

Whitish Patch over Soft Palate: A Case Report of Incidental Finding of Basaloid Squamous Cell Carcinoma

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Abstract. Introduction: Whitish lesion over the oropharyngeal mucosal lesion is traditionally attributed to benign lesions such as leukoplakia, oral candidiasis or lichen planus, which can be diagnosed through histopathological examination. Yet, performing a biopsy is prudent in all cases of persistent whitish lesions to rule out a more sinister pathology such as malignancy. Herein, we report an incidental finding of a whitish lesion in the soft palate of a gentleman who presented with otalgia and otorrhea, which turned out to be basaloid squamous cell carcinoma (BSCC). Therefore, we highlight the importance of thorough, meticulous and complete Ear, Nose and Throat examinations in all patients as they enable early diagnosis of a sinister pathology in this patient.

Keywords: Basaloid squamous cell carcinoma, Conventional squamous cell carcinoma Immunohistochemistry, Squamous cell carcinoma, Soft palate; Oropharyngeal carcinoma

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1. INTRODUCTION

Basaloid squamous cell carcinoma (BSCC) is a rare histologically distinct variant of squamous cell carcinoma (SCC) which was initially introduced by Wain et al. in 1986.¹⁻⁵ It was then included in the revised edition of WHO classification in 1991.¹⁻⁴ The tumour arises most frequently in the head and neck region with relative frequency of 2%.^{3,6-8} The most common sites being larynx, hypopharynx, tonsil and base of tongue.^{1,6,7,9} Other less common sites in upper aerodigestive tract areas include the floor of the mouth, oral mucosa, palate, sinonasal tract, nasopharynx, trachea and oesophagus.^{6,7,9-11} BSCC encompasses less than 1% of oropharyngeal carcinoma^{1,3} and an estimated 0.5% to 1.5% of all laryngeal SCC.⁸ According to Weidong Shen et al, the incidence rates were 0.45 per 100,000 for BSCC and 0.25 for head and neck BSCC in the United States from year 2000 until 2013.¹² Typically, BSCC manifests at an advanced stage with cervical lymph nodes and distant metastases and has been reported to be have an aggressive

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nature compared with those with SCC.^{1,3,7} It is estimated that 5% of all node-positive SCCs are classified as BSCC.⁷ Despite all attempts to control the disease, BSCC presents with increased morbidity and mortality and frequently are fatal within 12 months from the time of diagnosis.¹ The overall 3-year survival rate of BSCC is estimated to be around 28.5%.³ Given the aggressive nature and the relative rarity of BSCC, we present a case report involving an incidental finding of whitish patch over the soft palate which turned out to be BSCC.

2. CASE PRESENTATION

A 46-year-old Indian gentleman presented with a two-month history of right-sided intermittent otorrhea and otalgia. The patient has been treated with multiple ear drops and oral antibiotics by various general practitioners but to no avail. Besides that, the patient has no reduced hearing, tinnitus, vertigo, and no other recurrent nasal or throat symptoms. The patient denied having dysphagia, odynophagia, hoarseness, neck swelling, or any discomfort in the oral cavity region. His social history revealed that he is a chronic smoker and consumes alcohol occasionally.

Upon examination, the patient was well-built and appeared comfortable under room air. Otoloscopic examination revealed an inflamed right external auditory canal with minimal pus and an intact tympanic membrane. The left ear examination was unremarkable. Nasoendoscopic examination showed no tumour, lesion or signs of infection. However, upon intraoral examination, we noted a leukoplakic patch over the left soft palate region extending to the anterior pillar (**Figure 1**). Further examination with flexible nasopharyngolaryngoscopy examination was unremarkable, and neck palpation revealed no neck nodes. Aural toileting was performed, and the patient was treated with ear drops for right otitis externa. As for the whitish lesion, the patient was treated with oral Aid gel and was given a one-week appointment. One week later, the leukoplakic patch remained persistent over the left soft palate.

A biopsy of the whitish lesion was performed under topical anaesthesia. The histopathological findings showed microinvasive squamous cell carcinoma. We proceeded with staging computed tomography (CT) of the brain to the abdomen, which revealed a localised mucosal thickening of the left soft palate with no local extension or distant metastasis. The patient underwent wide local excision of the left soft palate lesion under general anaesthesia. Histopathological findings revealed stratified squamous epithelium showing dysplasia (**Figure 2**), where the features were suggestive of basaloid squamous cell carcinoma. Immunohistochemistry staining shows the basaloid component expresses BerEP4 (**Figure 3**). Immunohistochemistry staining shows the squamous component expresses epithelial membrane antigen (**Figure 4**)

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The patient was counselled for selective neck dissection and kept in view for radiotherapy and chemotherapy. Initially patient opted for radiotherapy and was referred to the Oncology Unit in another tertiary hospital. However, after further discussion with family members he refused treatment even palliative care due to socio-economical reason and defaulted follow up despite multiple counselling. Thus, we are unable to monitor the patient's progress.



