopathological and immunohistochemical features confirmed the diagnosis of EHE.

Case Report

A 34-year-old Indian male presented to the department of Oral Medicine and Radiology NIMS Dental College Jaipur (India) with a chief complain of painless swelling on the base of the tongue since 8 months. The swelling was initially small and gradually reached the current size. The patient felt discomfort in normal movement of the tongue. Past medical history and family history of the patient were non- contributory to the presenting symptom. Intra oral examination revealed a dome shaped swelling of the dorsum of the tongue extending to the right lateral border of the tongue measuring about 3×2cm in diameter. The color of the mucosa was similar to the adjacent mucosa with a slightly yellowish tinge, without any sign of discharge and ulceration. (Figure 1)

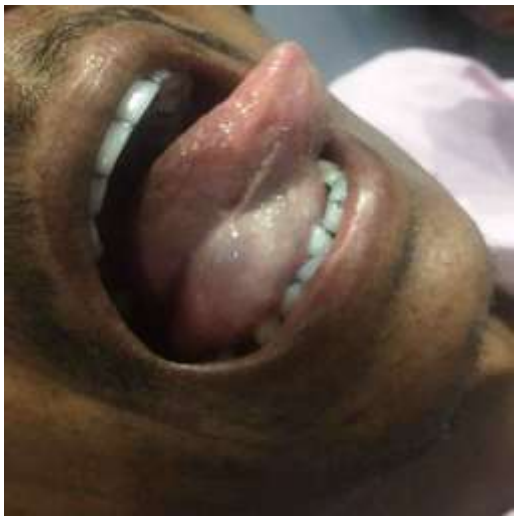

Figure 1: Clinical picture of the swelling of the dorsum surface of the tongue

On palpation, the swelling was found to be soft and fluctuant with absence of induration. The lesion was nodular and its consistency was found to be elastic. No other swelling and other pathology was found on careful history taking. A provisional diagnosis of lipoma was given due to the yellowish tinge of the swelling, granular cell tumor was considered as a differential diagnosis and the patient was referred to the department of oral surgery for the biopsy. A surgical excision of the lesion was planned and the whole lesion was removed under local anesthesia. The lesion was excised after dilatation and dissection of the surrounding tissue. After irrigation, suturing of the wound was performed using 4.0 vicryl suture material. A follow up period of 2 years was uneventful. The excised tissue was sent to the department of Oral and Maxillofacial Pathology for microscopical evaluation.

Histopathological examination of hematoxylin and eosin stained soft tissue sections revealed an unencapsulated tissue mass showed diffuse proliferation of neoplastic epitheloid cells with hyperchromatic nuclei, (Figure 2a) few epitheloid cells showed intracytoplasmic vacuoles, (Figure 2b) some vacuoles contained RBCs inside, numerous vascular spaces were seen having erythrocytes inside and lined by epitheloid cells. (Figure 2c) Epitheloid tumor cells were seen invading the muscles at places. The connective tissue stroma was fibrocellular. Immunohistochemical staining for different markers was done objectively and the intensity of

