



# Recurring basal cell carcinoma involving exclusively intra-oral mucosa: a case report

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## Abstract:

Basal cell carcinoma (BCC) is the most common skin cancer, but oral involvement is extremely rare. Here, we showed a case of a 71-year-old Caucasian male patient presenting an asymptomatic submucosal nodule in the left buccal mucosa on the same side of a previous BCC skin lesion. Intraoral examination revealed a circumscribed sessile and fibrous mass covered by normal mucosa. An incisional biopsy was performed. Microscopically, the lesion showed uniform, ovoid, dark-staining basaloid cells with medium-sized nuclei and little cytoplasm arranged in islands and strands, invading the underlying connective tissue. These islands demonstrated palisading of the peripheral cells and occasionally central areas with epidermoid differentiation. The final diagnosis was nodular basal cell carcinoma. Although uncommon, recurrent BCC may occur in the oral cavity.

**Keywords:** Basal cell carcinoma, Oral surgery, Oral pathology, Recurrence.

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## INTRODUCTION

Basal cell carcinoma (BCC) is the most frequent cutaneous malignant neoplasm<sup>1</sup>. Most BCC cases occur in men after the sixth decade of life. They are more prevalent in light-skinned people, particularly those living in hot weather with outdoor occupational activity<sup>2</sup>. Chronic and unprotected exposure to ultraviolet radiation from sunlight is considered the most critical risk factor associated with BCC's carcinogenesis. It is noted that BCCs are pretty unusual in black people, where the skin is naturally protected from the effects of ultraviolet radiation by their deep melanin pigmentation<sup>3</sup>. Added risk factors include exposure to ionizing radiation, tanning, UV photo therapies<sup>4</sup>, arsenic exposure<sup>5</sup>, immunosuppression<sup>6</sup>, and, more rarely, genetic syndromes<sup>7</sup>.

According to the WHO Classification of Skin Tumors, ten different histological subtypes of BCC are recognized and divided into lower- and higher-risk groups based on recurrence. All subtypes share steady histological characteristics represented by basaloid cell islands and nests from epidermal basal layers and follicles with peripheral palisade arrangement, scant cytoplasm, and hyperchromatic nuclei<sup>8</sup>. The most frequent clinical presentation is a firm nodule with a depression in the middle, which may progress into an ulcer. BCC usually is painless and grows gradually; however, it may be locally invasive and potentially destructive<sup>9</sup>.

About 80% of BCC cases are diagnosed on the face, which is usually a sun-exposed region. The incidence of BCC in areas less exposed to the sun is uncommon and suggests the involvement of other factors in their carcinogenesis<sup>10,11</sup>. Therefore, the primary BCC involving oral mucosa is extremely rare. Most described cases affect the gums and are not true BCC but rather peripheral ameloblastomas<sup>12</sup>. Likewise, the extension or recurrences of cutaneous BCC in intraoral locations are rarely reported<sup>13,14</sup>. In this paper, we report a case of a recurrent CBC that presented the first clinical sign in the oral cavity.

## CASE REPORT

A 71-year-old male patient presented to the Oral Diagnostic Center, School of Dentistry, University of São Paulo (FO-USP, Brazil), complaining of a lesion in the buccal mucosa. His medical history revealed type 2 diabetes, hypertension, and a cutaneous BCC in the left cheek, treated three years earlier. He reported receiving intense and unprotected sun exposure from a young

age while working as a farmer and in other outdoor assignments.

An intraoral examination revealed an asymptomatic fibrous and lobulated sessile mass covered by normal oral mucosa, measuring approximately 2,5 cm on the left buccal mucosa (Figure 1). Multiple yellow papules corresponding to Fordyce granules were also noticed in the region. Extraoral examination showed a scar on the left cheek corresponding to the healing site of the previous BCC, and it also coincided with the location of the lesion observed intraorally (Figure 2). No pathological lymph nodes were identified.

Considering the clinical signs and BCC history, the main clinical hypothesis was BCC's recurrence. An intraoral incisional biopsy was performed under local anesthesia. The histopathologic examination revealed uniform, ovoid, dark-staining basaloid cells



**Figure 1.** Intraoral examination shows a lobulated circumscribed sessile mass covered by normal mucosa on the left buccal mucosa.



