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Case Report

Hemangioendothelioma of the lower lip masquerading as traumatic lesion: a rare case report and review of literature

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ABSTRACT

Hemangioendothelioma (HE) is an uncommon vascular tumor originating from endothelial cells lining blood vessels that can manifest in various anatomical locations, including the oral cavity. The spectrum varies from Intermediate between entirely benign hemangiomas to highly malignant angiosarcomas. Generally epithelioid HE (EHE), variants have a low degree of malignancy, with a tendency to local relapse but a less metastatic potential. Here we describe a rare case of epitheloid hemangiendothelioma, asymptomatic soft pinkish growth in the lower lip of a 65 years old Female, an excisional biopsy was performed and confirmed by histopathological diagnosis. This report adds valuable insight to the uncertainty in selecting the most suitable treatment with dilemma in management. A wide excision is the treatment of choice with regular follow-up is advised as potential for high recurrence.

Keywords: HE, Lower lip, Epitheloid, Treatment

INTRODUCTION

Hemangioendothelioma (HE) surrounds multiple vascular proliferations including both benign and malignant neoplasms. In 1908 Mallory, initiated the terminology 'HE' encompassing all proliferations that originate from endothelial cells.[1] In 1961, Stout and Kauffman described it as a group of vascular lesions having low metastatic potential and high tendency for local persistence.[2] In 1982, Weiss and Enzinger presented HE, restricted to vascular neoplasms showing a borderline biological behaviour, intermediate between benign hemangiomas and highly malignant angiosarcomas.[3,4] The clinical and histological attributes are intermediary between a hemangioma and angiosarcoma; therefore, the term EHE was advanced.[5] WHO proposed, EHE as an exception, low-grade malignant vascular tumour characterized by endothelial cells with an epithelioid shape, plausible metastases that reports of 1% all vascular tumors. The reports of the oral cavity to date are scarce. The etiopathogenesis is unknown but thought to be trauma that causes inflammatory response.[6] Oral demonstration typically is ulcerated soft tissue mass that resembles friable granulation tissue which initially is widely non-specific, resembling reactive lesions such as angioma, chronic periodontal disease, pyogenic granuloma, facial granuloma, peripheral giant cell granulomas, insect bites, Kaposi's sarcoma, salivary gland tumor, lymphoma, lipoma, and squamous cell carcinoma.[7] When presenting on the lower lip, it is generally characterized by an insidious onset and a slow evolution typically presenting as a painless/slightly tender mass causing lip asymmetry, discomfort while speaking/eating. It requires a unique diagnostic and therapeutic considerations due to anatomical features and cosmetic significance. Histologically, it is prominent by proliferation of round, eosinophil-infiltrated endothelial cells, cytoplasm vacuolation, frequent angiocentric inflammation, and

myxohyaline stroma. The gold standard diagnosis is based on histopathological and clinical characteristics of the lesion.[8] We present a case that manifested as a painless enlargement on lower lip and provisionally diagnosed as fibroma and confirmed by the histopathological findings.

CASE REPORT

A 65 year, old female patient presented with chief complaint of soft pinkish growth on the lower lip region since 30 days. After asking about history of present illness, the patient experienced irritation on her lower lip in right labial mucosa and observed a firm growth. General examination was within normal limits with no lymphadenopathy. On inspection extra-orally, face is symmetrical with no obvious facial swelling. On intraoral soft tissue examination, lips are competent, labial mucosa on right mandibular vestibule shows pathology that was solid, sessile pedunculated with raised edges, pinkish in colour, on bi-digital palpation the growth was soft to firm, non-fluctuant, immovable and attached to the underlying mucosa with intermittent pain radiating to the entire lower lip, tenderness and diffused slight swelling in the affected area with no discoloration or bleeding on provocation, measuring 0.5×1 cm with slight redness around the growth, patient was unable to chew food due to discomfort on biting.

Figure 1: Lesion on the lower lip.

