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Case Report

Basaloid Squamous Cell Carcinoma of Gingiva: A New Case and Review of Literature

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Abstract

Introduction: Basaloid squamous cell carcinoma is a rare aggressive malignancy that is a distinct variant of squamous cell carcinoma. Basaloid squamous cell carcinoma (BSCC) of the oral mucosa other than the tongue is uncommon. Its aggressive clinical behavior is characterized by a high incidence of local recurrence, regional lymph node metastases and mortality rate. Because of the advanced stage at presentation, oral BSCC is prognostically worse.

Presentation of Case: We reported a case of 45 year-old women who presented with a painful, reddish and irregular mass on the left mandibular gingiva and was diagnosed as Stage IV BSCC on the gingiva.

Conclusion: Patients with BSCC have advanced disease at presentation. Accurate histopathologic distinction between the basaloid tumors is of considerable clinical importance. Survival rate of BSCC is less than poorly differentiated squamous cell carcinoma and should have separate treatment protocol from that of conventional squamous cell carcinoma.

Keywords: Basaloid squamous cell carcinoma; gingiva

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Introduction

Worldwide, oral cancer accounts for 2%–4% of all cancer cases. In some regions the prevalence of oral cancer is higher reaching around 45% in developing country like India. In 2004-2009 over 300,000 new cases of oral and oropharyngeal cancer were diagnosed worldwide. During the same time period, over 7,000 affected individuals died of these cancers [1]. Most cancer in the head and neck is squamous cell carcinoma (HNSCC) and the majority is oral squamous cell carcinoma (OSCC). OSCC is probably the eighth most common cancer world-wide but parts of Northern France and East Europe, particularly Hungary, and parts of South America and South East Asia have particularly high prevalences. It is a disease found particularly in low income communities and is still mainly a problem of older people, 90% being in over 45 year age. Warnakulasuriya points out that OSCC remains a lethal disease for over 50% of cases diagnosed annually largely reflected by the fact most cases are in advanced stages at the time of detection despite easy accessibility for regular examination [2]. Percentages of morbidity and mortality in males are 6.6/100,000 and 3.1/100,000 respectively, while in females the same percentages are 2.9/100,000 and 1.4/100,000.[1] Etiology and pathogenesis of basaloid cell carcinoma is similar to conventional squamous carcinoma. Most patients have a long history of smoking and alcohol drinking. In some cases there is a history of previous radiation to the head and neck region. Both represent independent risk factors for the development of squamous cell carcinoma. Smokeless tobacco and other exogenous carcinogens such as occupational, environmental and nutritional factors may also play role in the pathogenesis of this cancer. EBV was detected in few cases using in situ hybridization technique from nasopharyngeal sites. Recent studies detected a higher frequency of HPV and HSV in basaloid tumors than in conventional squamous cell carcinomas of the head and neck. Basaloid squamous cell carcinoma in non smoker young patients revealed infection with HPV, high risk genotype 16. The expression is so significant, to the extent that it led some authors to consider the expression may be important for the diagnosis of this type of squamous cell carcinoma [3]. In countries where the habit of betel-tobacco chewing is widespread, buccal mucosal involvement is more frequent. But, cancer of gingival and alveolar ridge are generally seen in the area of placement of the tobacco quid in those who practice this habit. Consequently the mandibular gingiva is more commonly involved than maxillary gingival [4]. Wain *et al*. [5] first proposed that basaloid squamous cell carcinoma (BSCC) was a distinct variant of squamous cell carcinoma (SCC). In 1991, the World Health Organization included this tumor in the revised classification for the upper respiratory tract and ear [6]. The most frequent sites of occurrence in the upper aerodigestive tract are the base of the tongue, the larynx and the pyriform sinus [7]. Ide *et al*.[8] reported 46 cases of BSCC in the oral mucosa, with a single case of BSCC in the gingiva. It is generally accepted that head and neck BSCC tends to have an aggressive clinical course than stage-matched conventional SCC, with frequent local recurrences; and regional and distant metastases. Here, a case of BSCC arising in the gingiva is reported and the literature reviewed for establishing the clinicopathologic characteristics of oral BSCC. The differential diagnosis with other basaloid oral carcinomas should be made cautiously.

