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Large cell neuroendocrine carcinoma of the submandibular gland: Case report and literature review

Nobuko Yamamoto [a,*], Shujiro Minami [a], Masanori Kidoguchi [a], Akihito Shindo [a], Yutaka Tokumaru [a], Masato Fujii [b]

[a] Department of Otolaryngology, National Tokyo Medical Center, Japan
[b] National Institute of Sensory Organs, National Tokyo Medical Center, Japan

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ABSTRACT

Large cell neuroendocrine carcinoma (LCNEC) of the salivary gland is extremely rare. We report on a case of LCNEC in the submandibular gland. A 58-year-old male had a four-month history of an enlarging mass in his left submandibular region. He underwent lymph node resection and metastasis of LCNEC was suspected. Magnetic resonance imaging of the neck showed a solid submandibular gland tumor with marginal blurring. Positron-emission tomography and upper gastrointestinal endoscopy showed no evidence of malignancy other than in the left submandibular gland. He underwent left submandibular gland resection and left upper neck dissection. The final diagnosis was LCNEC of the submandibular gland; surgical margin was negative. Fourteen months later he is free of tumors. This is the first report of LCNEC of the submandibular gland. LCNEC of the salivary gland shows high-grade malignancy like that of the lung. According to past reports, two of four patients died despite multidisciplinary treatments. There are no standard treatments for LCNEC of the salivary glands. More studies are needed to define prognostic factors and establish therapeutic methods.

1. Introduction

Travis et al. first proposed large cell neuroendocrine carcinoma (LCNEC) as a new category of pulmonary neuroendocrine tumors in 1991 [1]. Previously established histologic criteria of pulmonary neuroendocrine tumors were used for the diagnosis of typical carcinoid, atypical carcinoid and small-cell lung carcinoma. They found that a spectrum of high- and low-grade tumors existed among atypical carcinoid tumors and distinguished the high-grade tumors as LCNEC rather than atypical carcinoid. LCNEC has been reported in many other organs, such as the uterine cervix [2], thymus [3], stomach [4] and urinary bladder [5]. In the head and neck region, LCNEC is not recognized as a specific entity in the 2005 World Health Organization classification. However recent studies have shown that tumors fulfilling the criteria for LCNEC in the head and neck should be separated as a new entity because of their high-grade malignancy [6]. In the salivary glands, LCNEC is now categorized under large cell undifferentiated carcinoma according to the 2005 World Health Organization classification. Nagao et al. reported that LCNEC differs from other large cell undifferentiated carcinoma in the presence of the neuroendocrine pattern, including the rosette-like structures and the organoid and peripheral palisading growth patterns, as well as the immunohistochemical or electron microscopic features [7]. LCNEC in the salivary gland is a newly proposed clinicopathologic entity and extremely rare; a literature search found that only five cases have been reported. All of them were LCNEC of the parotid glands. Here we report on a case of LCNEC of the submandibular gland.

2. Case report

A 58-year-old male was referred to us with suspicion of submandibular lymph nodes metastases of LCNEC. He had a four-month history of an enlarging mass in his left submandibular region and had visited his family doctor. The mass was considered to be swollen submandibular lymph nodes. He underwent lymph node resection for the biopsy at the clinic. Pathological diagnosis was metastasis of LCNEC and he was referred to our institute. Physical examination found a 2 cm × 2 cm firm mass in the left submandibular area. Facial nerve paralysis was not present and no other mass was detected on neck palpation. Magnetic resonance imaging (MRI) of the neck showed a solid submandibular gland

* Corresponding author at: Department of Otolaryngology, National Tokyo Medical Center, 2-5-1, Higashigaoka, Meguro-ku, Tokyo 152-8902, Japan, Tel.: +81 3 3411 0111.
E-mail address: nobukoy@a2.keio.jp (N. Yamamoto).

