

Metastasis of Upper Gingival Squamous Cell Carcinoma to Buccinator Lymph Node: Case Report and Review of the Literature

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Abstract

Background: Metastasis to the lymph nodes is the most prognostic factor in patients with oral cancer. The antegrade lymphatic flow in patients with normal anatomy and physiology makes metastasis of upper gingival cancer to buccinator lymph nodes unlikely and uncommon. **Case Presentation:** A 50-year-old woman presented with a locally advanced squamous cell carcinoma 87 × 28 mm on her upper left anterior region of gingiva, along with metastatic buccinator nodes in the left and right respectively 26 × 23 mm and 24 × 22 mm, cervical lymph nodes and retropharyngeal lymph node without distant metastasis. Metastatic buccinator lymph nodes were independent of the primary tumor and round in shape. She underwent a multidisciplinary treatment by induction chemotherapy consisting of Docetaxel-Cisplatin-5 Fluoro Uracile. Two weeks after, she was treated with adjuvant radiotherapy (69.96Gy/33 fractions) with concurrent Cisplatin chemotherapy 40 mg/m² per week for five weeks. After two months, she returned with a scale four of performance status and died five days later. **Conclusion:** Metastasis to buccinator lymph nodes from upper gingival cancer is rare, and indicates a poor prognosis when present. We suggest that the possibility of metastasis to the buccinator node should be considered thoroughly in planning treatment for locally advanced oral cancer.

Keywords

Buccinator Lymph Nodes, Facial Lymph Nodes, Oral Cancer, Squamous Cell Carcinoma, Upper Gingiva

1. Background

Lymph node metastasis is the most prognostic factor in patients with oral cancer.

Primary cancers in the oral cavity region frequently metastasize to level I–III nodes, whereas metastasis of oral cancer to facial lymph nodes (FN) is rare 16% [1] [2]. FN have been subcategorized as malar, infraorbital, buccinator, and mandibular lymph nodes [2] [3]. Buccinator is among those FN which is a rare metastasis for oral cavity cancer and its location is in the buccomasseteric region, as shown in **Figure 1**. The buccomasseteric region is bounded by the buccinator medially and the zygomaticus major laterally, while the masseter is located posteriorly (**Figure 2**). It consists of the buccal fat, the angular branch of the facial artery, the facial vein, the buccal artery, nerves, the terminal part of the parotid duct and the facial node. Superiorly this space leads to the masticator space with often incomplete facial boundaries between [4]. Buccinator lymph nodes (BN) are present in the buccinator space along the branches of the facial vessels [5]. Metastasis of oral cancer to BN is uncommon. The aim of this report is to analyze the clinical characteristics and course of Buccinator lymph nodes metastases in patients with upper gingival squamous cell carcinoma.

2. Case Presentation

A 50-year-old woman came to our hospital for a locally advanced squamous cell carcinoma on her upper left gingiva, after a consultation with her dentist who made the biopsy. This patient has no past medical history, and is a non-smoker. The symptomatology started five months before with an oral lesion with a painless mass in the left upper gingiva with a bilateral cheek swelling. Consultation by a dentist who made the biopsy. This patient was referred to our hospital. Intra-oral examination showed a tumor with induration on the left anterior region of the upper gingiva. A submucosal mass independent of the gingival tumor, was palpable in the left and right buccal region. It was a well-rounded, mobile mass 15 mm in the left and 25 mm in the right. Submandibular and cervical lymph nodes on the left side were also palpable. A computed tomography (CT) scan with contrast showed a large gingival tumor 87 × 28 mm, with destruction of the adjacent maxillary bone, metastatic left-cervical lymph node 21mm and left parapharyngeal node 21 mm. CT imaging showed no metastases to the lungs and no liver metastasis on ultrasound. Magnetic resonance imaging (MRI) showed a left gingival maxillary process 52 × 35 mm, which infiltrates the upper lip, upper maxillary arch, and hard palate. A non-homogeneously enhanced mass was identified in the left and right buccinator space along the facial vessels, anterior to the anterior edge of the masseter muscle, and lateral to the buccinator muscle respectively 26 × 23 mm and 24 × 22 mm (**Figure 3**). Moreover, T1-weighted MRI showed a thin layer with high signal, indicative of fatty tissue between this mass and the primary tumor, indicating that the mass was independent of the primary tumor. Based on its anatomic location, the mass appeared to be metastatic disease to BN. Metastatic BN was round in shape, hypoechogenic, with well-defined borders, and without an echogenic hilus. Greyscale sonogram showed some metastatic cervical lymph nodes level Ib, level II (30 × 23 mm), level V (10 mm) on the left; bilateral level III

nodes (17 × 16 mm on the left). A left retropharyngeal node appeared in the T2-weighted MRI and filled the glosso tonsillar sulcus. According to the AJCC 2017, the tumor was diagnosed as a cT4aN2cM0 squamous cell carcinoma of the upper gingiva.