No history of any episode of lip biting or trauma on the lower lip, habits or any drug allergy. On past medical history patient was hypertensive under prescribed medication from 2 years {Telmisartan 40 mg OD}. Provisional diagnosis was made of irritational fibroma. Routine blood investigations of CBC were under normal parameters, HIV and HBsAG were non-reactive. After taking consent excisional biopsy was performed and sent for pathological assessment.The histopathological analysis with serial sections of tissue stained with hematoxylin and eosins shows para keratinized stratified squamous epithelium of variable thickness overlying fibro cellular connective tissue, stroma shows presence of small-to-medium sized, thin-walled lobular vessels showing multicellular canalized vascular channels lined by plump epithelioid endothelial cells with intracytoplasmic vacuoles. The presence of proliferating epithelioid endothelial cells protruding into the vascular lumina shows a “tombstone” appearance, eosinophils can also be appreciated at various areas near the blood vessels, collagenous areas enclosing granulation tissue with budding blood vessels are seen, confirming the diagnosis of HE. Patient has been asymptomatic since then and is being followed-up on a regular basis for every 3 months. So far, no recurrence has been observed.

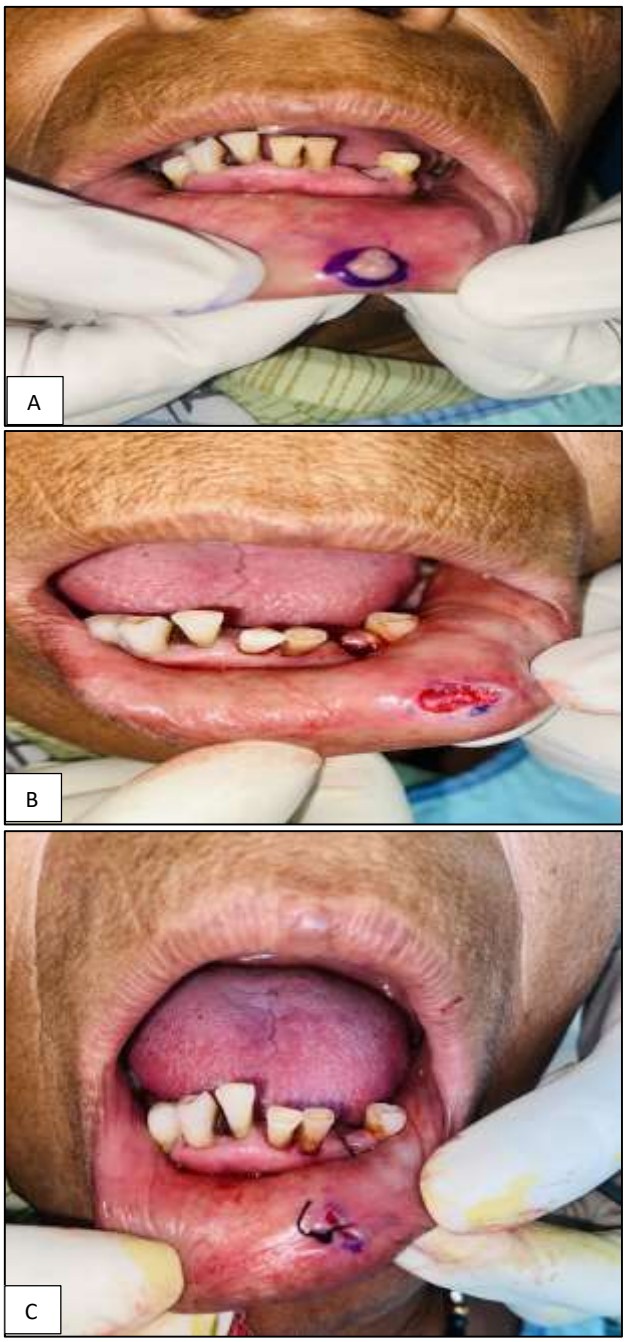

Figure 2 (A-C): Intra-operative-marking of the lesion, excision of the lesion and closure of the lesion.

