CASE REPORT

Epithelioid hemangioendothelioma of tongue: A case report with immunohistochemical studies

M. Uehara a,*, K. Shibahara a, S. Fujita b, T. Tobita a, S. Ohba a, A. Fujisawa a, M. Nonaka a, T. Inokuchi a

a Division of Oral and Maxillofacial Surgical Reconstruction and Functional Restoration, Department of Developmental and Reconstructive Medicine, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8588, Japan

b Division of Oral Pathology and Bone Metabolism, Department of Developmental and Reconstructive Medicine, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8588, Japan

Received 22 September 2005; accepted 23 September 2005

Summary A very rare case of epithelioid hemangioendothelioma (EH) in the tongue is reported. The immunohistochemical studies for Factor VIII, proliferating cell nuclear antigen (PCNA) and vascular endothelial growth factor (VEGF) were performed. The tumour cell kinetics in EH was evaluated by PCNA immunohistochemistry. PCNA labeling index in the tumour was 57.0%. Furthermore, strong immunohistochemical expression of VEGF was recognized in the cytoplasm of tumour cells. The intense expression of VEGF in EH may indicate its aggressive proliferative activity and metastatic behavior.

KEYWORDS
Epithelioid hemangioendothelioma; Tongue; Immunohistochemistry

Introduction

Epithelioid hemangioendothelioma (EH) is a rare vascular tumour, which was described first by Weiss and Enzinger.1 This tumour shows an intermediate malignant potential between hemangioma and angiosarcoma.2 EH rarely occurs in the oral cavity, to our knowledge, only 15 cases have been reported.3–15 In those cases, only two cases of EH in the tongue have been reported.6,13 The behavioral nature of EH in the tongue is unknown because of the rarity. We describe here the EH manifested in the tongue together with its immunohistochemical findings.

Case report

A 72-year-old Japanese man presented with 2 months history of a slowly growing painless swelling in the tongue dorsum. The patient’s medical history was noncontributory. The extraoral examination was negative for swelling, tenderness, or lymphadenopathy. A hemispheric swelling (7×7 mm) involved in the left side of the tongue dorsum...
was moderately firm without ulceration (Fig. 1). To make the diagnosis, biopsy was performed under local anesthesia. Histologically, the haematoxylin–eosin (H–E) stained specimen showed a submucosal nodule composed of plump cells with large nuclei and distinct cell border. Scattered vascular channels containing erythrocytes were seen in the dodule, where mitotic figures were sparsely found (Fig. 2). These findings made diagnosis of epithelioid hemangioendothelioma (EH). The lesion was excised with the safety margin of 10 mm. No tumour involvement was microscopically shown in the surgical margin.

Reticulin staining as well as immunohistochemical staining for factor VIII (1:200 diluted, DAKO N1505) were performed to confirm the diagnosis. The reticulin staining highlighted fibrous materials surrounding the individual tumour cells (Fig. 3). This staining demonstrated a dense reticulin network that surrounds individual tumour cells, and this finding is one of the features of tumour originated from endothelial cell. The positive reaction to anti-factor VIII was demonstrated in the cytoplasm of the tumour cells. This vascular marker was more accentuated at the sites where vascular lumina were formed (Fig. 4).

Furthermore, the proliferative activity of this tumour was evaluated by immunohistochemical staining of proliferating cell nuclear antigen (PCNA; 1:100 diluted, Santa Cruz FL-261) (Fig. 5). Both labeled and unlabeled tumour cells in the square field (0.25 mm × 0.25 mm) were counted at a magnification of 400×. The PCNA labeling index (LI) was calculated as the percentage of the PCNA-positive cells in 1000 tumour cells counted from randomly selected four fields. The PCNA LI amounted to 57.0%. Immunohistochemical expression of vascular endothelial growth factor (VEGF; 1:200 diluted, Santa Cruz A-20) in the tumour was also investigated to reveal its behavioral nature. VEGF was stained strongly in the cytoplasm (Fig. 6).

![Figure 1](image1.png)  **Figure 1** Mass of the tongue dorsum without ulceration.

![Figure 2](image2.png)  **Figure 2** Submucosal nodule composed of plump cells with large nuclei (haematoxylin and eosin staining ×200).

![Figure 3](image3.png)  **Figure 3** Reticular fiber around the cells (reticulin staining ×400).

![Figure 4](image4.png)  **Figure 4** The strongly positive factor VIII in the cytoplasm of the tumour cells (immunohistochemical staining ×400).
Weiss et al. reported the prognosis of 46 cases of EH, which were followed up for 48 months on average. They described that local recurrence included 6 cases (13%), and metastasis to regional lymph nodes and/or other organs 14 cases (31%). Therefore, radical excision of the lesion with adequate margin was obtained, taking into account the risk of local recurrence in this case.

The present case expressing the high LI of PCNA is suggestive of its clinical outcome as well as aggressive proliferative activity. In addition, angiogenesis plays an important role in tumour growth and metastasis. VEGF is a dimeric polypeptide growth factor, and its mitogenic activity is specific for vascular endothelial cells. The intense expression of VEGF in EH may indicate its aggressive proliferative activity and metastatic behavior as well.

Because of its remarkable cellularity and the mitotic activity, EH can be confused with carcinoma. The immunohistological staining for factor VIII helps to differentiate EH from carcinoma. Critical therapy and follow-up must be required because of its semi-malignant potential.

References

18. Toi M, Hoshina S, Takayanagi T, Tominaga T. Association of vascular endothelial growth factor expression with tumor...
