Title: Intravascular papillary endothelial hyperplasia arising from the upper lip

Author(s): Matsuzaka, K; Koike, Y; Yakushiji, T; Shimono, M; Inoue, T

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INTRODUCTION

Intravascular papillary endothelial hyperplasia (IPEH) is a benign, non-neoplastic, vascular lesion first described by Masson in 1923(12). It is characterized histologically by papillary fronds lined by proliferating endothelium(17). IPEH in the oral area is relatively uncommon; it usually presents as a cutaneous lesion(2,3,9). We report a relatively rare case of an IPEH in the upper lip.

CASE REPORT

A 28-year-old male first noticed a painless swelling in his right upper lip in 2001 and was admitted to the hospital of the Tokyo Dental College on the 11th of October, 2002. The lesion was covered with normal mucosa, and the patient had no history of trauma in that area. Under the clinical diagnosis of a fibrous polyp, the tumor was resected. The specimen was fixed with 10% formalin, and paraffin sections were prepared for light microscopy.
using routine procedures. The sections were stained with H-E, and immunohistochemical staining was also performed using primary antibodies to factor VIII related antigen, collagen type IV, vimentin, and proliferating cell nuclear antigen (PCNA).

PATHOLOGICAL FINDINGS

Under the normal oral epithelium, a few lobulated tumor masses were lined by an incomplete fibrous capsule of variable thickness separated from the surrounding tissue. Thrombus was observed, but no necrosis was present (Fig. 1a). Mitotic bodies were often noted (Fig. 1b). Other areas of the lesion showed larger spaces filled with papillary structures bearing fibrous stalks and a single layer of endothelium, but the capillary formation was poorly defined (Fig. 1c). The masses were filled with endothelial cells arranged in columns. Immunohistochemically, some of these endothelial cells were positive for factor VIII related antigen (Fig. 1d). In contrast, vimentin immunoreacted with both endothelial cells and mesenchyme (Fig. 1e). Although staining for type IV collagen was negative in the endothelial cells, it was positive in the basement membrane of the surrounding tissue in the large space (Fig. 1f). Many PCNA positive cells were observed among the endothelial cells (Fig. 1g, h).

DISCUSSION

Some vascular lesions are common in the oral area, but IPEH is a benign, non-neoplastic, vascular lesion that is uncommon in the oral area. It is characterized histologically by papillary fronds lined by proliferating endothelium. IPEH is in fact the proliferation of endothelial cells or vascular malformation, the main significance of this intravascular endothelial hyperplasia is its microscopic resemblance to angiosarcoma and its possible misdiagnosis as such. It is important to recognize such lesions histologically because they may mimic the appearance of angiosarcoma in their proliferation of endothelial cells, mitotic activity, and papillary projections. However, these lesions lack cellular anaplasia and an infiltrative pattern of growth, both important features of angiosarcoma. In this case, many mitotic cells were observed, but no abnormal mitotic figures, solid areas, or necrotic foci, all of which are frequently seen in angiosarcoma. We suggest that these mitotic cells were involved in the process of thrombus production. Hemangioendothelioma is also an important lesion in the differential diagnosis of IPEH. Weiss et al. reported that hemangioendothelioma has a malignant potential intermediate between those of simple hemangioma and angiosarcoma. Kaposi’s sarcoma, which may occur in oral area, is easy to exclude, because the fascicular pattern of spindle-shaped fibroblast-like cells and vascular slits which typify that condition were not evident in this case. Although malignant endovascular papilloma and endothelioma may show some resemblance to IPEH, the bizarre intravascular papillary proliferation of atypical endothelial cells is absent. IPEH can be distinguished from other lesions, because it is frequently well-circumscribed or encapsulated, with the proliferative process entirely limited by the vascular wall and characterized by papillary fronds. Further, IPEH is generally associated with a thrombus, which precedes the formation of the fronds and severs as a matrix for their development. The present case was not completely encapsulated, but we also observed a thrombus.

Furthermore, the principal significance of the lesion lies in the fact that it may be mistaken for angiosarcoma. Table 1 shows the locations of IPEH in the literature, showing that it is slightly more frequent in the lower lip around the oral area. IPEH comprises approximately 2% of the benign and malignant vascular tumors of the skin and subcutaneous tissues. Only three IPEHs, including the present case, were experienced, among the 573 vascular lesions in 15,671 materials in our hospital from 1966 to 2002. One of these
Fig. 1  Microscopic findings

a: Loupe finding of Hematoxylin-Eosin staining. The lobulated masses are lined by an incompletely fibrous capsule, and a thrombus is observed (arrowhead).  
b: Hematoxylin-Eosin staining. Mitotic cells are frequently observed (arrowhead).  
c: Hematoxylin-Eosin staining. A papillary structure can be seen in the vessel, and the vessel wall was indicated by an arrowhead.  
d: Immunohistochemical staining for factor VIII. Endothelial cells were reactive.  
e: Immunohistochemical staining for vimentin. The endothelial cells and the mesenchyme both reacted.  
f: Immunohistochemical staining for type IV collagen. The basal membrane was reactive (arrowhead).  
g, h: Immunohistochemical staining for PCNA.
IPEH specimens was from the lower lip of a 57-year-old female, another was from the tongue of a 74-year-old male, and the present case is from the upper lip. Thus the incidence of IPEH is only 0.5% of vascular lesions from the oral area in our hospital. IPEH and angiosarcoma may be exceedingly difficult to distinguish, but there are several important hallmark characteristics of IPEH: (1) the proliferative process is entirely confined to an intravascular space, (2) most of the papillary structures are associated with thrombi, (3) the papillae consist of fibrohyalinized tissue that is covered by no more than two endothelial cell layers, (4) the endothelial cells may be hyperchromatic, but extreme nuclear atypia and frequent mitotic figures are absent, (5) tissue necrosis is absent. This case adequately exhibits the above-mentioned characteristics of IPEH, except for the mitotic figures. Immunohistochemically, the vascular origin of the lesion was demonstrated by its positive reaction for vimentin and partially for factor VIII related antigen. Furthermore, vimentin reacted not only with mesenchymal cells but also with endothelial cells. Tosios described that the cells react with vimentin in the earlier stages of the development of the lesion, followed by factor VIII related antigen in the final stages of organization. On the other hand, the papillary-structured area proliferated in a space surrounded by a basement membrane that was immunoreactive for type IV collagen. PCNA positive cells were also frequently seen in this case, indicating that the proliferating activity was high. Therefore, we concluded that this rare case is IPEH with high proliferation activity.

ACKNOWLEDGEMENT

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REFERENCES


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**Reprint requests to:**

Dr. Kenichi Matsuzaka
Department of Clinical Pathophysiology,
Tokyo Dental College,
1-2-2 Masago, Mihama-ku,
Chiba 261-8502, Japan
Tel: 043-270-3581
Fax: 043-270-3583
E-mail: matsuzak@tdc.ac.jp