

A Case Of Basaloid Cell Carcinoma Of The Floor Of The Mouth

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Citation

M Fukasawa, Y Akazawa, S Kasugai, K Mikami, Y Saito, M Akutsu, Y Kato, K Ido, H Ohto, I Maeda, I Koizuka. *A Case Of Basaloid Cell Carcinoma Of The Floor Of The Mouth*. The Internet Journal of Oncology. 2016 Volume 12 Number 1.

DOI: [10.5580/IJO.37893](https://doi.org/10.5580/IJO.37893)

Abstract

Basaloid squamous cell carcinoma (BSCC) is a rare carcinoma of the head and neck region. It has a worse prognosis than squamous cell carcinoma (SCC), and the control of distant metastasis is associated with prognosis. Treatment for distant metastasis often poses a problem.

We report a case of BSCC (T1N0M0) of the floor of the mouth in a 68-year-old man, who underwent total laryngectomy with bilateral neck dissection and postoperative radiotherapy was given for laryngeal cancer of SCC (T3N2bM0) at the age of 64. We performed tumor resection of the floor of the mouth and confirmed multiple metastases in the lung with CT images taken three months after surgery. We performed a course of Cetuximab combination chemotherapy for the metastases in the lung and observed a complete response for one year.

We compared BSCC of the floor of the mouth with SCC of the larynx by immunostaining. BSCC exhibited strong positive staining for p53 and Ki-67. Therefore, BSCC might be more invasive and has a higher cellular proliferative capacity than SCC. Our results indicated that BSCC is an aggressive tumor and Cetuximab combination chemotherapy might be one of the useful treatments for distant metastasis.

INTRODUCTION

Basaloid squamous cell carcinoma (BSCC) is a rare distinct variant of squamous cell carcinoma (SCC) [1]. BSCC is considered aggressive based on the clinical behavior, having frequent local recurrences and regional and distant metastasis. A treatment method similar to that for SCC is considered sufficient for localized treatment. However, distant metastasis is often a problem, and at present, there has not been much research on chemotherapy. [2, 3]

We used Cetuximab combination chemotherapy for multiple metastases of BSCC of the floor of the mouth to the lung and observed a complete response (CR) for one year via computed tomography (CT). Using immunohistochemical studies, we compared SCC of laryngeal cancer, BSCC of the floor of the mouth, and the metastatic lung cancer. We reviewed the clinical course of this case according to the current literature. The patient provided written informed consent.

CASE REPORT

A 68-year-old man visited our hospital regular follow up after laryngeal cancer treatment. Medical history showed that he had h/o alcoholism, gastric ulcer, hemorrhoids, and laryngeal cancer (when he was 64-years-old). He has since stopped smoking after having smoked 40 packs/year and also stopped excessive alcoholic dependency after the operation of his laryngeal cancer. He underwent total laryngectomy with bilateral neck dissection for laryngeal cancer (T3N2bM0) in June 2010 followed by postoperative radiotherapy (59.4 Gy). The course after treatment was uneventful without local recurrence or metastasis of the disease for 48 months after the operation. However, he noticed a mass on the floor of the mouth in January 2014 and we confirmed a firm protruding mass of 1 cm in size on the sublingual caruncle. We performed magnetic resonance imaging (MRI) and computed tomography (CT). Axial gadolinium-enhanced T1-weighted images of MRI showing a high mass lesion and heterogeneous signal intensity and

T2-weighted images showing iso-signal intensity and diffusion-weighted images showing high signal intensity (Fig. 1a, 1b, and 1c). Because the tumor size was too small it was hard to be seen from CT images (Fig. 1d). We performed a biopsy for the tumor and pathologically, BSCC was suspected.

We performed tumor resection of the floor of the mouth and made a diagnosis of BSCC (pT1N0M0). We confirmed multiple metastases in the lung with CT images taken three months after surgery (Fig. 1e). While the results of PET/CT showed abnormal accumulation in the colon, neither of the lungs showed any abnormal accumulation. Therefore, we performed a lower digestive tract endoscopy, and confirmed a lesion suggestive of early colon cancer. Thoracoscopic left upper lobe segmental resection was performed to identify the primary site of the multiple lung tumors. The diagnosis was metastases in the lung from the BSCC of the floor of the mouth. We performed a course of Cetuximab combination chemotherapy for the metastases in the lung (weekly Cetuximab [week 1, 400 mg/m²; subsequent weeks, 250 mg/m²] with CDDP [100mg/m², day 1] and 5-FU [1000mg/m²/day, days 1-4]). Because the patient could not endure itchy caused by skin reaction that was an adverse event, i.e. disorder of grade 1 with perionychia and dermatitis, we could not continue the treatment although partial response was obtained through the CT images. CR was achieved after chemotherapy for three months as seen with CT images. There was no recurrence observed in the CT images taken one year after chemotherapy (Fig. 1f).

