Intravascular papillary endothelial hyperplasia (IPEH) is a rare, benign lesion of vascular origin caused by an exuberant endothelial cell (EC) proliferation. It can occur in any blood vessel in the body but has a propensity for the skin and subcutaneous tissues of the head and neck region, fingers and trunk. It is rarely seen in the oral cavity but, awareness of this lesion is very crucial as it is one of the most misdiagnosed lesions of the maxillofacial region. Furthermore, misinterpretation as a malignancy, can subject the patient to unnecessary aggressive therapy (additional surgery or irradiation). Hence, a thorough knowledge of this lesion is important in order to arrive at a correct diagnosis.

Intravascular papillary endothelial hyperplasia has a nonspecific clinical presentation in the oral cavity and sites commonly involved are the lips, tongue, buccal mucosa, mandibular vestibule and gingiva. It is generally seen in the third and fourth decades of life and is more common in females. On a computed tomography scan, IPEH often presents as a homogeneous, nonhomogeneous and contrast enhancing or nonenhancing lesion. This is related to the varying amounts of parenchymal tissue and anastomotic, stagnant, or low-flow vascular channels. Hence, imaging plays little role in the diagnosis of this lesion. Cytology of IPEH is often characterized cohesive sheets of polygonal pleomorphic cells with vesicular nuclei and prominent multiple nucleoli in a hemorrhagic background and can be misdiagnosed as a malignant neoplasm like metastatic embryonal carcinoma, adenoid cystic carcinoma, squamous cell carcinoma etc. Histologically, it is characterized by an exuberant papillary EC proliferation toward the lumen of an enlarged blood vessel from the area of an organizing thrombus. The lesion was surgically excised under local anesthesia. The patient was followed for 1-year with no evidence of recurrence. This paper discusses the various aspects of IPEH of the oral cavity such as pathogenesis, clinical features, histopathology treatment, and prognosis.

Address for correspondence:
Dr. Sachin Sarode
E-mail: drsachinsarode@gmail.com

In the present paper, we discuss a case of extra-vascular type of oral intravascular papillary endothelial hyperplasia (Masson’s tumor) of lower lip: A case report and review of the literature
CASE REPORT

A 54-year-old female presented to the Department of Oral Pathology and Microbiology with a chief complaint of asymptomatic swelling on the left side of lower labial mucosa since 4 months [Figure 1]. The patient gave a history of trauma 4 months back at the site of the lesion. Physical examination revealed a nontender, nodular lesion of approximately 3 cm in diameter on the left side of the lower labial mucosa [Figure 1]. The lesion was slightly elevated with an oval form, soft-firm consistency, and bluish color. The lesion was covered by normal oral mucosa with no evidence of ulceration on the surface. The patient had no family history of similar lesions.

Under the clinical diagnosis of mucocele/hematoma the patient underwent an excisional biopsy under local anesthesia. Gross pathologic examination revealed a well-circumscribed, purple-red, soft tissue mass, measuring 3 cm × 4 cm with a friable cut surface [Figure 2]. There was no evidence of mucous material or calcified material inside the lesion.

Histopathologically, section showed tumor tissue surrounded by hemorrhagic areas [Figures 3 and 4]. The hemorrhagic areas were in continuation of papillary or tuft-like connective tissue projections, which appears to be present within dilated vascular space [Figure 4]. These tuft-like papillae were covered with one or two layers of plump ECs around cores of fibrous connective tissue, which occasionally appear to be hyalinized [Figure 5]. A smooth transition was observed between the tumor tissue (IPEH) and hemorrhagic areas [Figure 6]. The IPEH changes appear to be going from center of the hemorrhagic areas to the periphery. In the deeper areas, proliferating ECs formed solid islands. There was no evidence of nuclear atypia, hyperchromasia or mitotic figures and no necrosis or invasion of surrounding tissues. The overlying epithelium was normal. 1-year after resection, the patient had no evidence of recurrence.