The patient received induction chemotherapy, consisting of 75 mg/m² cisplatin, 75 mg/m² Docetaxel both on day 1 and 750 mg/m²/day 5-fluorouracil by continuous infusion (i.v.) for five consecutive days. Examination after three cycles of chemotherapy showed marked shrinkage of the primary tumor. A slight reduction in BN size was observed. According to the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines, version 1.1 [6], this patient showed a partial response to treatment. Two weeks after the end of neoadjuvant chemotherapy, the patient was treated with adjuvant radiochemotherapy concomitant with concurrent Cisplatin chemotherapy 40 mg/m² per week for five weeks. With the development of radiotherapeutic equipment and computer technology, Volumetric Modulated Arc Therapy (VMAT) has been used with a dose of 69.96 Gy in 2.12-Gy daily fractions, 59.4 Gy in 1.8 Gy daily fractions and 54 Gy in 1.63 Gy daily fractions respectively for high-risk, intermediate risk and low risk in 33 fractions over 56 days. The patient was immobilized in the supine position with a head, neck,

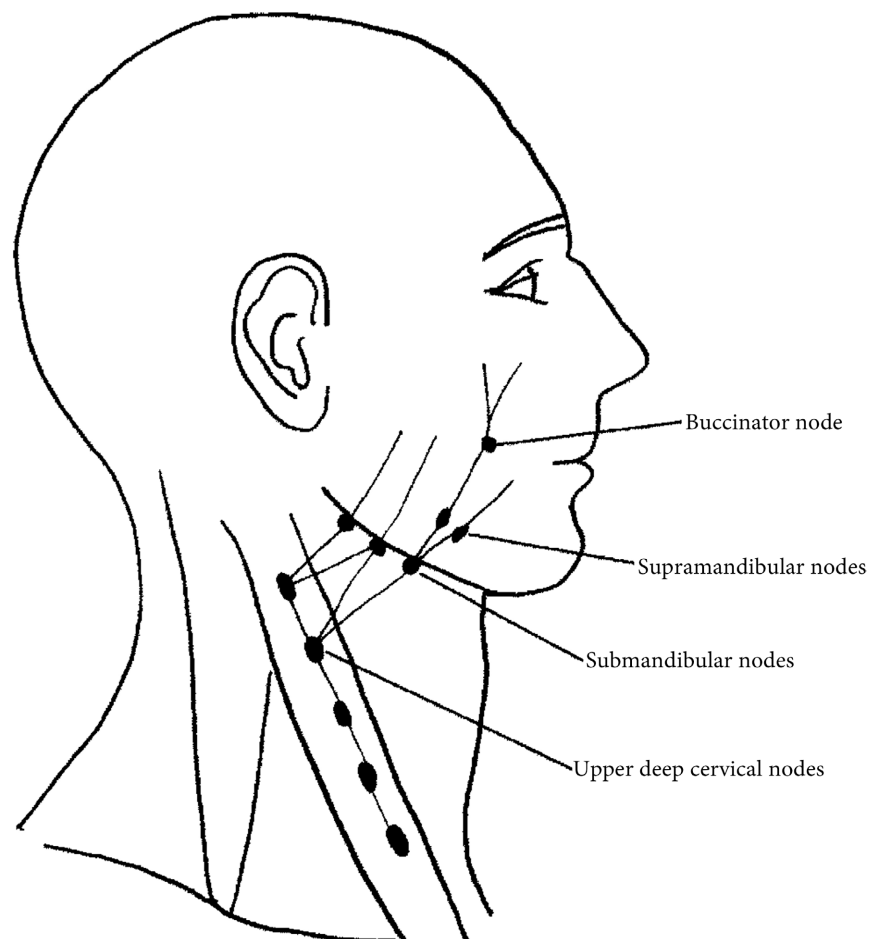


Figure 1. Location of the buccinator node.