Figure 1 Red arrow shows leukoplakic patch over the left soft palate.

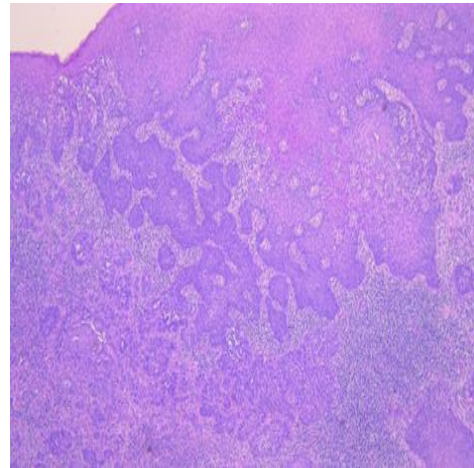


Figure 2 Low power (x200) of the tumour shows malignant basaloid cells arising from the epidermis, disposed in micronodular pattern. Squamoid differentiation is also observed intermingling with the basaloid tumour.

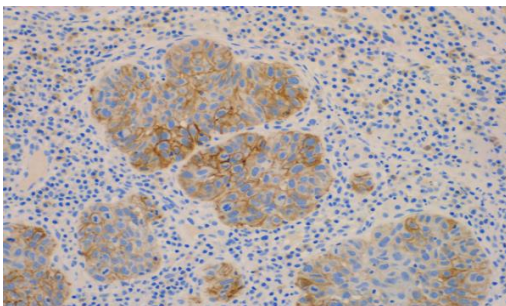


Figure 3 Immunohistochemistry staining shows the basaloid component expresses BerEP4

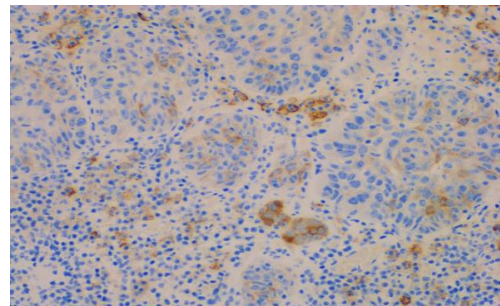


Figure 4 Immunohistochemistry staining shows the squamous component expresses epithelial membrane antigen (EMA)

3. DISCUSSION

BSCC is categorized as malignant surface epithelial tumours and defined as clinically unfavourable and rare variant of SCC composed of a prominent basaloid component and squamous cell differentiation as per WHO classification of head and neck tumours 2017.^{3,4,9} Wain et al. described BSCC as a high-grade and histologically distinct variant of SCC in 1986.⁵ The most common sites being larynx, hypopharynx, tonsil and base of tongue.^{1,6,7,9} It encompasses less than 1% of oropharyngeal carcinoma.^{1,3} It has a high tendency to be multifocal, deeply invasive and metastatic even at the initial presentation.^{6,9} The differential diagnosis of this entity includes adenoid cystic carcinoma, neuroendocrine carcinoma, basal cell adenocarcinoma, adenosquamous carcinoma, and common (well differentiated, moderately differentiated, and poorly differentiated) SCC.^{3,4,9,13,14}

BSCC occurs predominantly in male patients in their 60 and 70s.^{1,4,6,7,9} Tobacco, alcohol abuse and a previous history of radiation to the head and neck region are considered the main risk factors.^{1,4,6,7,9} The patient in our case was a chronic smoker and consumed alcohol occasionally. It is worth noting that BSCC has also been associated with HPV infections particularly HPV type 16, which tend to be more frequent in the oropharynx, in women, and in non-smokers who consume no or little alcohol.^{2,3,7,13-16} Oropharyngeal tumours especially tonsillar cancer are most likely to be HPV positive among head and neck carcinomas of different origin.^{13,16,17} Kleist et al. demonstrated significant associations between HPV and oropharyngeal BSCC.¹³ Whereas, Mellin et al. described a significant association between female gender and increased risk for HPV positive tumours.¹⁶