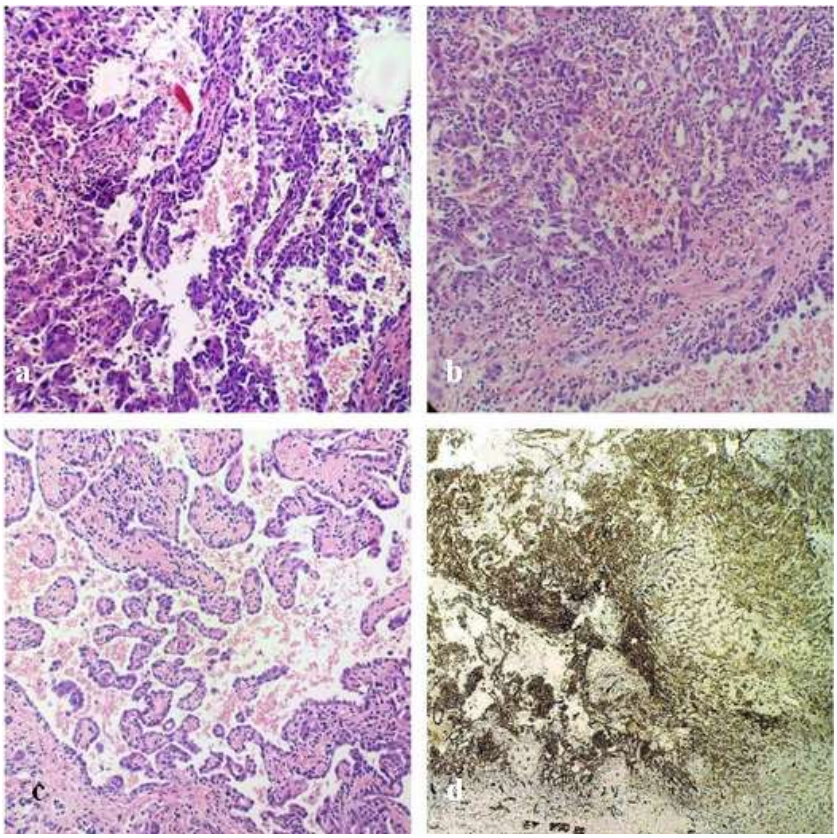

Figure 2a: An uncapsulated lesion with numerous epitheloid cells and vascular areas (Hematoxylin and Eosin staining 20 X), **b:** nests of neoplastic epitheloid cells with intracytoplasmic vacuolation (Hematoxylin and Eosin staining 20 X), **c:** Intracytoplasmic inclusion of epitheloid endothelial cells containing erythrocytes (Hematoxylin and Eosin staining 20 X), **d:** Positive immunohistochemical expression for CD 31 (40 X)

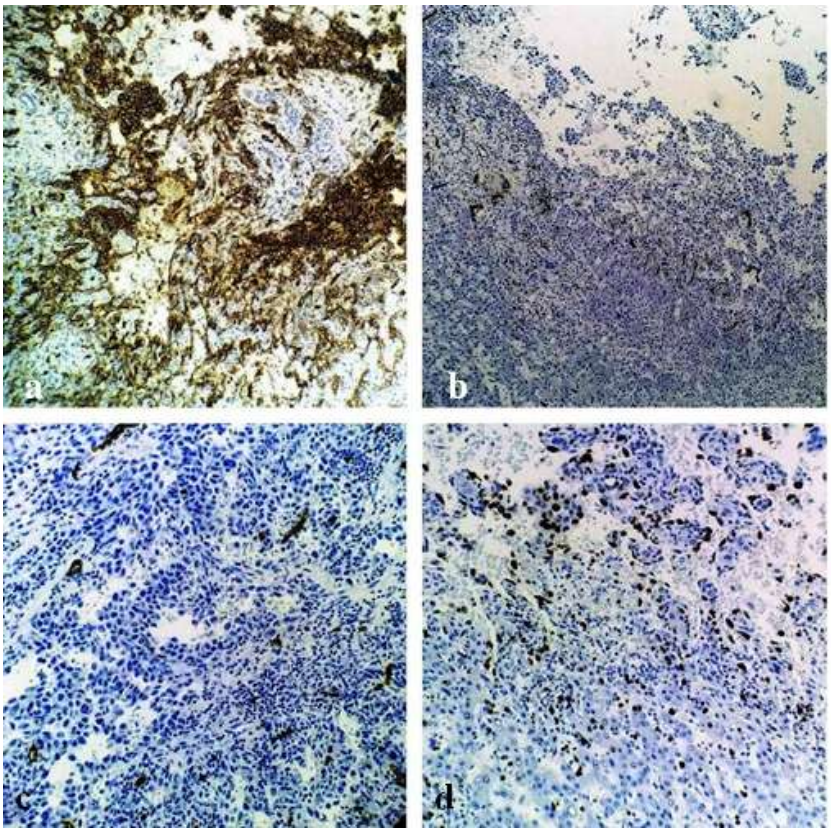

Figure 3a: Diffuse positive expression of the tumor cells for factor VIII (40 X), **b:** Weak expression of tumor cells for CD 34 (20 X), **c:** Negative expression of the tumor cells for smooth muscle actin (40 X), **d:** Weak expression of the tumor cells for Ki 67 (20 X)