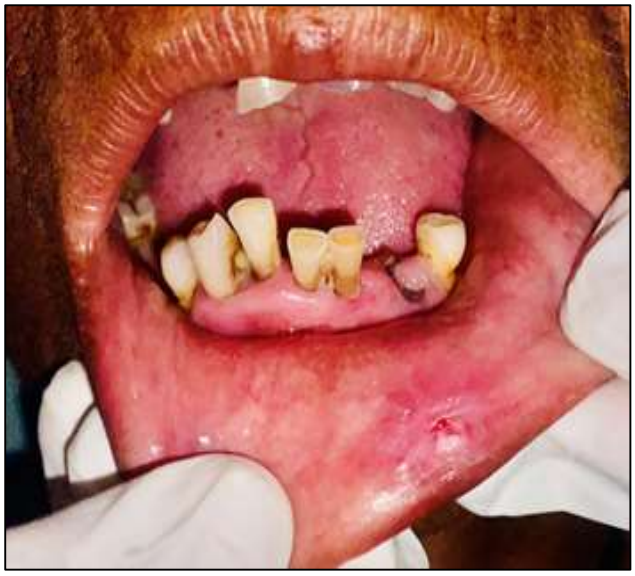

Figure 3: Follow up on day 7.

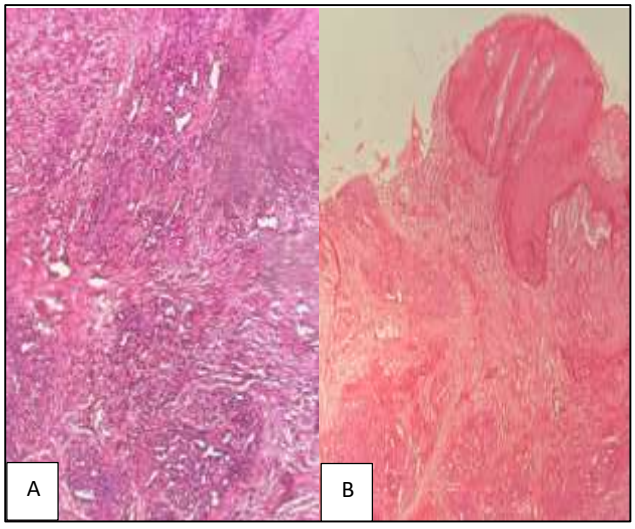

Figure 4 (A and B): Microscopic image shows parakeratinized stratified squamous epithelium, stroma shows the presence of thin-walled lobular vessels showing multicellular canalized vascular channels lined by plump epithelioid endothelial cells with intracytoplasmic vacuoles, proliferating epithelioid endothelial cells, eosinophils can also be appreciated at various areas with budding blood vessels are seen (H and E stain1).

DISCUSSION

HE is described as all the proliferations arising from endothelial cells surrounding a vascular lumen. HE involving the skin and soft tissue includes papillary, retiform, kaposiform, epithelioid, pseudomyogenic, and composite type.[8] EHE was originally described by Weiss and Enzinger in 1982 as a benign vascular tumor of soft tissue and bone with features intermediate between hemangioma and angiosarcoma.[3]