Case report

A 45-year-old women complained of swelling and pain in left mandibular gingiva. Patient was apparently alright before 1 month after which she noticed a small swelling on lower left posterior region of the gingiva. The swelling was initially small pea sized which rapidly increased to attain the present size. Patient also complains of diffuse, dull continuous pain in the same region which is radiating upto the neck, pre & post auricular region on same side since 10 – 15 days; and also complains of dysphagia. Pain is aggravated on eating food, mouth opening. Her medical history was noncontributory. Patient has the habit of tobacco and lime chewing 10-15 times a day since 20 years and keeps the mixture in the left buccal vestibule. Patient also applies mishri on gums and teeth 4-5 times a day since 20 years. Extra oral examination revealed facial asymmetry due to diffuse, ill defined

swelling on left side of face which is firm in consistency and fixed to underlying structures; extending from 2cm posterior to angle of mandible upto 1 cm anterior to corner of mouth; and superiorly extending from 2cm below the zygomatic arch and inferiorly upto to submandibular region on left side & entire submental region (Figure 1). On palpation, the submandibular, pre and post auricular lymph nodes on left side; and submental lymph nodes were enlarged, tender, hard and fixed to underlying structures. Intra oral examination revealed ulceroproliferative growth which was reddish pink, irregular, 5 x 2 cm mass on left mandibular posterior buccal gingiva and obliterating the buccal vestibule in the region of 35 to 38 (Figure 2). On palpation the lesion was firm to hard in consistency and bleeds on provocation; the borders are indurated and lesion is fixed to underlying structures. There were no other oral mucosal anomalies. An incisional biopsy was performed and was reported as BSCC histopathologically. The lesion was staged as T3 N2b M0. The patient was referred to higher center for further treatment.

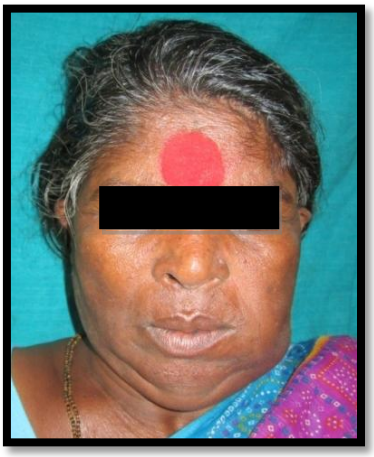


Figure 1

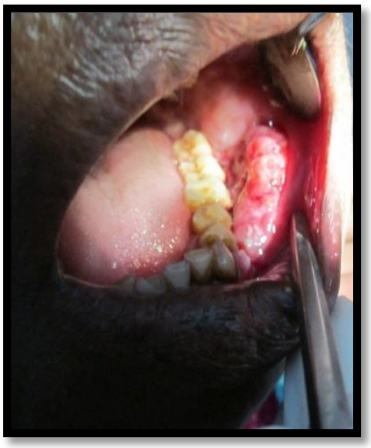
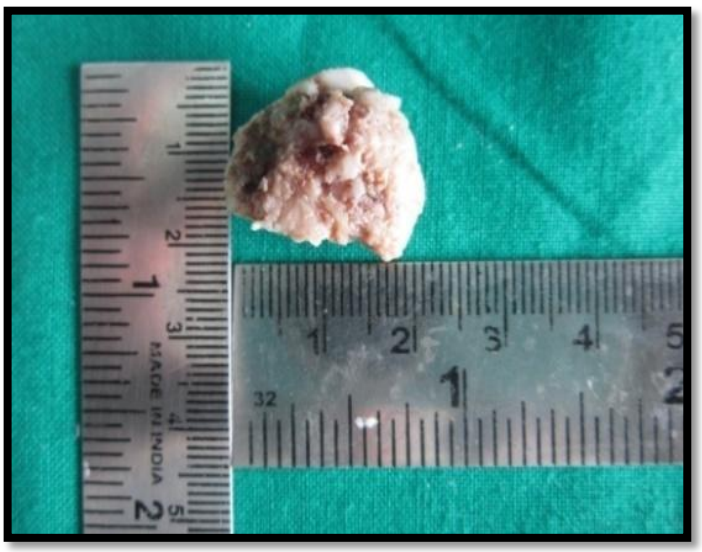


Figure 2

Gross specimen of the incisional biopsy from the region of 36 on macroscopic examination showed a circular mass of size approximately 2.2 X 2.1 X 1.8 cm, grayish white in color and firm in consistency. The outer surface was nodular whereas the undersurface was rough and irregular (figure 3).