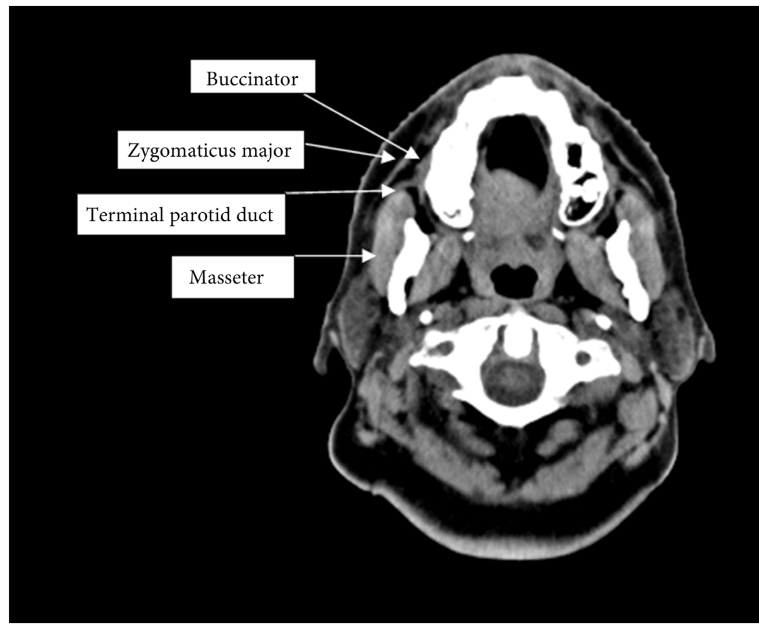


Figure 2. Buccomasseteric region bounded by zygomaticus major, masseter, buccinator inserting into pterygomandibular raphe and terminal parotid duct.

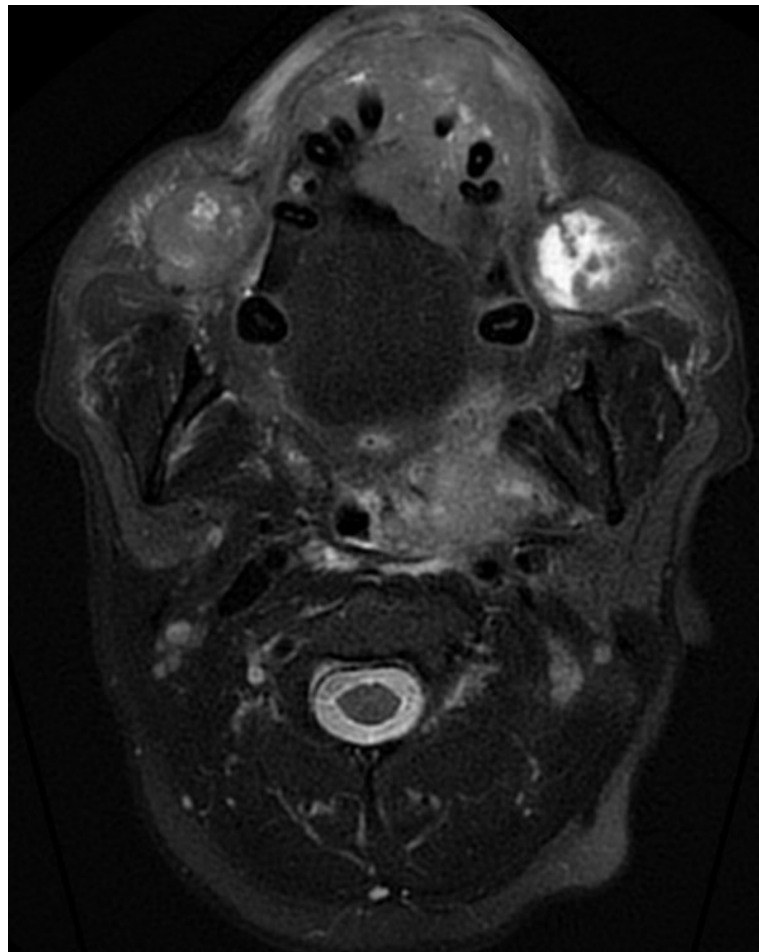


Figure 3. Left and right buccinator nodes for the actual case.

and shoulder thermoplastic mask. Two set images, with and without contrast, were obtained from the CT simulator for treatment planning purposes. This patient was scanned with serial 3-mm slices from the vertex through the clavicles. The delineation of gross tumor volume (GTV), was based on a combination of clinical, endoscopic, and imaging findings that include the primary disease, lymph nodes > 1 cm in diameter. Three CTVs were defined as follows: $CTV_{69,96} = GTV + 5 \text{ mm margin}$; $CTV_{59,4} = CTV_{69,96} + 5 \text{ mm margin} + \text{cervical lymph nodes Ib to Iva} + \text{one level node upper and lower to the BN}$, $CTV_{54} = CTV_{59,4} + 5\text{mm}$. During the radiation treatment, Grade 2 mucositis and dermatitis were established.