HISTOPATHOLOGICAL STUDY

The tumor had a firm elevated, outgrowth surface. It measured 1.6 × 1.5 × 0.5 cm in size and was located on the sublingual caruncle region. Microscopically, invasive growth of basaloid epithelial tumor cells forming nests was detected in the subepithelial layer of the BSCC of the floor of the mouth (Fig. 2a). The tumor cells showed a high nuclear grade and numerous mitotic figures (Fig. 2b). The epithelium adjacent to BSCC foci displayed epithelial dysplasia (Fig. 2c and 2d). Squamous component was present in the foci of the tumor nest (Fig. 2d). While invasive keratinizing SCC present at the SCC of the larynx (Fig. 2e and 2f), histological sections of the BSCC of multiple metastases in the lung didn't have keratinizing SCC and closely resembled the BSCC of the floor of the mouth (Fig. 2g and 2h). The epithelial component of the present tumor fully met the criteria of the BSCC.

IMMUNOHISTOCHEMICAL STUDY

Immunohistochemistry for p16, p53, Ki-67, and epidermal growth factor receptor (EGFR) was performed on 5- μ m-thick sections obtained from selected paraffin-embedded blocks containing tumor. Paraffin-embedded tissue sections were deparaffinized in xylene and rehydrated in graded alcohol. Antigen retrieval was performed with a citrate buffer (pH 6.0) or 1 mM Tris-EDTA (pH9.0) depending on the antibodies. Antibodies against p16 (anti clone 4A4), p53 (anti clone DO-7), Ki-67 (anti clone MIB-1) and EGFR (anti clone SP4) were used.

All tumor cells of SCC of larynx, BSCC of the oral floor and metastatic lung cancer were immunonegative for p16 (Fig. 3a, 3e, and 3i). The expressions were observed with diffusely immunopositive for p53 at the BSCC (origin and metastasis) and partially immunopositive at the SCC of Larynx (Fig. 3b, 3f, and 3j). The expressions were observed with diffusely immunopositive for EGFR for SCC of Larynx and BSCC of the floor of the mouth and partially immunopositive for metastatic lung cancer (Fig. 3c, 3g, and 3k). The positive rates of Ki-67 in SCC of the larynx, BSCC of the oral floor and metastatic lung cancer were approximately 30%, 70% and 90% (Fig. 3d, 3h, and 3l). The immunohistochemical stainings are shown in Figure 3 and Table 1.

Figure 1

The BSCC of oral floor in a 69-year-old man. We performed magnetic resonance imaging (MRI) and computed tomography (CT). (a) Axial gadolinium-enhanced T1-weighted images shows a high mass lesion and heterogeneous signal intensity area; (b) T2-weighted images shows iso signal intensity; (c) Diffusion-weighted images shows high signal intensity; (d) It is difficult to be shown due to small tumor size, but CT indicated strong contrast enhancement effect moderately on the right side from the anterior of the floor of the mouth. (e) CT images of the multiple lung metastases three months after surgery. (f) CR is obtained based on CT images of multiple metastases in the lung one year after a course of Cetuximab combination chemotherapy.