DISCUSSION

Intravascular papillary endothelial hyperplasia was first described by Pierre Masson[14] in 1923 as an intravascular papillary proliferation, formed within the lumen of an inflamed hemorrhoidal plexus in a 68-year-old man. He named the lesion as “vegetant intravascular haemangioendothelioma”. The more descriptive term which is more frequently used in the English literature “intravascular papillary endothelial proliferation”, was coined by Clearkin and Enzinger in 1976.[15]

Many investigators consider it an unusual form of thrombus undergoing organization, characterized by exuberant endothelialization of thrombus fragments.[2,15‑18] Fragmentation of the thrombus may result from the forces of intravascular pressure as well as its contraction. The close association of most of the lesions with thrombotic material favors this hypothesis.[16,17,19]

Stimulation of excessive EC proliferation by locally produced angiogenic growth factors is another interesting hypothesis proposed by Pins et al.[1] Levere et al.[20] demonstrated elevated levels of basic fibroblast growth factor (bFGF) in cases of IPEH compared with non-IPEH organizing thrombi. bFGF was proposed to be released by macrophages in response to trauma or irritation leading to excessive proliferation of ECs as an autocrine growth factor. As bFGF may also be secreted by ECs, proliferation of ECs will in turn lead to secretion of more bFGF which, by positive feedback, would cause a cascade of EC proliferation.[21] Currently, IPEH is considered to be a reactive vascular proliferation following traumatic vascular stasis. At the ultrastructural level, IPEH closely resembles granulation tissue, which...
Extra-vascular masson’s tumor

Further supports the theory that this process is reparative.\textsuperscript{22} Irey and Norris,\textsuperscript{23} suggested a hormonal influence in the pathogenesis of IPEH due to the female predilection of this lesion. However this has not been further substantiated.

Most commonly it affects the skin and subcutaneous tissues of the face and scalp with the oral cavity being less frequently involved. The present case showed lower labial mucosal involvement of IPEH in 54-year-old female patient. In the literature, a slight variation in age is reported by Buchner et al.\textsuperscript{18} (age range: 30–63 years; mean 53 years), Tosios et al.\textsuperscript{6} (age range: 24–83 years; mean 52.3 years), Makos et al.\textsuperscript{7} (age range 26–60 years; mean 42.6 years) and Sarode et al.\textsuperscript{13} (age range: 9 month to 79 years; mean 45.5 years). Female predilection were reported by Buchner et al.\textsuperscript{18} (1.2:1), Tosios et al.\textsuperscript{6} (3.5:1), Makos et al.\textsuperscript{7} (1.3:1) and Sarode et al.\textsuperscript{13} (1.14:1). The site most frequently involved is the lower lip followed by the tongue, buccal mucosa, upper lip, gingiva, labial commissure, mandibular vestibule, hard palate, floor of the mouth and angle of mouth.\textsuperscript{6,7,13,18}

Intravascular papillary endothelial hyperplasia usually manifests as a soft to firm painless mass, sometimes tender ranging in size from 0.5 to 1.8 cm in diameter and imparts a reddish blue color to the overlying skin or mucous membrane [Figure 1].\textsuperscript{18,24–28} IPEH are generally slow-growing in character, with their duration varying from as less as 15 days 29–6 years.\textsuperscript{18} The lesions are sharply demarcated from the adjacent mucosa, slightly raised and mostly solitary though rarely multiple nodules can be found.\textsuperscript{7} In the present case, patient gave a history of trauma 4 months back at the site of lesion. History of minor trauma has been estimated from 4%\textsuperscript{1} up to 10%.\textsuperscript{29} In oral lesions, Tosios et al.\textsuperscript{6} reported the contribution of minor trauma to be 7%.

Figure 3: Photomicrograph showing scanner view of hemorrhagic area (black arrow) and highly cellular tumor tissue (white arrow) (hematoxylin and eosin, ×40)

Figure 4: Photomicrograph showing connective tissue stroma (white arrow), vascular space (black arrow), hemorrhagic areas (white arrow head) and tumor tissue (black arrow head) (hematoxylin and eosin stain, ×100)

Figure 5: Photomicrograph showing tumor tissue containing small papillary hyalinized areas surrounded by endothelial cells (black arrow) (hematoxylin and eosin stain, ×400)

Figure 6: Photomicrograph showing the transition between the tumor tissue and hemorrhagic areas (hematoxylin and eosin, ×400)
Hashimoto et al.\textsuperscript{[16]} in 1983 described three distinct types of IPEH as “pure”, “mixed” and “extravascular”. Pure (55.8%) arises de novo in a dilated vascular space with no causative comorbidity. Mixed (39.9%) found superimposed over a preexisting vascular anomaly such as arteriovenous malformations, hemangiomas, pyogenic granulomatosis, and chronic illnesses such as paroxysmal nocturnal hemoglobinuria, which is associated with venous thrombosis. Extra-vascular (4.3%) associated primarily with trauma-induced hematoema formation, which acts as a template for EC proliferation. As the present case is associated with a history of trauma and hematoema formation (as depicted from the histopathological examination), the final diagnosis of extravascular IPEH was made.