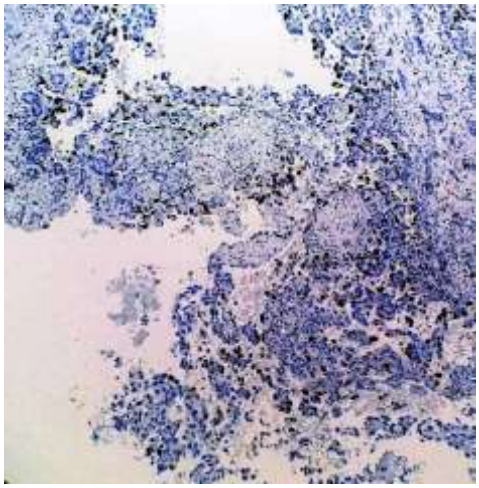

Figure 4: Weak expression of the tumor cells for BCL2 (20 X)

staining was scored by a scoring system described by Shen *et al.* [8] Immunohistochemical examination revealed a diffuse positive expression for endothelial markers including CD 31(Figure 2d) and factor VIII (Figure 3a) weak expression of CD 34 (Figure 3b) Smooth muscle actin (SMA) (Figure 3c) was used to rule out the possibility of angioleiomyoma, which was found to be negative. Ki 67 for proliferation index (Figure 3d) and Bcl2 for apoptosis (Figure 4) was done both of them were found to be negative, revealing that the lesion was not aggressive. With the correlation of histopathological and immunohistochemical features a final diagnosis of EH was rendered. With the diagnosis of EHE, ultrasound of abdomen and computed tomography of the chest was performed in order to rule out any primary lesion. The examinations showed no abnormality.

Discussion

Hemangioendothelioma is a vascular tumor intermediate malignant potential. [1] On histopathological basis, it is classified into three different variants including epitheloid hemangioendothelioma (EHE), kaposiform hemangioendothelioma polymorphous, and spindle cell type. The present case showed histopathological features consistent to EHE. [2-3, 9] Tumor of intermediate behavior are tend to show local invasion and metastasis but lesser than with the malignant ones. [1] The present case also revealed an invasion of tumor cells into the muscular tissue. EHE occurs rarely in oral cavity only thirty one cases have been reported in the literature so far. [2] Intra-orally, gingiva is the common site followed

Table 1: Microscopical differential diagnoses of EHE

S. NO	Differential Diagnosis	Differentiating features
1	Carcinoma	Histopathologically, carcinoma usually does not show a highly vascular tissue unlike EHE. Immunohistochemically endothelial markers CD 31, CD 34, and factor VII can be used to rule out the possibility of epithelial origin. Vimentin shows positive expression in EHE and negative expression in carcinoma.
2	Epitheloid angiosarcoma	Epitheloid angiosarcomas show cellular atypia and high mitotic index. Immunohistochemically markers like Ki67, can be used for determine the proliferation rate.
3	Angioleiomyoma	Hemangioendothelioma (HE) may mimic angioleiomyoma especially spindle cell type, Smooth muscle actin shows a negative expression for HE while a positive expression for angioleiomyoma.
4	Angiofibroma	Te fibrous component of the stroma in EHE is relatively less pronounced in EHE. Angiofibromas usually show negative expression for endothelial markers.
5	Hemangiopericytoma	Hemangiopericytomas show numerous large vascular channels with stag horn pattern.