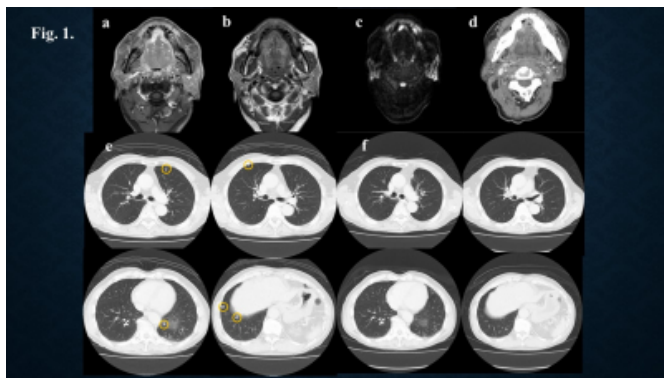


Figure 2

Hematoxylin and eosin stain (a, b, c, d) Histological sections of the BSCC of the oral floor (a) Invasive growth of basaloid epithelial tumor cells forming nests in the subepithelial layer. (b) The tumor cells showed basaloid feature with a high nuclear grade. (c, d) Epithelium adjacent to BSCC foci displayed epithelial dysplasia. Squamous component is present in foci of the tumor nest. (e, f) The keratinizing SCC of the larynx is present in the subepithelial layer. (g, h) In the BSCC of multiple metastases in the lung, the cancer cell nests resemble those of the BSCC of the oral floor closely.

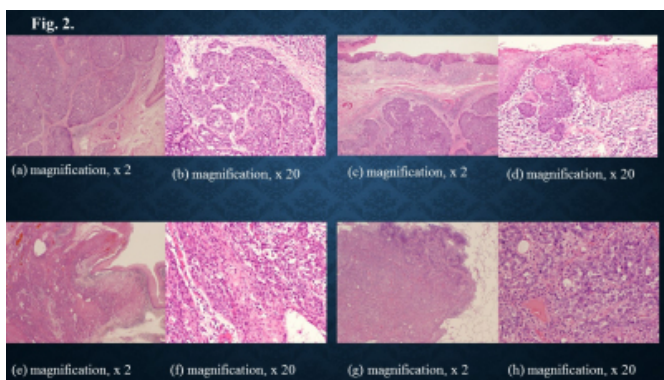


Figure 3

(a, b, c, d) Immunohistochemistry of the keratinizing SCC of the larynx. (e, f, g, h) Immunohistochemistry of the BSCC of the oral floor. (I, j, k, l) Immunohistochemistry of the BSCC of multiple metastases in the lung. a, e, i: All tumor cells are immunonegative for p16. b: The tumor cells are partially immunopositive for p53. f, j: The tumor cells are diffusely immunopositive for p53. c, g: The tumor cells are partially immunopositive for EGFR. k: The tumor cells are focally immunopositive for EGFR. d, h, l: Immunochemical study for ki67: a, h, and l of ki67 labeling index were approximately 30%, 70%, and 80%.

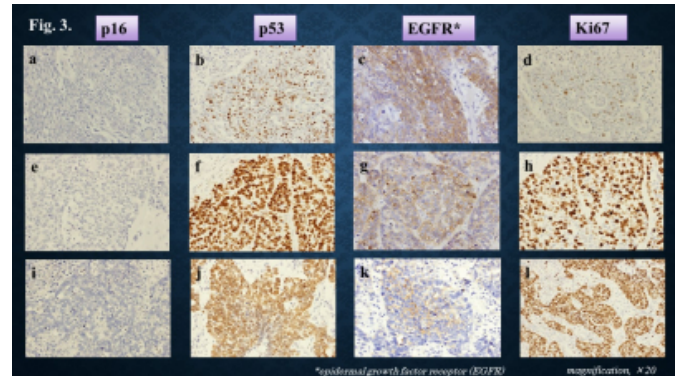


Table 1

Immunohistochemistry results for p16, p53, Ki-67 and EGFR performed on the BSCC of the floor of the mouth, multiple metastases in the lung and SCC of the larynx

	SCC of the Larynx	BSCC of the floor of the mouth	BSCC of the metastasis in the lung
EGFR	positive ++	positive ++	positive +
Ki-67 positive ratio	approximately 30%	approximately 70%	approximately 90%
p16	negative	negative	negative
p53	positive +	positive +++	positive +++

DISCUSSION

BSCC was first described by Wain et al., in 1986 [1] as a rare malignant tumor that presents in the head and neck region. BSCC was officially recognized as a distinct clinico-pathologic entity in the World Health Organization (WHO) 2005 classification, where it was described as an aggressive variant of SCC characterized by an advanced stage at the time of diagnosis and a poor prognosis [2]. The tumor always has metastases in the regional lymph nodes or involving the lungs, bone, skin and brain. Clinically, some authors have reported that it is an aggressive tumor with high rates of nodal and distant metastasis [3-6]. The lung is the main target for distant metastases of BSCC [3]. Winzenburg et al. [4] showed significant differences in the survivals of

BSCC with and without lymph node metastases, with survivals of 18.6 and 47.6 months respectively. Some authors have reported that metachronic second primary tumors have a high incidence of about 15.0 % in the head and neck BSCC [3]. In contrast, Banks et al. [7] reported that the frequency of a second primary tumor in patients with oral BSCC was 5.0 %. In this current case, the patient had laryngeal cancer and colon cancer in his 60's.