Figure 3



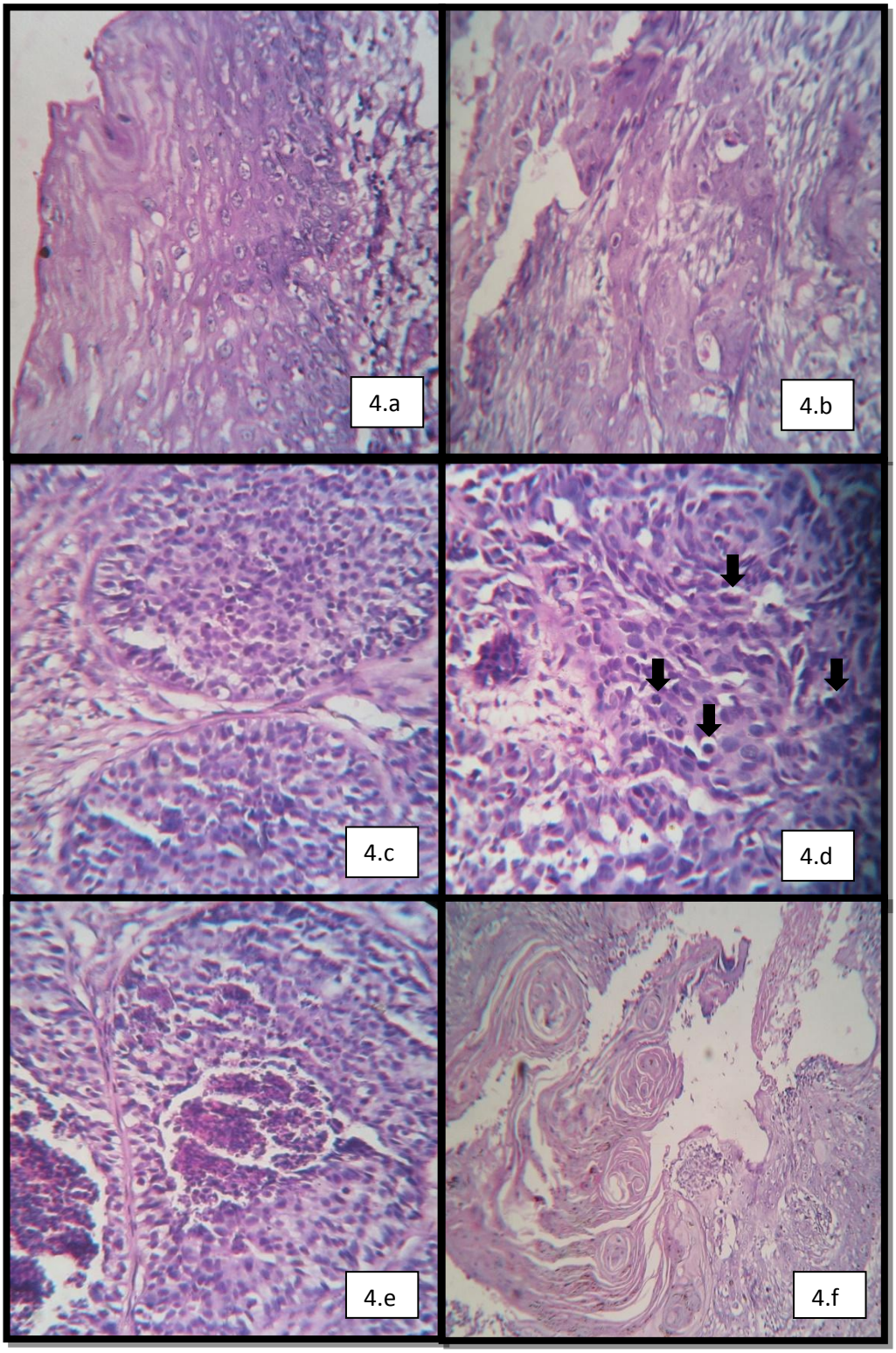


Figure 4.a) Surface epithelium showing dysplastic features involving entire thickness of epithelium (H and E, X40); 4.b) Infiltrating strands of tumor epithelial cells in connective tissue (H and E, X40); 4.c) Islands showing peripheral palisading of basaloid cells (H and E, X40); 4.d) Tumor cells showing numerous mitotic figures (arrows, H and E, X40); 4.e) Tumor islands showing comedo-like necrosis (H and E, X40); 4.f) Infiltrating strands of tumor epithelial cells showing keratin pearl formation (H and E, X10).

