

Case Report

Lymphoepithelial Carcinoma in the Lateral Tongue: The Case Report

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Abstract: Lymphoepithelial carcinoma (LEC) of the tongue is a rare subtype of squamous cell carcinoma. Histologically, it is an undifferentiated carcinoma with rich lymphocyte and plasma cell infiltration. The most common location for LEC in the head and neck is the salivary glands, and LEC of the oral cavity is extremely rare. The second case report of LEC in the lateral tongue is presented. In addition, a review of the literature was performed, and the relationship between LEC and Epstein–Barr virus infection was considered.

Keywords: Lymphoepithelial carcinoma; oral cavity; lateral tongue



Citation: Ono, S.; Marunaka, H.; Yanai, H.; Kawai, H.; Takabatake, K.; Nishida, K.; Toji, T.; Nakano, K.; Nagatsuka, H.; Yoshino, T.

Lymphoepithelial Carcinoma in the Lateral Tongue: The Case Report. *Reports* **2021**, *4*, 24. <https://doi.org/10.3390/reports4030024>

Academic Editor: Toshio Hattori

Received: 26 April 2021

Accepted: 11 August 2021

Published: 12 August 2021

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1. Introduction

Lymphoepithelial carcinoma (LEC) is a squamous cell carcinoma morphologically similar to non-keratinizing nasopharyngeal carcinoma, undifferentiated subtype [1]. Schminke first described LEC of the nasopharynx in 1921 [2]. Histologically, LEC consists of atypical epithelial-derived cells that have pale cytoplasm and large, round vesicular nuclei. It is characterized by lymphoid cells breaking up the tumor into tiny aggregates. Epstein–Barr virus (EBV) is associated with head and neck LEC (HNLEC).

HNLEC is a tumor diagnosed most commonly in the salivary glands, and only 18 cases in the oral cavity appear to have been reported so far. To the best of our knowledge, no case of LEC in the lateral tongue has been reported in the English literature. A case of LEC in the lateral tongue is presented, along with a review of the literature on oral LEC and a discussion of the relationship between oral LEC and EBV infection.

2. Case Report

An 82-year-old man with a previous history of alcohol and tobacco use and esophageal cancer 8 years earlier noticed a mass on the left edge of the tongue. Malignancy was suspected on examination of a biopsy specimen, and he was referred to our hospital. On clinical examination, a hard, slightly bulging mass with a smooth surface, approximately $2 \times 1 \text{ cm}^2$, was found (Figure 1a). The tumor was localized in the posterior edge of the left edge of the tongue, and there was no cervical lymph node enlargement on computed tomography (CT) (Figure 1b). The nasal cavity, nasopharynx, and larynx appeared normal on endoscopy. The tumor was resected, and macroscopically, the excised tumor was a pale yellowish, solid mass, $1.7 \times 1.0 \times 1.2 \text{ cm}^3$ in size (Figure 2). Histologically, the tumor cells

showed proliferation of pale staining, cohesive epithelial cells with prominent surrounding and infiltrating lymphocytes (Figure 3). The tumor cells are polygonal and contained large round vesicular nuclei with prominent nucleoli. No keratinization was found in the tumor, and was similar to nasopharyngeal carcinoma. On immunohistochemistry, the tumor cells were positive for cytokeratin AE1/AE3, p40, and p53. On in situ hybridization, the epithelial cells were negative for EBV-encoded small RNA (EBER) (Figures 4 and 5). The diagnosis of LEC was made. After surgery, no recurrence was observed at the 7-month follow-up visit.