The exact etiology is debated, but attributing factors which can be reactive are linked to hypersensitivity reactions, inflammatory vascular manifestations, infections, or trauma.[9] It predominantly affects males, mean age of oral HE is 37.7 years and is more prevalent in Asians. In addition, sex hormones and high levels of serum estrogen may be involved in the growth of the lesion, Association with HIV has also been reported in the literature.[7] At the molecular overlook, angiogenic stimulators act upon promoters for proliferation of endothelial cell. A study suggests that for proliferation of monocyte chemoattractant protein-1 stimulates the angiogenic nature of endothelial cell.[9] The clinical appearance of oral lesion is nonspecific, manifesting as a macula, ulcer, crust, or nodule with a sessile or pedicled base, smooth or lobulated surface, appearing as a benign nodular lump, occasionally ulcerated, may be single or grouped, and its coloration varies from red to brown. The frequently reported symptom is pain caused by thrombosis or occlusion in the affected vessel. The most frequently affected sites are the lips, buccal mucosa, tongue, and palate Although in the present case it was found to be the rarity on the lip, appearing as a benign lump with raised borders, the mass was painless and nontender.[6-8] Histopathological examination is considered the gold standard to determine the definitive diagnosis of HE, it is well circumscribed lesion composed of small to medium sized thin blood vessel showing lobular arrangement with canalized vasculature. The hallmark feature is proliferation of blood vessels covered by prominent endothelial cell proliferation, protruding into the vascular lumina shows tombstone, hobnail cobblestone-like appearance, and chronic inflammatory infiltration of perivascular and interstitial infiltrate of lymphocytes, plasma cells and especially eosinophils around the vessel with intracytoplasmic vacuoles and exhibits nuclear atypia ovoid in appearance, solid growth patterns, necrotic foci, and increased mitotic activity invasion into underlying tissues.[8,10] Immunohistochemistry diagnosis often involves (IHC) markers such as CD31, CD34, SMA, VEGF, Factor VIII, FLI-1 and Vimentin, along with a low Ki67 index and ERG negativity to understand the aggressiveness of the lesion,In 2024 Dong Ren et al. identified unique fusion genes YAP1-TFE3 or WWTR1-CAMTA1 including ACTB::FOSB, POTEL::FOSB, EGFL7::FOSB which upregulate FOSB expression. Epithelioid endothelial cells of oral HE has been shown to be immunoreactive for CD34 and factor VIII. Additionally, HE cells express positivity for podoplanin, Lyve-1, and Prox-1, supporting a lymphatic lineage.[9-11] The main differential macroscopic diagnoses of oral EH are Kaposi's sarcoma, pyogenic granuloma, lymphoma, squamous cell carcinoma, and salivary gland tumor.[7] As it is a rare disease of the oral mucosa, it is frequently confused histologically with epithelioid angiosarcoma and bacillary angiomatosis.[8] HE diagnosis involves histopathological examination, IHC marker analysis, and sometimes molecular characterization to confirm the final diagnosis and rule out differential diagnoses. The primary

treatment method involves surgical excision. In cases where complete excision isn't possible, or in instances of recurrence, alternative treatments such as corticosteroids, laser, cryotherapy, pulsed light, intralesional chemotherapy, topical imiquimod, systemic propranolol, and interleukin-5 therapy may be employed, albeit rarely for oral HE. Malignant transformation rate is 13-20%, in cases with larger lesions with positive margins and those with higher mitotic figures per field present a higher risk of metastatic disease, regional nodal resection with adjuvant radiotherapy to a dose of 60 Gy is considered and systemic therapy include cytotoxic chemotherapy such as single-agent gemcitabine, (VEGFR) vascular endothelial growth factor receptor inhibitors such as bevacizumab, sorafenib and (mTOR) mammalian target of rapamycin inhibitors such as sirolimus, tyrosine kinase inhibitors like pazopanib, which has shown efficacy in controlling metastasis with minimal side effects.[7,9] Recurrence rates in oral HE are 10 to 15% after excision, varies based on factors like age, disease, duration, and lesion characteristics, higher for multiple lesions than unilesional, have been successfully treated with re-excision without leaving deep scars.[7] The article presents a case study of a 65-year-old female patient who developed HE without history of trauma, surgical excision has been effective as in our case with no signs of recurrence observed. Due to the rarity of HE, treatment protocols rely on case-by-case approaches and necessitates comprehensive follow-up strategies.

CONCLUSION

In conclusion, HE of the lower lip is a unique entity within the spectrum of vascular tumors. While uncommon, prompt diagnosis, tailored management, and cosmetic preservation are key considerations. The interdisciplinary collaboration integrating clinical, histopathological, and molecular insights, clinicians can optimize outcomes for patients with these rare and challenging lesions. We emphasize the importance of regular follow-ups due to EHE's recurrence potential and malignant nature. Considering its unpredictable behaviour and high propensity for distant metastasis, citing a case with a two-year follow-up showing no recurrence. Despite advancements in understanding these neoplasms, further research is needed to elucidate the molecular mechanisms driving these neoplasms and to establish standardized treatment protocols with multimodality approach should be considered to get the best treatment outcomes.

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