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Case Report
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Large cell neuroendocrine carcinoma of the tongue base: case report of an unusual location with immunohistochemical analysis

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Abstract. A case of large cell neuroendocrine carcinoma (LCNEC) of the tongue base is described. It was characterized by solid tumor nests with central necrosis and rosette formation resembling basaloid squamous cell carcinoma. Immunohistochemical examination revealed that this tumor had neuroendocrine differentiation. It was diagnosed as LCNEC of the tongue base.

Pulmonary LCNEC is a well-established entity, but LCNEC also occurs in other organs. This is the first report of mucosal LCNEC in the oral cavity. Basal cells in the normal squamous epithelium around the tumor indicated positivity for neural cell adhesion molecule and N-cadherin. These cells were considered neuroendocrine-related cells in the lingual squamous epithelium, which are related to the tumorigenesis of mucosal LCNEC in the tongue base.

Keywords: tongue base; large cell neuroendocrine carcinoma; immunohistochemistry.

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Large cell neuroendocrine carcinoma (LCNEC) of the lung is a well-established clinicopathologic entity that is morphologically and biologically different from atypical carcinoid and small cell carcinoma[4,10], although such cancer occurs in other organs, including the salivary glands[3,6]. A large-scale histological review revealed that LCNEC accounted for 3% of surgically resected pulmonary tumors, and the overall 5-year survival was 57%, which is one of the poorest for subgroups of primary lung cancers[11]. In the head and neck region, LCNEC has only been reported in the parotid gland[3,6]. To the best of the authors' knowledge, no report has shown that it occurs as a mucosal tumor in the oral cavity.

Case report

The patient was a 79-year-old Japanese man who had had liver carcinoma (well-differentiated hepatocellular carcinoma) and hypopharyngeal carcinoma, which had been completely resected about 1 year before. Partial hepatectomy was performed, followed by total pharyngo-lar-

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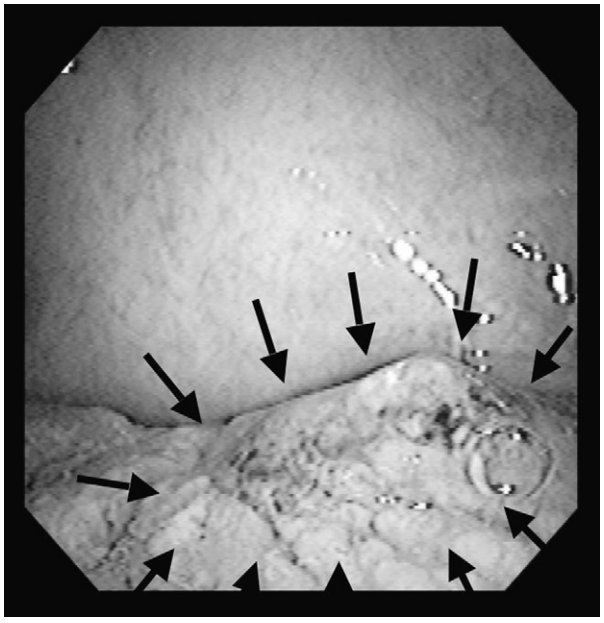

Fig. 1. Intraoral endoscopy showing the dome-like mass (arrows) with erosive surface on the left side of the tongue base.

yngo-esophagectomy and bilateral neck dissection for hypopharyngeal cancer that was diagnosed as moderately differentiated squamous cell carcinoma (SqCC). He had been followed up, and a mass, 10×10 mm, had been found on the left side of the tongue base with intraoral endoscopy (Fig. 1). This lingual base tumor was not connected to the hypopharyngeal carcinoma, clinically, macroscopically or microscopically: the hypopharyngeal carcinoma and the tongue base tumor were separate and distinct clinical entities. Positron emission tomography, computed tomography and magnetic resonance imaging indicated that there were no distant and satellite metastases or direct invasion of hepatocellular carcinoma, hypopharyngeal carcinoma and other lesions. PET examination showed no other primary lesions, for example, in the lungs. After 1 month, partial resection without neck dissection was performed for the lingual base tumor. No adjuvant therapy or postoperative radiotherapy has been performed. There has been no recurrence or distant metastasis of LCNEC about 18 months after surgery.