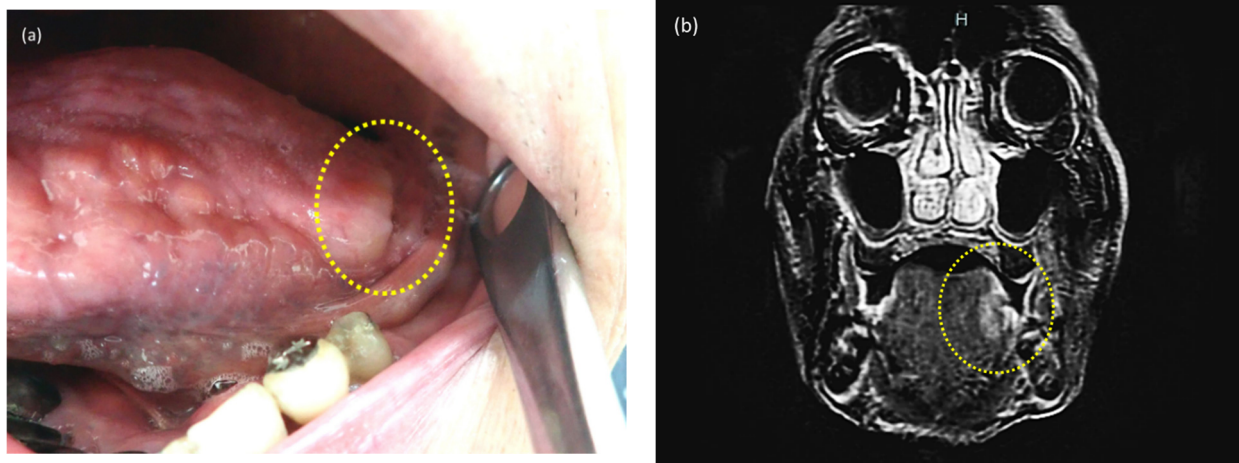


Figure 1. Gross findings of the tumor. (a)The tumor is seen in the posterior edge of the left side of the tongue. (b)The tumor is localized in the left side of the tongue.



Figure 2. Gross findings of the resected material that view from the left. The tumor is in the anterior vallate papilla. The surface of the tumor is smooth, and the central depression of the tumor is the biopsy scar.

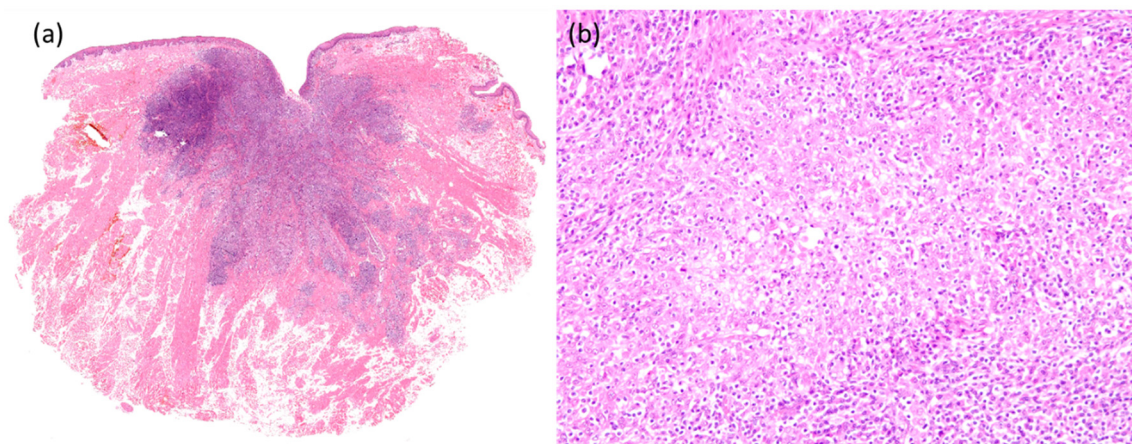


Figure 3. Histological findings of the tumor. (a) The tumor infiltrates the muscles of tongue (20×). (b) The tumor exhibits a cluster of light staining neoplastic cells with abundant lymphocytic stroma (100×).

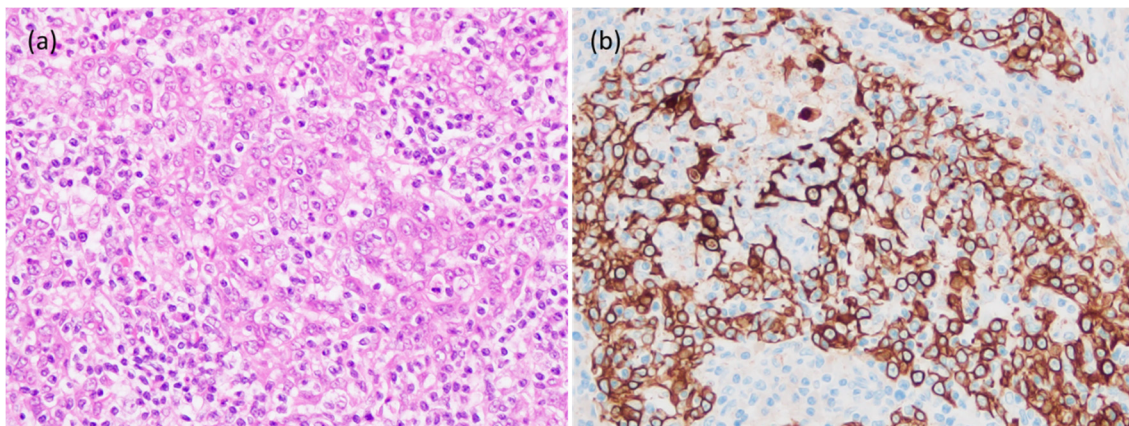


Figure 4. Histological and immunohistochemical findings of the tumor. (a) The tumor cells are polygonal with enlarged vesicular nucleoli and lightly eosinophilic cytoplasm, and abundant infiltration of lymphocytes is seen (200×). (b) The tumor cells are positive for cyokeratin AE1/AE3 (200×).

