CASE REPORT

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PRIMARY LYMPHOEPITHELIOMA-LIKE CARCINOMA OF MINOR SALIVARY GLAND: A CASE REPORT WITH IMMUNOHISTOCHEMICAL AND IN SITU HYBRIDIZATION STUDIES

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Abstract: Background. Lymphoepithelioma-like carcinomas (LEC) of salivary glands represent rare epithelial malignancies, with most cases affecting the parotid gland. To our knowledge, there was only one LEC arising from the minor salivary gland described in the English-language literature.

Methods. We report the second LEC of the minor salivary gland in the buccal area of a 50-year-old Taiwanese woman, who underwent surgical resection and adjuvant radiotherapy and remained alive and well after 120 months of follow-up. Histologically, irregular tumor nests of undifferentiated epithelial cells with syncytial cell boundaries were found embedded within rich lymphoplasmacytic stroma. The tumor cells also showed strong c-KIT expression and evidence of Epstein-Barr virus (EBV) infection.

Conclusions. Our case suggests potential pathogenic implications of both c-KIT and EBV in LEC of the minor salivary gland that can be cured by the combination of surgery and radiotherapy and has a very favorable long-term prognosis. © 2005 Wiley Periodicals, Inc. Head Neck 28: 182–186, 2006

Keywords: lymphoepithelioma-like carcinoma; minor salivary gland; Epstein-Barr virus; c-kit

Lymphoepithelioma-like carcinoma (LEC), also referred to as malignant lymphoepithelial lesions or undifferentiated carcinoma with lymphoid stroma, has a marked racial predilection for Southeastern Chinese and Eskimos. It is considered the malignant counterpart of benign lymphoepithelial lesion (BLE) and histologically indistinguishable from the similarly named neoplasms of nasopharyngeal origin. Two thirds of LECs arise de novo, whereas the remaining third develop in the setting of a preceding or concurrent BLE. As with LEC of nasopharyngeal origin, Epstein-Barr virus (EBV) has been strongly implicated in the oncogenesis of LECs, which can be detected by variable methods, including in situ hybridization for EBV-encoded small RNAs (EBER) mRNA.

c-KIT (CD117) is a transmembrane receptor–type tyrosine kinase that is structurally and
functionally analogous to platelet-derived growth factor and colony-stimulating factor-1 receptors. c-KIT expression has been previously documented in a wide variety of human neoplasms resulting either from constitutional mutation of various exons in the *c-kit* gene or from paracrine/auto-crine loop feedback pathways. A recent study indicated that c-KIT is highly frequently expressed in a handful of LECs of major salivary glands, raising the possibility that c-KIT might also confer growth advantage on LECs.

To date, only one case of an intraoral LEC of presumed minor salivary gland origin, affecting a 69-year-old white woman, has been reported in the English-language literature. It was associated with concurrent BLE and neck lymph metastasis at initial diagnosis. In this report, we describe the second LEC of the minor salivary gland that occurred in an Asian patient without associated BLE in conjunction with immunohistochemical and EBV studies.

**CASE REPORT**

A 50-year-old woman was initially seen with a progressively enlarged, painless, firm mass beneath the right buccal mucosa for 1 year without a history of smoking, alcohol, or beetle nut consumption or relevant systemic disease. The overlying mucosa of the tumor was unremarkable. The CT scan revealed neither enlarged neck lymph nodes nor abnormality of the nasopharynx, lending further support for the primary nature of this tumor. She received wide local excision followed by adjuvant radiotherapy with a total dose of 6520 cGy with curative intent. The patient is alive with no evidence of disease after 120 months of long-term follow-up.
Pathology. Grossly, the tumor, measuring 2.0 × 1.6 × 1.0 cm, was yellowish white, firm, and multinodular in appearance. Microscopically, residual lobules of minor salivary glands were found juxtaposing or intermingling with several separated, various-sized tumor nodules (Figure 1A) beneath an intact nondysplastic stratified squamous epithelium (Figure 1B). The tumor was predominantly composed of large, polygonal, undifferentiated tumor cells with vesicular nuclei and prominent nucleoli that were arranged in cohesive nests within abundant lymphoplasmacytic infiltrates, focally forming germinal centers. The cell borders between adjacent cells were indistinct, creating a syncytial cytoplasmic appearance (Figure 1C). Mitotic figures averaged one to two per high-power field. Necrosis, keratinization, and benign lymphoepithelial lesions were all absent. Immunohistochemically, the tumor was diffusely positive for epithelial membrane antigen (EMA), AE1/AE3 cocktail, and CD117 (Figure 2A) but negative for cytokeratin 7, cytokeratin 20, and latent membrane protein-1 (LMP-1). The labeling indices of Ki-67 and p53 were approximately 10% and 25%, respectively. In situ hybridization for detection of EBV by use of EBER1-specific antisense oligoprobe disclosed abundant EBER1 in undifferentiated carcinoma (Figure 2B) but not in the surrounding lymphoid stroma.

DISCUSSION

Hilderman et al\textsuperscript{2} were the first to recognize epithelial malignancy in the salivary gland showing features similar to those of BLE. Although LEC accounts for only 0.4% of all salivary gland neoplasms as reported by the Armed Forces Institute of Pathology Tumor Registry,\textsuperscript{3} more than 100 cases have been described to date, with most affecting the parotid glands or, less commonly, the submandibular glands.\textsuperscript{4,5} LEC accounted for 7% of all malignant salivary gland tumors in Taiwan, an incidence 14 times higher than in the Western population. Nevertheless, the presentation of primary LEC affecting the minor salivary gland was hitherto never described in Asians, except for one previous case derived from the same buccal area of an elderly white woman in the English-language literature.\textsuperscript{1} As for malignancies of intraoral minor salivary glands, the most common histologic type is mucoepidermoid carcinoma followed by adenoid cystic carcinoma and adenocarcinoma, not otherwise specified, etc.\textsuperscript{6} Therefore, this case represents an extremely rare type of carcinoma of the minor salivary glands.

More than 40% of patients with LECs originating from the major salivary glands have metastases to lymph nodes at presentation, 20% have local recurrences or lymph node metastases develop, and approximately 20% eventually experience distant metastases within 3 years after therapy.\textsuperscript{3} The clinical stage of disease has a significant impact on prognosis, because advanced disease in the form of large size or lymph node metastases corresponds to poor survival. The favorable outcome observed in our minor salivary gland LEC can be mostly ascribed to the early stage at initial presentation. However, accurate survival rates in patients with LECs of the sali-
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CONCLUSION

We have described an additional LEC of the minor salivary gland, which, using surgical excision with adjuvant radiotherapy, showed a satisfactory outcome after long-term follow-up. The tumor cells were strongly positive for EBER1 and c-kit protein, providing further insights into the tumorigenesis of salivary gland LECs.

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