by tongue and palate. [10] Only nine cases of EHE occurring on the tongue have been reported in the literature. [2-3] The present case is being only the 10th presentation of EHE on the tongue. EHE generally affects the middle-aged patient although few cases have been reported in children also. [1-4] The mean age of occurrence is 31 years, and in present case the age of the patient was 34 years. A review of oral EHE by Gordón‐Núnez *et al.* [4] revealed that most of the cases of oral EHE clinically presented as reddish, erosive, or purplish soft tissue growth. However, the present case was contrary to their finding and the color of the lesion in the present case was found to be similar to the adjacent mucosa, which clinically imitated a lipoma. Most of the cases of oral EHE initiated as a painless mass although ulcerated lesions have been reported too. [12] The etiology of EHE is not very clear; recently Tanas RM *et al.* [13] proposed that reciprocal translocation of chromosome 1 and 3 is responsible for the fusion of two different genes namely WWTR1 and CAMTA1. This fusion was found to be positive in 90% cases of hemangioendothelioma. [13-14] Microscopically, oral EHE is characterized by proliferation of vascular epitheloid type endothelial cell with inta-cytoplasmic vacuoles; few of the vacuoles may show erythrocytes inside, invasion of the epitheloid cells in underlying muscle tissue may or may not be present. [4] A population of spindle shaped cells may also be seen. The connective tissue stroma in most of the cases is found to be fibro- vascular with numerous vascular channels. [3] Some histopathological features are considered more aggressive including increased population of spindle cells, focal necrosis, increased mitotic figures, cellular atypia, and metaplastic bone formation. [2, 4] The present case showed classical features of EHE and was devoid of aggressive features although invasion of epitheloid endothelial cells was seen in the muscle tissue. Microscopical differential diagnoses of EHE include carcinoma, epitheloid angiosarcoma, angioleiomyoma, angiofibroma, and hemangiopericytoma. (Table 1) [4-7]

Immunohistochemically, endothelial cells of EHE show positive expression for endothelial markers include CD 34, CD 31, factor VIII, and Ulex europaeus antigen. [2, 8] However, in present case the tumor cells showed positive expression for CD 31 and Factor VIII but a weak expression for CD 34. The diagnosis of EHE is based on the correlation of histopathological and immunohistochemical findings. Recently fluorescence in situ hybridization (FISH) based bioassay for WTRA1 and CAMTA1 has been developed that offers the pathologists to identify the fusion of the two genes, which is specific for EHE. Treatment of choice for oral EHE is a wide surgical excision with a proper follow up considering the recurrence and malignant potential of the lesion. [13] The Chimeric WWTR1/ CAMTA1 transcription factor offers a therapeutic target for EHE and offers some insight on the mechanism of both genes. [13-14] In present case the biological behavior of the lesion was assessed immunohistochemically, using proliferation (Ki67) and anti-apoptotic marker. (Bcl2) An extensive review of literature revealed that nine lesions showed recurrence out of 30 published cases. The present case showed no recurrence after 2 years of follow up period.

Conclusion

Oral EHE is a rare vascular lesion and a great imitator clinically, that usually mimics an inflammatory lesion and pyogenic granuloma. Microscopically, it imposes a significant diagnostic challenge to the oral pathologists

owing to its similarity with different vascular lesions and carcinoma. Immunohistochemistry is advisable for such lesions to arrive at the final diagnosis. Tumor markers Ki67 and BCL2 are useful to determine the biological behavior of the tumor. Due to the remarkable cellularity and high mitotic index, EHE can be confused with carcinoma. A proper differentiation is mandatory to avoid the aggressive treatment, which is needed in carcinoma.

The differentiation between EHE and carcinoma can be achieved by vascular markers i.e. CD 34, CD 31, and Factor VIII.

Conflict of Interest

The authors declare that they have no conflict of interest.

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