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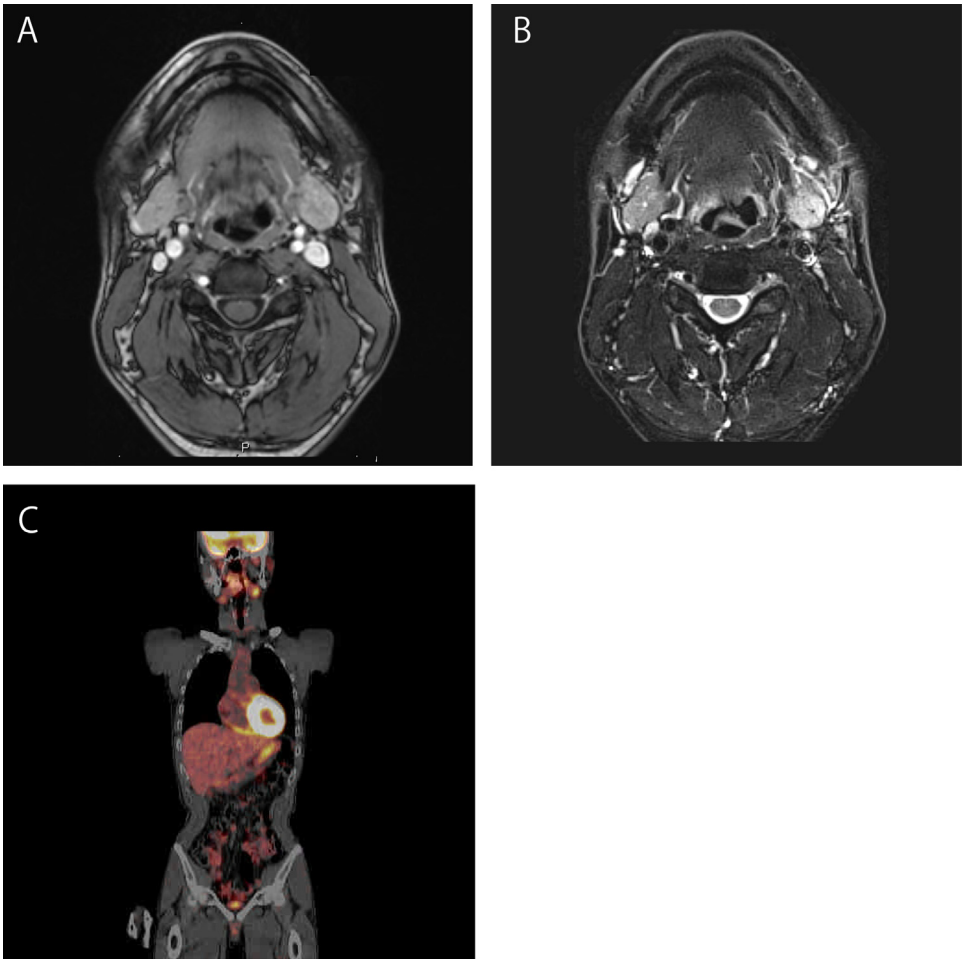

Fig. 1. The tumor in the left submandibular gland was hyposignal on T1-weighted images (A) and hypersignal on T2-weighted images (B). Its marginal was blurring. PET (C) showed abnormal accumulation in the left submandibular gland and gastric wall.

tumor with marginal blurring, which was hyposignal on T1-weighted images and hypersignal on T2-weighted images (Fig. 1). There was an enlarged lymph node immediately lateral to the left submandibular gland. Positron-emission tomography (PET) and upper gastrointestinal endoscopy were also performed and there was no evidence of malignancy other than in the left submandibular gland (Fig. 1). Therefore the left submandibular gland was considered the primary site of the tumor. The patient subsequently underwent the left submandibular gland resection and the left selective neck dissection levels I–III. There was a white solid mass, which had well defined borders and measured 20 mm × 20 mm × 12 mm, in the submandibular gland. Microscopic examination of the mass found proliferating tumor cells showing nests and a trabecular pattern. The tumor cells were large and polygonal with a moderate amount of mildly eosinophilic cytoplasm. Their nuclei displayed coarse and vesicular chromatin with conspicuous nucleoli. The mitotic counts of the tumor cells were over 30 per 10 high-power fields (Fig. 2). Under immunohistochemical staining for neuroendocrine markers, synaptophysin and CD 56 were positive (Fig. 3), and chromogranin was negative.

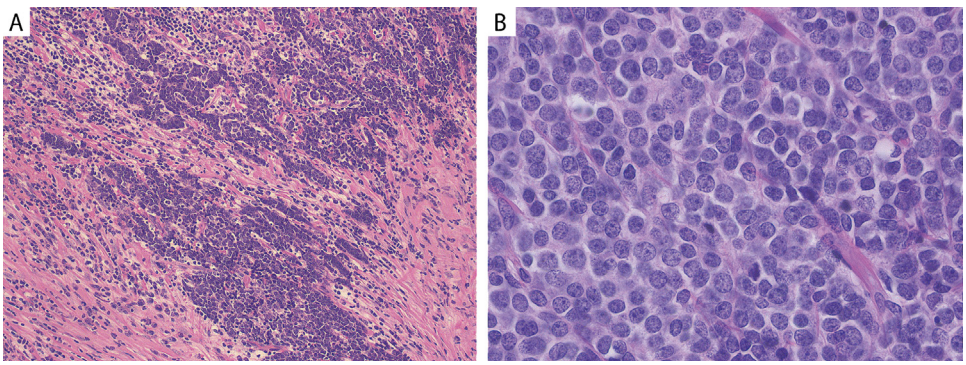

Fig. 2. Microscopically tumor cells proliferated showing nests pattern and a trabecular pattern (A: H-E stain, 100×). The tumor cells were large and polygonal with a moderate amount of mildly eosinophilic cytoplasm. Their nuclei displayed coarse and vesicular chromatin with conspicuous nucleoli. The mitotic counts were over 30 per 10 high-power fields (B: H-E stain, 400×).