Histopathologically, Haematoxylin and eosin stained tissue section showed (figure 4.a-4.f) surface epithelium

which is absent at places and other areas shows dysplastic features involving the whole thickness of epithelium. The basement membrane is indistinct and discontinuous. The underlying connective tissue shows infiltration of dysplastic epithelial cells in the form of strands, cords, islands and sheets. The infiltrating cells shows dysplastic features like cellular and nuclear pleomorphism, increased nuclear cytoplasmic ratio, numerous abnormal mitotic figures, individual cell keratinization and keratin pearl formation. Numerous islands comprising of basaloid cells are evident. At places the islands contain densely packed basaloid cells whereas some areas show islands with central comedo necrosis and periphery of the island shows tall columnar cells with palisaded nuclei. The basaloid cells comprise of hyperchromatic nuclei and scanty cytoplasm. The epithelial islands are separated by loosely and haphazardly arranged bundles of collagen fibers, mild to moderate amount of chronic inflammatory cells like lymphocytes and plasma cells, numerous small blood capillaries are also seen. At places areas of extravasation are seen. Overall features were suggestive of Basaloid squamous cell carcinoma.

Discussion

BSCC is the designation initially introduced by Wain *et al*. in 1986. Since then, the incidence of this tumor is constantly increasing. As early as 1927, Quick and Cutler mentioned the existence of undifferentiated SCC of the nasopharynx, tonsil and tongue base where BSCC occurs more frequently, but they provided no histopathologic details other than this type of tumor is highly malignant and radiosensitive. They recommended the name "transitional cell epidermoid carcinoma". According to Ferlito *et al*., 158 cases have been identified in the literature. Similar, if not identical, tumours have been reported in a wide variety of non head and neck sites [9]. Basaloid squamous cell carcinoma is a rare high grade variant of SCC [10]. In the head and neck, it occurs most commonly in the pyriform sinus, larynx, and base of the tongue [7]. Overall clinical findings of oral BSCC are essentially similar to previously reported results in other anatomic sites. Interestingly, although more than 80% of head and neck BSCC affected males, oral tumors occurred almost equally in both sexes. Greater number of patients with oral BSCC will be needed to explain this discrepancy. Like the conventional SCC, tobacco use and alcohol consumption appear to represent risk factors. Epstein–Barr virus or human papilloma virus may play a role in the development of site specific nasopharyngeal and genital or anal canal BSCCs, but Ide *et al*. [8], did not find evidence of viral infection in their two cases of oral BSCC. BSCC of the oral mucosa is rare. The histologic features of BSCC have been described in many reports [5,7,8,11]. The neoplasm is composed chiefly of basaloid cells with the typical finding of foci of squamous differentiation and the basaloid cells have dark hyperchromatic nuclei and a scant cytoplasm. The neoplasm has squamous differentiation ranging from focal squamous differentiation to Carcinoma in situ (CIS) to invasive SCC. The neoplasm occasionally shows palisading of the peripheral tumor cells, comedonecrosis, and intratumoral cystic spaces. To confirm the epithelial differentiation, earlier investigators used AE1/AE3 stains, although the percentage of positivity varies greatly among different reports [7,10,12,13].

Clinical features of 41 cases of oral BSCC are summarized in Table 1. Oral BSCC has the following characteristics:

(1) a strong predilection for the base of tongue;

(2) an occurrence in an older population with a mean age of 61 years;

(3) male predominance;

(4) an advanced clinical Stage III or IV presentation;

(5) an aggressive clinical course characterized by a high incidence of cervical lymph node metastases at the initial

presentation;
(6) local recurrence;
(7) subsequent lymph node metastases and
(8) death from disease.

These results indicate that the tendency for oral BSCC to present with disease of more advanced stage may be attributed in part to the poor prognosis. Because of the limited number of cases, divided among five anatomical locations in the oral mucosa, no meaningful data are available for therapeutic approaches in each specific site. In 41 cases, 38 patients were treated surgically, 21 of who received radiation therapy, 9 received adjuvant chemotherapy and eight patients had a combination of irradiation and chemotherapy and 3 patients did not undergo any treatment. According to Ide *et al*. [8], few cases of BSCC in the oral mucosa have been reported in the English-language literature, with a single case of BSCC in the gingiva. Later Eiji Hirani *et al*. [14], in 2009 published a review on 6 cases of BSCC occurring in gingiva. The present case adds 1 more case of BSCC occurring in gingiva, making the number to 8.