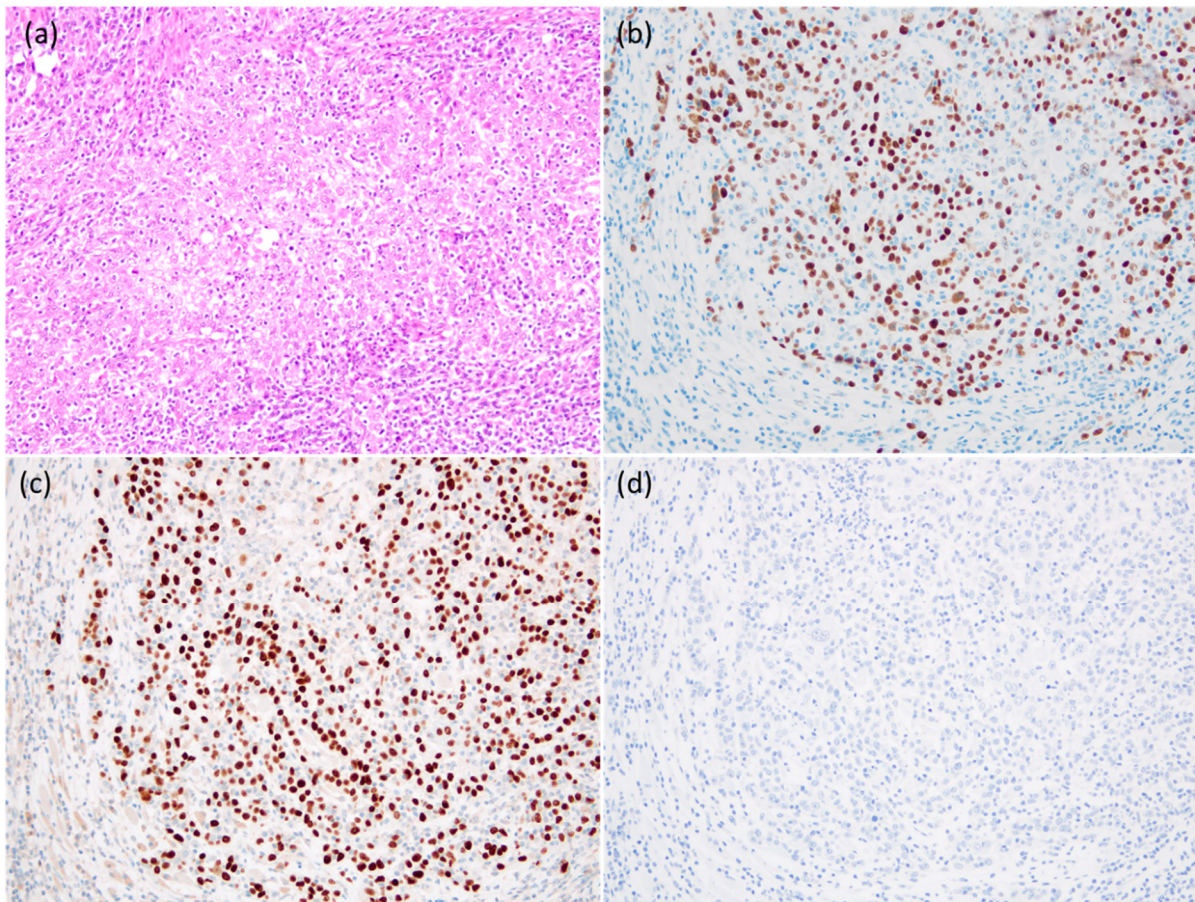


Figure 5. Histological, immunohistochemical and in situ hybridization findings of the tumor. (a) Histological finding of the tumor (100 \times). On immunohistochemistry, p53 (b) (100 \times), and p40 (c) (100 \times). The tumor cells are negative on EBER (d) (100 \times) in situ hybridization.

3. Discussion

LEC is a subset of poorly differentiated squamous cell carcinoma with intermingled lymphocytes. LEC outside of the nasopharynx is rare, and only 18 cases of oral LEC have been reported (Table 1). Oral LEC developed commonly in the minor salivary gland, lip, and palate. This is the second report of LEC arising in the lateral tongue. The age of patients ranged from 11 to 82 years (average 56.4 years), and there was no sex predilection. All tumors were within 3 cm (range: 0.5 to 2.6 cm) in size. Six patients (33.3%) had metastases to the cervical lymph nodes. Although one patient who refused treatment died of tumor 34 months after diagnosis, the prognosis of patients with oral LEC was excellent.