Two months later, at the end of the adjuvant chemo radiotherapy, the patient returned to our Hospital with scale four of performance status. CT imaging showed multiple metastasis to the lungs and liver. The patient died five days later.

3. Discussion

Facial nodes are inconsistently observed and frequently absent in upper gingival squamous cell carcinoma. When present, these nodes are located in the subcutaneous space along the branches of the facial vessels [5]. Most of the afferent drainage of BN is from the skin and subcutaneous tissues of the upper and lower eyelids, nose, and cheek. Moreover, the lymphatics of the perilabial and buccal mucosa drain directly into these nodes [7]. The efferent drainage of BN is to the submandibular nodes [3] [5]. Metastasis to BN from oral cancer especially in upper gingiva is uncommon. Kimura reported in his study that patients with cheek swelling had imaging findings that were suggestive of cancer spread into the buccal space [8]. This finding may support the cheek swelling presented in our case. To our knowledge, there have been 15 patients with oral cancers with metastasis to BN reported in the literature (Table 1) [3] [9]-[13].

In these study, metastasis to BN were present in three upper gingival cancer. As far as the authors are aware to date, with our case, four cases have been described in upper gingival squamous cell carcinoma with BN metastasis [3] [9]-[13]. These literature reviews show the possibility of node metastasis in upper gingival carcinoma to Buccinator region and precisely its scarcity. Tart *et al.* reported that BN can be present before diagnosis or during treatment or even after the treatment. They described in their study that four were involved at the first examination, two during the initial treatment and the remaining four after that [3]. Our patient reported in this report presented the BN at the time of diagnosis and this BN metastasis has been considered during the treatment in the radiation field with a good response in the BN area. We may consider the possibility of BN involvement in upper gingival cancer even this metastasis is absent at the time of diagnosis. Kimura *et al.* reported that cancer from upper gingival anterior region spread frequently into the buccal space than from those in the molar region and face and neck space involvement by upper gingival cancer was not observed in patients who did not have cancerous alveolar ridge destruction [8]. These findings may support the above hypothesis. Squamous cell carcinoma was the most common pathologic

type, being present in nine (69 %) of these 15 patients [3] [9]-[12]. Hyo-Cheol Kim described that buccal space lymph node metastasis is typically associated with squamous cell carcinoma of the face. These results are similar to the histologic type of this case. BN appears as a well-circumscribed mass with rim enhancement and central low attenuation on the CT scan or as high signal intensity on the T2-weighted images [14]. This mass is an individualized mass round in shape at the buccinator region as described in our report. When BN metastasis is present in oral squamous cell carcinoma (OSCC), it indicates an advanced disease [1] [15]. It has been shown that tumour stage has a marked correlation with the prognosis of OSCC [16]. The standard strategy for advanced OSCC comprises a multidisciplinary approach including radical surgery and postoperative radiotherapy with or without systemic chemotherapy [17] [18]. After a multidisciplinary decision, this case was deemed inoperable cancer. She received three cycles of induction chemotherapy (ICT) with docetaxel-cisplatin-5-fluorouracil (TPF) followed by chemoradiation therapy. More controversial is the use of ICT followed by radiotherapy or chemoradiotherapy as a routine treatment in patients with inoperable disease [19]. TPF has now been established as an ICT regimen that yields better response rates and a milder toxicity profile than earlier induction regimens, including Cisplatin-5 Fluorouracile (PF). Two key randomized phase III trials have established standard practices for the safe administration of TPF: the European trial TAX 323/EORTC 24971 and the American trial TAX 324. The TAX 323/EORTC 24971 study delivered four cycles of TPF 75 mg/m² docetaxel, 75 mg/m² cisplatin, both on day 1 and 750 mg/m²/day 5-FU by continuous intravenous (i.v.) infusion for five consecutive days followed by radiotherapy and conferred significant survival benefits in a population of patients with previously untreated, unresectable locally advanced squamous cell carcinoma in the head and neck (LA SCCHN) [20]. Results indicated that TPF with radiotherapy prolonged progression free survival (PFS) (median, 11.0 versus 8.2 months in the TPF versus PF arms of TAX 323, respectively), reduced risk of death by 27%, and prolonged overall survival (OS) (median, 18.8 months versus 14.5 months in the TPF versus PF arms of TAX 323, respectively) over PF ICT [21]. Patients with a high risk of distant failure (DF) and LA SCCHN with multiple involved nodes, large-volume nodal disease, and low nodes appear to gain certain benefits from the sequential chemotherapy approach. In DeCIDE, patients with N2–N3 disease experienced a trend in improved recurrence-free survival and lower cumulative incidence of SCCHN-related death with TPF chemoradiotherapy (versus chemoradiotherapy) [20]. With regard to cisplatin scheduling, weekly doses ranging from 30 to 40 mg/m² or daily administration at 5 to 7 mg/m² or at 100 mg/m² administered over several days have been increasingly used instead of a standard dose of 100 mg/m² every 21 days. The principle intent of this modification was to improve treatment compliance in order to increase the cumulative cisplatin dose and, consequently, the efficacy of combined therapy. Another rationale for more frequent administration of cisplatin would be to provide radiosensitizing chemotherapy during a larger proportion of the course