Numerous recent studies have statistically shown that oropharyngeal BSCC generally shows a better prognosis than laryngeal and non-oropharyngeal BSCC.^{12,13} So it is important not to confuse cases affecting the oral cavity from those affecting the oropharyngeal region.⁴ Recent investigations also suggested that BSCC associated with HPV has a more favourable prognosis than those that are not.^{4,7,13,14} In the study by Lindel et al, the local control rate was higher in HPV positive patients, although with possible confounding factors, such as smoking and alcohol status.¹⁵ The increased radiosensitivity may be caused by the HPV E6 protein, which interferes with the p53 protein, and also by the HPV16 E2 gene, which interferes with the regulation of apoptosis and cell cycle control.¹⁵ However, Cabanillas et al. found a conflicting result where there is no evidence of HPV DNA found in nine cases of pharyngeal BSCC.¹³

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When compared with patients with conventional SCC, the prognosis of patients with BSCC remains poor or uncertain.^{2,4,7,10,18-20} The rate of distant metastasis was six times higher in the cases of BSCC.² Approximately 64% of patients with BSCC develop cervical lymph node metastasis.^{6,20} Distant metastasis involving the lung, bone, skin and brain develops in up to 44% of cases.^{6,20} As the BSCC was diagnosed early, our patient did not have any metastasis at the point of imaging. Winzenburg et al. first identified that distant metastases occurred in 52% of patients with BSCC and 13% of patients with poorly differentiated SCC.² Soriano et al. showed that patients with SCC were associated with notably higher survival rates when compared with patients with BSCC.² However, there are conflicting results by some authors. According to de Sampaio Góes et al, the prognosis did not differ between patients with BSCC of the oral cavity and those with conventional SCC.² Linton et al. demonstrated that patients with oropharynx BSCC had a better prognosis than those with SCC.⁷

The gold standard to diagnose BSCC is based on histopathological examination of the tissue.^{2,6,9,19} The classical histological criteria of BSCC include the presence of dysplastic squamous epithelium infiltrating into the connective tissue, tumour cells showing basaloid appearance with peripheral palisading, increased mitotic activity, hyperchromatic nuclei, comedo necrosis and occasional squamous differentiation.^{1,2,4,7,9,19} Immunohistochemistry (IHC) has been found to be helpful in diagnosing BSCC.^{2,3,6,9,13} Tellechea et al. proposed BerEP4 as an IHC marker of BSCC, and this has been documented in other small series to be efficacious as well.¹³ Our patient demonstrated a typical histologic picture of BSCC. It is worth noting that BSCC exhibits a different clinical course and prognosis compared to the conventional SCC, hence warranting a different treatment course.⁴

Although there is no established consensus for treatment, BSCC demands an aggressive multimodality treatment.^{2,11,18} The treatment of choice in most of the published literature is complete surgical excision with selective neck dissection supplemented with radiotherapy and, in patients with metastatic disease, chemotherapy.^{1,2,11,18-20} Regional control rates of patients who underwent neck dissection and radiotherapy was reported to be high than those who did not.¹⁴ Although chemotherapy is recommended due to its high incidence of distant metastasis, a standard chemotherapy regimen for BSCC has not yet been established.^{2,3,19} Recently, Reiko li et al. reported a case of a 36-year-old man who was successfully treated with induction chemotherapy followed by radical surgery and adjuvant proton beam therapy for a locally invasive BSCC of the nasal cavity where the patient survived for five years without recurrence.¹¹ In addition, Bonner et al. advocated that immunotherapy elicited an improved treatment effect w

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hen compared with radiotherapy alone and resulted in a reduced mortality rate in advanced SCC of head and neck cancer.²¹

Despite all attempts to control the disease, BSCC presents with increased morbidity and mortality and frequently are fatal within 12 months from the time of diagnosis.^{1,18} The overall 3-year survival rate of BSCC is estimated to be around 28.5%.³ According to a study conducted by Weidong Shen et al, the five-year cumulative incidence of cause-specific death after diagnosis of HNBSCC was 26.5%.¹² Therefore, close surveillance is crucial and a long-term study with a large number of patients is warranted to determine the optimal treatment protocols for BSCC.

4. CONCLUSION

We highlight the importance of complete and meticulous ENT examination in all patients with head and neck symptoms. Asymptomatic and persistent whitish oral lesion needs to be investigated thoroughly, including histochemical examination of the lesion, regardless of age, gender and risk factor. Oropharyngeal BSCC requires emergent surgical and chemoradiotherapy owing to its aggressive nature and high propensity for local and distant metastasis.

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