Histologically, the present case showed proliferation of non-keratinized epithelial cells with massive infiltration of lymphocytes. On immunohistochemical examination, tumor cells were diffusely positive for cytokeratin AE1/AE3 and p40. These results confirm the character of the tumor cells as squamous epithelium.

Previous reports showed an association between EBV and oral LEC, especially in Asian cases. Of the 12 Asian cases, 9 (75%) were positive. In contrast, no cases in North and South America, Europe, and Africa showed an association with EBV. In the present case, the tumor cells were negative on EBER in situ hybridization.

Table 1. Summary of previous and current reports of LEC in the oral cavity. M: Male, F: Female, EBV: Epstein–Barr virus, NM: not mentioned, +: positive, -: negative, LN: lymph node, S: surgery, R: radiotherapy, C: chemotherapy.

Study	Age (Years)	Gender	Country	EBV	Site	Size	Metastasis	Treatment	Follow-Up (Month)	Residual, Metastasis
Ahuja (1999) [3]	63	M	China	+	Roof of oral cavity	2.5 cm	NM	NM	NM	NM
	47	F		+	Palatinum	NM	cervical LN	NM	NM	NM
Chow (2002) [4]	58	M	China	+	Palatinum	2.0 cm	cervical LN	R	30	No
	56	F		+	Palatinum	1.5 cm	No	R	12	No
	80	F		+	Retromolar region	NM	cervical LN	patient refused	34	Died
Lu (2005) [5]	50	F	Taiwan	+	Minor salivary gland, cheek	2 × 1.6 × 1 cm ³	No	S+R	120	No
Tanuja (2008) [6]	11	M	India	+	Mandible	NM	cervical LN	C + R	36	No
Hsieh (2010) [7]	50	M	Taiwan	+	Buccal mucosa	2 cm	No	C + R	NM	residual tumor
Zeng (2015) [8]	38	F	China	+	Hard palate	2.6 × 2.4 × 1.7 cm ³	No	S	12	No
Weiss (1989) [9]	64	M	United States of America	-	Floor of mouth	NM	NM	NM	NM	NM
Worley (1997) [10]	69	F	United States of America	-	subepithelial mass in the left buccal area	0.5 cm	cervical LN	S + R	12	No
Mahomed (2008) [11]	73	M	South Africa	-	Lower lip	1 × 1 cm ²	No	S	20	No
Rytkönen (2011) [1]	30	M	Finland	-	Maxilla	NM	No	S + R	11	No
Dardo (2012) [12]	56	M	Italy	-	Minor salivary gland and upper lip	2.5 cm	No	S	24	No
Gultekin (2014) [13]	41	M	Turkey	-	Lower lip	1 cm	cervical LN	C + R	36	No
Almeida (2019) [14]	82	F	Brasil	-	Lower lip	NM	No	S	24	No
Takeda (2021) [15]	72	F	Japan	-	left tongue edge	1.2 × 0.6 cm ²	No	S	12	No
Present case	82	M	Japan	-	left tongue edge	1.7 × 1.0 × 1.2 cm ³	No	S	7	No
Hsiung (2005) [16]	50	F	Taiwan	NM	Minor salivary gland in right buccal area	NM	No	S + R	116.5	NM

The tumor cells of the present case showed overexpression of p53. This finding suggests that mutation of *TP53* may play a key role in carcinogenesis of this tumor. In the previous studies, p53 status was studied in only two cases. One case with EBV showed p53 expression in only 25% of the tumor cells, suggesting wild type [5]. In contrast, one EBV-negative LEC showed overexpression of p53 on immunohistochemistry [14]. Although the number of cases is limited, there may be different mechanisms of tumorigenesis in oral LEC.

Lymph node metastasis was present in 6 of 18 cases, and it was more common in EBV-positive cases. The EBV status of oral LEC may have some role in nodal metastasis.

In conclusion, the second case of LEC in the lateral tongue was presented. This EBV-negative case might have been caused by *TP53* mutation, another possible mechanism of tumorigenesis of oral LEC. To identify prognostic factors, study of additional cases is needed.

Author Contributions: S.O.: pathology fellow responsible for working up the case. Write-up of the manuscript and final submission. H.M.: Otolaryngology pathology assistant professor contributed to review the manuscript. H.Y.: pathology professor responsible for the interpretation and final diagnosis of case. H.K., K.T., and K.N. (Keisuke Nakano): Oral pathology assistant professor responsible for interpretation, review, and editing of final manuscript. T.T., and K.N. (Kenji Nishida): pathology assistant professor contributed to the data collection. H.N.: oral pathology professor, consultant during the interpretation and get-ting to the final diagnosis. T.Y.: pathology professor, reviewed manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Conflicts of Interest: None of the authors have any conflicts of interest to declare.

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