Intravascular papillary endothelial hyperplasia is generally well circumscribed or encapsulated showing the characteristic papillary fronds lined by proliferating ECs. There are several bundles of papillae with one or more stalks attached to the wall of a dilated vascular space or as multiple isolated papillae floating freely in the lumen. These tuft-like papillae are covered with one or two layers of plump ECs around cores of fibrous connective tissue which occasionally appear to be hyalinized [Figure 5]. Inflammatory cells are scanty. Hemosiderin deposits can be observed in the connective tissue cores.\textsuperscript{[18,30]} Thrombi in varying degrees of organization can usually be seen and appear to merge with the papillary structures [Figures 3,4 and 6]. Yonezawa and al\textsuperscript{[31]} also demonstrated expanded elastic fibers on the blood vessel by Victoria blue staining. The microscopic picture of IPEH is pathognomonic, and hence special investigations like immunohistochemistry are not generally required for diagnosis.

Clinical presentation of the lesion is nonspecific and may mimic a variety of lesions such as mucocele, intravenous pyogenic granuloma, hemangioma, traumatic fibroma, hematoema, nevus, salivary gland tumor, phlebitis, lymphangiomata, Kaposi’s sarcoma, angioendothelioma, papular angioglioma, Kimura’s disease, bacillary angiomatosis, intravenous atypical vascular proliferation and malignant melanoma.\textsuperscript{[13]} Histologically IPEH is often mistaken to angiosarcoma.\textsuperscript{[5,19,24]} Differential characteristics of IPEH include: Circumscribe lesion, intraluminar location, papillary formation related to thrombotic material, fibrohyalinized stuck of the papillae, one or two covering layers of ECs, not true endothelial fronts, possibly hyperchromatic ECs, uncommon piling up of endothelium, obscure cellular pleomorphism, rare mitotic activity, rare foci of necrosis and absence of irregular and inosculated capillary vessels.\textsuperscript{[3,4,13]}

Other histological differentiation of the oral cases includes hemangioma,\textsuperscript{[32]}mucocele,\textsuperscript{[32]}intravenous pyogenic granuloma,\textsuperscript{[6]}Kaposi’s sarcoma,\textsuperscript{[3,32]}spindle cell hemangiendothelioma,\textsuperscript{[6]}malignant endovascular papillary angioendothelioma or Dabska’s tumor\textsuperscript{[3,4,6]} and intravascular endothelioma.\textsuperscript{[4]}

Essentially all cases are cured by simple total excision with healthy margins. Cohen et al.\textsuperscript{[33]} used sclerotherapy (intra-lesional injection of a sclerosing agent “sodium tetradecyl sulfate”, causing compression and fibrosis of the blood vessels) followed by surgery with good esthetic results and minimal intra-operative bleeding. Endoscopic surgery has been used to treat an extensive IPEH of the sinonasal cavity.\textsuperscript{[34]} Recently, IPEH has been successfully treated by the beta-adrenergic antagonist nebivolol.\textsuperscript{[35]}

The prognosis of IPEH is excellent. Follow up of some large series showed no evidence of local invasion or metastasis.\textsuperscript{[36]} Nevertheless, IPEH may recur if it arises in a primary vascular lesion, which may itself recur\textsuperscript{[13,16,30]} or if the lesion is incompletely excised.\textsuperscript{[37]} Therapy in these cases should be planned according to the nature of underlying lesions. It has also been suggested that in recurrent cases exhibiting strong immunolabeling of proliferative markers the possibility of angiosarcoma should be investigated.\textsuperscript{[38]}

REFERENCES


How to cite this article: Sarode GS, Sarode SC. Extra-vascular type of oral intravascular papillary endothelial hyperplasia (Masson’s tumor) of lower lip: A case report and review of the literature. Indian J Dent Res 2015;26:101-5.

Source of Support: Nil, Conflict of Interest: None declared.