Macroscopically, an undulated mass with surface erosion was observed on the left side of the tongue base. On the cut surface, an ill-circumscribed grayish-white tumor with invasion to the muscle layer was seen (Fig. 2).

Histological examination of the lingual base cancer indicated solid malignant epithelial nests and cord-like structures

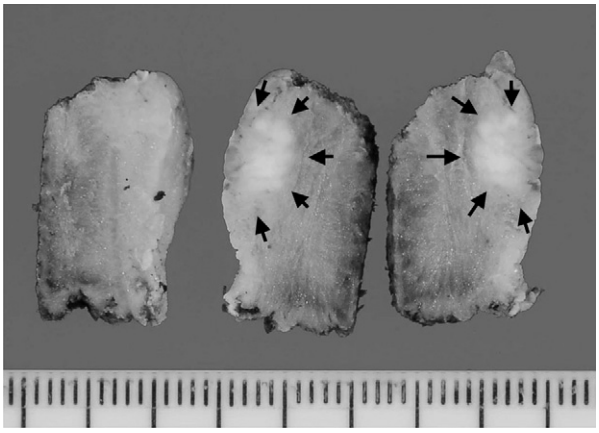

Fig. 2. Macroscopicallly an ill-defined, grayish-white mass (arrows) with erosion was seen on the cut surface under the mucosal membrane.

of large polygonal cytoplasms with areas of central necrosis and high mitotic figures (13 per 10 high-power fields). The nuclear chromatin was coarsely granular and nucleoli were prominent. The nests had smooth rounded margins and hyalinized stroma was partly seen in them. Many rosette structures were observed (Fig. 3A and B). The cancer cells were diffusely positive for neural cell adhesion molecule (NCAM), N-cadherin, high-molecular-weight keratin (HMWK: 34betaE12), p63, p53, p16, cytokeratin (CK) 5/6, CK19, protein gene product 9.5 and neuron-specific enolase (NSE) (Fig. 3C,D and E). They were negative for chromogranin-A, thyroid transcription factor-1 (TTF-1), hepatocyte, CK7, CK14 and CK20. Ki-67 labeling index was 82% (Table 1). The authors diagnosed this tumor as LCNEC arising from the lingual base mucosa. Some basal cells in the normal squamous epithelium around the tumor were focally positive for NCAM and N-cadherin, (Fig. 3F) but not for NSE, CK20 and S-100 protein, whereas basal and suprabasal cells were positive for p63 and all layers of squamous epithelium were diffusely positive for HMWK. Normal squamous epithelium was negative for synaptophysin and chromogranin-A. The basal cells of the normal squamous epithelium derived from three surgical and autopsy specimens of the tongue base showed no positivity for NCAM and N-cadherin.

Discussion

LCNECs were formally diagnosed as poorly differentiated SqCC and previous reports have pointed out that LCNEC was often misdiagnosed as poorly differentiated SqCC or poorly differentiated adenocarcinoma[5,11]. Basaloid carcinoma of the lung also resembles LCNEC, but basaloid carcinoma lacks neuroendocrine features and TTF-1 expression[7,8]. The diagnosis of LCNEC in the present case is based on criteria established for tumors of the lung[10]. The criteria included large cells, with a polygonal shape, low nuclear to cytoplasmic ratio, coarse nuclear chromatin, frequent nucleoli, mitotic activity in excess of 10 mitoses per 10 high-power fields, with frequent necrosis, many rosette structures, and immunohistochemical evidence of neuroendocrine differentiation.

The most common cancer in the head and neck regions is SqCC. Basaloid squamous cell carcinoma, which is a rare variant of SqCC[1], partly resembles LCNEC, but basaloid SqCC lacks neuroendocrine