Table 1 Summary of clinical characteristics of oral BSCC.[8]

Number of affected sites,n= 53	Tongue	28
	Palate	3
	Buccal mucosa	1
	Gingiva	8
Gender (n= 41)	Mal e	23
	Female	18
Age (n= 41)	Range	39-83 years
	Average	61 years
Stage (n=41)	I	8
	II	10
	III	10
	IV	13
No metastasis		16
Metastasis (n= 25)	Local nodal metastasis	18
No treatment		3
Treatment (n=38)	Surgery	38
	Radiation	21
	Chemotherapy	9
	Radiation & Chemotherapy	8
Local recurrence		8
Outcome (n=41)	Distant metastasis	7
	Died of disease	15
	Alive with disease	4
	Alive without disease	18
	Not known	4

The differential diagnosis of BSCC includes adenoid cystic carcinoma (ACC), small cell undifferentiated carcinoma, basal cell adenocarcinoma (BCAC), adenosquamous carcinoma, and basosquamous carcinoma [8,15].Both the cytologic and histomorphologic characteristics of the solid type of ACC are quite similar to those

of BSCC. Klijanienko *et al*. indicated that distinguishing between BSCC and ACC may be difficult or impossible, especially when only a small diagnostic biopsy sample is available. Although one paper stated that immunohistochemistry was not particularly helpful in distinguishing between ACC and BSCC [16], several authors found that immunohistochemistry was helpful in distinguishing between the two [15,17]. Coletta *et al*. [15] found that the cells of ACC expressed CK7, signaling a ductal pattern possibly of salivary gland origin, whereas the basaloid cells in BSCC were positive only for CK14. Furthermore, the presence of basement membrane–like material positive for laminin and type IV collagen in the microcystic spaces is a feature of BSCC but not of ACC. Madur *et al*.[17] found that BSCC were negative for vimentin and S-100. Emanuel *et al*. found that the p63 staining pattern of BSCC differed strikingly from the staining pattern in ACC. BSCC consistently displayed diffuse p63 positively, with staining of nearly 100% of tumor cells. In contrast, ACC displayed a consistently compartmentalized pattern within tumor nests. Andreadis *et al*. found that BSCC and BCAC shared some similar microscopic features, such as basaloid epithelial cell aggregations in solid, membranous, trabecular, and tubular nests separated from each other by thin septa or thick bands of collagenous stroma, a characteristic peripheral palisading of nuclei, foci of necrosis and stromal hyalinization; and immunohistchemical findings are critically helpful in the differential diagnosis of these tumors. Immunohistochemically, CK7, vimentin, and S100 are positive in BCAC but not in BSCC. Cadier *et al*. stated that it was worthwhile to note that basaloid squamous carcinoma is quite distinct from basosquamous carcinoma, which is an atypical basal cell carcinoma of the skin, has squamous elements, is an aggressive tumor, and not uncommonly metastasizes, unlike normal basal cell carcinoma. The clinical course and prognosis of BSCC are thought to be worse than those of typical SCC, based on the high recurrence rates, regional and distant metastases, and lower survival rates [7,11]. However, few studies have evaluated the clinical course of BSCC located exclusively within the mouth, and the sample sizes are too small to be representative or to determine a prognosis [15]. Sampaio Goes *et al*. compared 17 BSCCs in the oral cavity with typical SCCs in the oral cavity and concluded that the prognosis of BSCC does not differ from that of typical SCC when matched for clinical stage. We could find English-language literature summarizing BSCC in the gingival and we summarized the reported cases, including the present case. Unfortunately, the sample size is too small to establish prognosis.

HISTOPATHOLOGICAL DIFFERENTIAL DIAGNOSIS[18]

- Basal cell ameloblastoma
- Adenoid cystic carcinoma (solid variant)
- Adenosquamous carcinoma
- Basal cell adenocarcinoma
- Salivary duct carcinoma
- Small cell undifferentiated carcinoma

According to the various studies performed in the literature, IHC analysis for BSCC showed different cellular components expressing different markers as shown in the Table 2 [15,19]:

Conclusion

Accurate histopathologic distinction between the basaloid tumors is of considerable clinical importance. Since the full extent of BSCC may not be evident in small or superficial biopsy, it is critical that the specimen includes the interface of tumor with surrounding tissue and surface epithelium. BSCC have advanced disease at presentation. Metastasis occurred in 52% cases of BSCC and 13% cases of poorly differentiated squamous cell carcinoma. Survival rate of BSCC is less than half of poorly differentiated squamous cell carcinoma. BSCC should have separate (exceptionally aggressive) treatment protocol from that of conventional SCC [9].

Table 2 Immunohistochemical analysis for BSCC

Cell type	IHC marker
SQUAMOUS DIFFERENTIATION	CK 13+ve areas seen in Basaloid areas.
	CK 1 +ve
	CEA +ve
BASALOID CELLS	CK 13 -ve
	CK 14 +ve (less reactive)
	CK 903 (less reactive)
	p53, p63, Ki 67 +ve
MICROCYSTIC SPACES	Anti- laminin antibody +ve
	Type IV collagen +ve

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