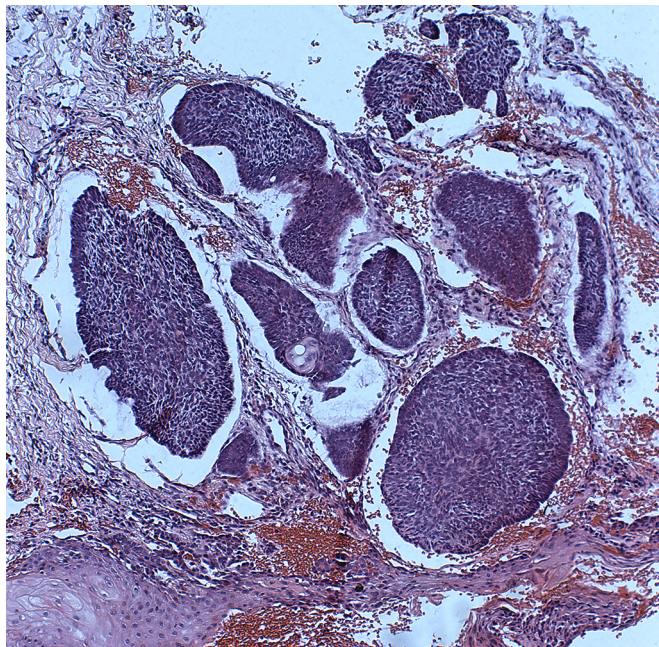
**Figure 2.** Extraoral examination showed a scar on the left cheek corresponding to the healing site of the previous BCC.

with medium-sized nuclei and little cytoplasm arranged in islands and strands, invading the underlying connective tissue and compromising surgical margins (Figure 3). At high power, these islands demonstrated palisading of the peripheral cells, occasionally areas with epidermoid differentiation and retraction spaces from the surrounding stroma (Figure 4). According to these findings, a diagnosis of basal cell carcinoma with areas of epidermoid differentiation was established.

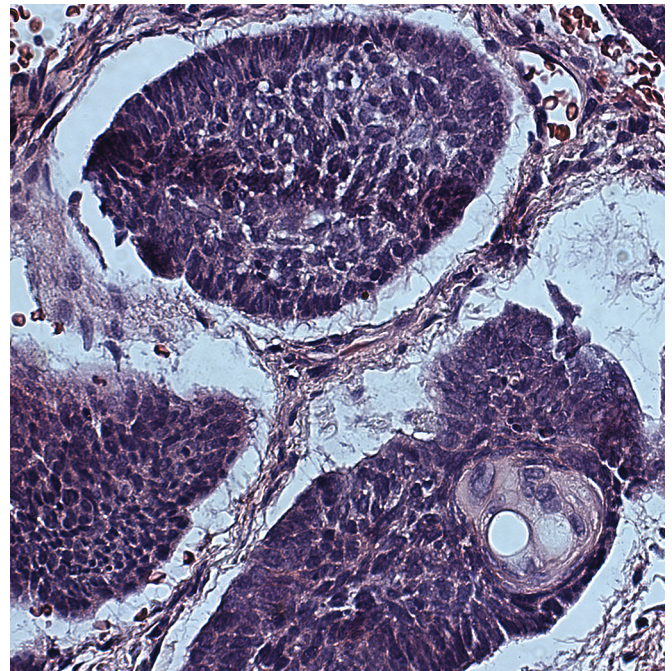
After diagnosis, the patient was referred to the Oncologic Center and underwent surgical treatment with a full-thickness resection with safe margins of labial commissure followed by a microsurgical free flap reconstruction (Figure 5). Histological analysis of surgical specimens confirmed a nodular basal cell carcinoma. During the six months of follow-up, the patient remains without evidence of recurrence or complications.

## DISCUSSION

Basal cell carcinoma (BCC) is the most common cutaneous malignancy, representing a critical issue in public health due to its high incidence and morbidity, mainly in areas closer to the equator<sup>2</sup>. In this report, the patient fits the age, skin tone, gender, and occupational activity related to chronic sun exposure that certainly



**Figure 3.** Photomicrographs of the biopsy specimen revealed uniform, ovoid, dark-staining basaloid cells with medium-sized nuclei and little cytoplasm arranged in islands and strands, invading the underlying connective tissue (H&E, 10X).



**Figure 4.** Neoplastic islands demonstrated palisading of the peripheral cells and occasionally areas with epidermoid differentiation. Note retraction spaces from the surrounding stroma (H&E, 40X).



**Figure 5.** Extraoral aspects of microsurgical free flap reconstruction.

played a critical role in the etiology of the lesion. In addition, the participation of arsenic in the carcinogenesis of this lesion cannot be ruled out since it is a chemical element extensively used as an herbicide and insecticide in agriculture in former times.

BCC originates from the basal layer of the epidermis and is considered a locally invasive tumor with slow spread and low metastatic rate<sup>7</sup>. BCC's main location is the head and neck region, specifically in areas more susceptible to sun damage, such as the eyelids, nose, lips, and scalp. Accordingly, when BCC occurs in unexposed areas, it may be related to other carcinogenic factors, including genetic disorders<sup>10,11</sup>. Nevoid basal cell

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carcinoma syndrome, also known as Gorlin syndrome (GS), is associated with a high susceptibility to developing numerous BCCs from early stages in life. In these patients, BCCs are not restricted to sun-exposed sites, including intra-oral cavity involvement reported in the literature<sup>15</sup>. Genetic alterations involving Patched (PTCH1), aberrant activation of hedgehog (HH) signaling pathway components, inactivation of the TP53, and mutations in other members of the RAS family are related to BCC carcinogenesis<sup>16</sup>.