of radiotherapy [22]. Compared with the result reported in these study, our treatment was the same, we followed the recommendations for this locally advanced cancer. She received neo-adjuvant chemotherapy, this regimen ICT showed a good response with marked shrinkage of the primary tumor after three cycles, chemoradiation therapy with full dose of radiation and cisplatin 40 mg/m² weekly. She received all prescribed treatment as recommended for this advanced oral squamous cell carcinoma. There were no interruptions of treatment but this patient died after two months of follow-up due to progression of disease with some distant metastasis; however, before treatment, it was a locally advanced disease, not a metastatic disease.

Gadoni *et al.* report a significant association between advanced tumour stage (S III - IV) and poor overall and disease-specific survival [23]. Kimura in his report showed three cases of upper gingival Squamous cell carcinoma (SCC) with BN metastasis with one case with no evidence of disease and two deaths from disease at 6 and 10 months of follow-up [9]. Our patient had the fewest follow-ups compared with the others. It has been shown that the presence of BN metastasis in upper gingival SCC has a poor prognosis. Metastasis of oral squamous cell carcinoma (OSCC) to FN has been reported to indicate advanced disease [1] [15] and to be a risk factor for local recurrence and poor prognosis [1] [2]. This poor prognosis may indicate that metastases of the buccinator nodes are as important as cervical node metastases in oral squamous cell carcinoma and should be considered in treatment planning, even if it is absent.

Table 1. Patients with metastasis to BN from oral cancer.

Patient	Reference	Site of primary tumor	Histology	Treatment	Prognosis
1	Tart <i>et al.</i> 1993	Buccal mucosa	Adenocarcinoma	ND	NED, 10 m
2	Tart <i>et al.</i> 1993	Alveolar (upper or lower were not described)	Carcinoma	ND	LTF
3	Tart <i>et al.</i> 1993	Retromolar trigone	ND	ND	DOD
4	Tart <i>et al.</i> 1993	Buccal mucosa	SCC	ND	AWD, 3 m
5	Miyazaki <i>et al.</i> 1999	Maxillary alveolar process	Plasmacytoma	S + RT	NED, 18 m
6	Kimura <i>et al.</i> 2000	Buccal mucosa	SCC	Palliative	DOD, 11 m
7	Kimura <i>et al.</i> 2000	Buccal mucosa	SCC	S + RT	NED
8	Kimura <i>et al.</i> 2000	Upper gingiva	SCC	S	NED
9	Kimura <i>et al.</i> 2000	Upper gingiva	SCC	RT	DOD, 6 m
10	Kimura <i>et al.</i> 2000	Upper gingiva	SCC	S	DOD, 10 m
11	Maruoka <i>et al.</i> 2005	Buccal mucosa	SCC	S† + RT	DOD, 8 y
12	Maruoka <i>et al.</i> 2005	Buccal mucosa	SCC	S	DOD, 11 m
13	Takada <i>et al.</i> 2018	Lower gingiva	SCC	CT + S + CRT	NED, 2 y
14	Tomioka <i>et al.</i> 2018	Buccal mucosa	ND	S + CT	NED, 6 y
15	Tomioka <i>et al.</i> 2018	Lower gingiva	ND	CT + S + CRT	NED, 2 y
16	Present case	Upper gingiva	SCC	CT + CRT	DOD, 2 m

Abbreviations: BN buccinator lymph node, M male, F female, SCC squamous cell carcinoma, ND not described, S surgery, RT radiotherapy, CT chemotherapy, CRT chemo-radiotherapy, AWD alive with disease, DOD death from disease, LTF lost to follow-up, NED no evidence of disease †Excisional biopsy of buccinator lymph node ‡Numbers are length of follow-up in years (y) and months (m).

4. Conclusion

Metastasis to buccinator lymph nodes from upper gingival cancer is rare, and indicates a poor prognosis. We suggest that the possibility of metastasis to the buccinator lymph nodes should be thoroughly considered in planning treatment for locally advanced oral cancer.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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