BSCCs of the oral cavity have been reported in literature, with a strong predisposition for the base of the tongue (61%) and the floor of the mouth (30%) [3, 8]. Other areas in the head and neck region that are most frequently affected are the hypopharynx and tonsils. BSCC of the upper aerodigestive tract typically occurs in old age and commonly affects males [9].

Microscopically, it is characterized by a biphasic pattern. The basaloid component typically consisted of cords and nests of basaloid cells, and keratin pearls or squamous cell components were interspersed among the basaloid islands. Basaloid cells with relatively light cytoplasm always showed a cribriform structure with comedonecrosis [6-8]. This case of tumor showed that the squamous cell component was complex with a basaloid component. Solid nests with the typical cell population, basaloid at the periphery and squamous at the center, are the most common growth patterns of BSCCs. It is very difficult to distinguish BSCC from SCC because the clinical features of BSCC are similar to conventional SCC. Therefore, diagnosis depends mainly on the histopathological and immunohistochemical features [3, 4, 7, 8]. Differential diagnosis for BSCC includes basal cell carcinoma, adenoid cystic carcinoma, poorly differentiated carcinoma and basal cell adenocarcinoma [5-7]. Immunohistochemically, BSCC expresses cytokeratins and epithelial membrane antigen (EMA), and is focally positive for carcinoembryonic antigen (CEA) [3]. Similar to conventional SCC, BSCC also shows strong association with tobacco and alcohol consumption [10]. Recent studies have shown that the human papilloma virus (HPV) might play a role in the pathogenesis of some of the cases of BSCC [11, 12].

Therefore, we compared BSCC of the floor of the mouth with SCC of the larynx by pathological immunostaining. From the results, BSCC exhibited strong positive staining for p53 and Ki-67 (Fig.3, Table 1). Immunohistochemical analysis revealed that the high positive rate of p53 was associated with a poor degree of differentiation and a poor prognosis. In addition, a high immunopositive rate of Ki-67

indicated that BSCC possessed high proliferative activity and conspicuous malignancy [13]. Strong positive expressions of Ki-67 and p53 suggested high proliferative and malignant activities. Therefore, the invasive ability and cellular proliferative capacity might be higher in the BSCC than SCC. As mentioned previously, it is thought that distant metastasis of the BSCC led to early or higher rates of discovery. We reported this case to be a non-HPV-related tumor after pathological examination. This is due to the negative expression of p16 and the highly positive expression of p53 at the BSCC. The cause of the BSCC is considered to be the patient's history of smoking and drinking. EGFR showed a moderate positive expression at SCC of the larynx and BSCC of the floor of the mouth, and a mild positive expression at the metastatic lung cancer. Cetuximab combination chemotherapy was extremely effective in this case study. So far, there is no established consensus for such treatment. Surgery of tumor and lymph nodes associated with radiotherapy is usually reported in most of the literature [6, 10]. With CDDP-5-FU treatment, there are reports that metastases in the lung of the BSCC disappeared, but the standard chemotherapy regimen for BSCC has not yet been established. We propose that establishment of the chemotherapy involving distant metastasis of the BSCC is necessary through accumulation of the clinical studies and research, including those using Cetuximab combination chemotherapy. Our results indicated that BSCC is an aggressive tumor and Cetuximab combination chemotherapy might be one of the useful treatments for distant metastasis.

CONCLUSION

We experienced one case of BSCC of the oral floor. The BSCC of the oral floor resulted in multiple metastases in the lung during an early postoperative period. We gave a course of Cetuximab combination chemotherapy and CR was obtained for one year. As distant metastasis is high and BSCC is a poor histologic type, examination of combined modality therapy including further chemotherapy, together with the accumulation of case studies will be necessary in future.

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