Primary intra-oral BCCs are very unusual and controversial mainly due to their histological resemblance with peripheral ameloblastoma (PA) and adenocarcinoma (AC); immunohistochemistry is helpful in the differential diagnosis. Usually, BCCs are positive for Ber-EP4 and negative for EMA and calretinin, which differs from AC and PA<sup>12,17</sup>. Recent reviews which investigated intraoral BCCs appointed that most previous cases reported in the literature were misdiagnosed and represented other lesions<sup>12,15</sup>. For these authors, the only truly primary intra-oral was reported in a 69-year-old man showing a 1.3 cm ulcerated plaque on the right buccal mucosa<sup>18</sup>. Shumway et al. (2011)<sup>15</sup> also presented a BCC in the buccal mucosa but diagnosed in a patient with GS. Later, Woods et al. (2014)<sup>12</sup> reported three new cases, one on the buccal mucosa and others on the anterior hard palatal mucosa and retromolar area, respectively. We also found another intra-oral BCC presenting as a multifocal black pigmentation on the buccal mucosa<sup>19</sup>. These observations imply that buccal mucosa may be a common intraoral BCC site when occurring in the oral cavity.

Extension or recurrences of cutaneous BCC in intraoral locations are rarely reported<sup>13,14</sup>. Two case reports highlighted the intra-oral involvement of skin BCC discovered during Mohs surgery, but still, patients presented noticeable clinical signs on the skin region of the oral commissure<sup>10</sup>. Otherwise, cases of aggressive skin BCC concomitantly extending to oral mucosa and maxillofacial bones are frequently reported<sup>20,21</sup>. Our case represents a recurrence of a skin BCC presenting the first and unique clinical signs in the buccal mucosa. To the best of our knowledge, this is the first report with these characteristics in the literature.

The gold standard of treatment in BCC is surgical excision with tumoral-free margins, with a low recurrence rate, around 2 to 8% of the patients in 5 years<sup>9,22,23</sup>. For patients with locally advanced BCC or with metastasis that cannot be successfully treated using

surgical methods, radiotherapy or systemic medication is recommended<sup>9,23</sup>. Several authors have attempted to identify recurrence risk factors for head and neck BCCs<sup>7,24-28</sup>. Surgical margins in BCCs of different histological subtypes have been extensively discussed in the literature. Kiely & Patel evaluated the surgical margins of 694 excised lesions. They noted that 5% showed peripheral margin infiltration, even with the average safety margin of around 4mm, and 1.4% showed deep margin infiltration. Compared to the nodular histological type, infiltrative lesions were 9.9 (95% CI: 2.3-43.3; p=0.002) times more likely to have deep margin involvement, while mixed lesions were 2.6 (95% CI: 1.2-6.0; p=0.022) times more likely to have peripheral margin involvement. Thus, the authors emphasize the importance of the excision of infiltrative basal cell carcinomas to at least the first anatomical plane to reduce the chances of recurrence<sup>25</sup>.

Armstrong et al. also addressed safety margins and histological grades as risk factors. In a 2-year follow-up, 3% (10 of 331) of surgically treated facial BCCs presented local recurrence. In recurrent cases, margin involvement was found in the peripheral regions (40%) and the deep areas (30%). For non-recurrent BCCs, margin involvement was lower, 10.9% (p=0.013) in peripheral regions and 12.1% (p=0.048) in deep areas. Histological classification showed a higher prevalence of the infiltrative (p=0.02) and micronodular (p=0.041) subtypes in recurrent lesions compared to non-recurrent cases<sup>24</sup>.

Although infiltrative lesions are related to a higher risk for local recurrence, the 5-year retrospective study by Hasan et al. identified that 77.8% (14 of 18) of lesions presented a nodular subtype. Only one case recurred with a modified histologic type, diagnosed as nodular in the primary lesion and as infiltrative in the recurrence. Since many primary lesions are removed with surgical safety margins less than 4mm, some authors believe it may be insufficient and contribute to recurrence. No correlation was noted with other factors studied, such as the size of the primary tumors and history of UV exposure [26]. Furthermore, TERTp mutation was also related as a potential biomarker of the aggressiveness of BCCs<sup>29</sup>.

## CONCLUSION

In conclusion, although oral involvement is rare, BCC can extend to the oral mucosa. We emphasize that health practitioners must be aware of clinical recurrence features in the oral cavity to establish an early diagnosis. Regular follow-up must be performed, regardless of the histological type.

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## Conflict of interest

We have no conflicts of interest to disclose. All authors declare that they have no conflicts of interest.

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