

Carcinoma Cuniculatum

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ABSTRACT

Introduction: Carcinoma cuniculatum (CC) is an uncommon variant of squamous cell carcinoma (SCC). It is a low-grade tumor, with an endophytic, burrowing growth pattern. The lesion initially presents as a condyloma or hyperkeratinized patch which eventually ulcerates, with sinuses that discharge keratinous material. A total of 57 cases have been reported in the head and neck region from 1977 to 2017, with 51 cases in the oral cavity.

Case report: A 75-year-old female patient presented with a complaint of a painful, nodular growth of the left buccal mucosa in relation to teeth 26, 27. The patient was on antidiabetic medications for 10 years and was taking Levothyroxine (125 µg/day). Patient does not have tobacco/areca nut chewing habit history. On intraoral examination, the lesion was pinkish white, soft, nodular, and measured 2 × 1.5 cm, which was tender and caused difficulty in chewing.

Conclusion: The most common site for CC in the oral cavity is alveolar mucosa, whereas the lesion in the present case was seen in the buccal mucosa. The CC is a locally aggressive lesion that predominantly occurs in the elderly, with low recurrence rates. Biopsy and meticulous histopathology examination become exigent for the proper diagnosis and treatment planning of oral CC.

Keywords: Carcinoma cuniculatum, Condyloma, Squamous cell carcinoma.

How to cite this article: Lavanya C, Kavitha L, Haridass S, Ranganathan K. Carcinoma Cuniculatum. Oral Maxillofac Pathol J 2018;9(1):16-19.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Carcinoma cuniculatum, also referred to as epithelioma cuniculatum, Buschke-Löwenstein tumor, and inverted verrucous carcinoma, is an uncommon variant of SCC. It was first described in the foot by Aird et al¹ in 1954, which is the most common site. Other reported sites include hand, wrist, finger, knee, buttock, nasal cavity, larynx, pharynx, esophagus, penis, face, and oral cavity.

Carcinoma cuniculatum is a low-grade tumor, with an endophytic, burrowing growth pattern. The lesion initially presents as a condyloma or hyperkeratinized patch that eventually ulcerates, with sinuses that discharge keratinous material.² It exhibits slow growth and local invasion and usually metastasizes to the regional lymph node.^{3,4}

When the tumor invades bone, there is chronic sup-puration, abscess formation, and bone sequestration, features that may be misdiagnosed as osteomyelitis. Suggested etiologic factors include human papillomavirus, alcohol and tobacco, chronic trauma, chronic inflammation, radiation, and chronic arsenic poisoning.³

A total of 57 cases have been reported in the head and neck region from 1977 to 2017, with 51 cases in the oral cavity. Here we present a case of CC of buccal mucosa in a 74-year-old female patient.

CASE REPORT

A 75-year-old female patient presented with a complaint of a painful, nodular growth of left buccal mucosa in relation to teeth 26, 27. The patient was on antidiabetic medications for 10 years and was taking Levothyroxine (125 µg/day). Patient does not have tobacco/areca nut chewing habit history. On intraoral examination, the lesion was pinkish white, soft, nodular and measured 2 × 1.5 cm (Fig. 1), which was tender and caused difficulty in chewing. The patient was advised routine hemogram, which revealed elevated levels of erythrocyte



Fig. 1: Pinkish white nodular growth in relation to 26 and 27 in the buccal mucosa

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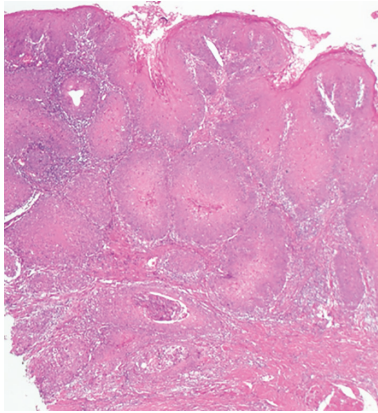


Fig. 2: Photomicrograph (hematoxylin and eosin, 4×) showing endophytic proliferation of stratified squamous epithelium enclosing keratin-filled crypts

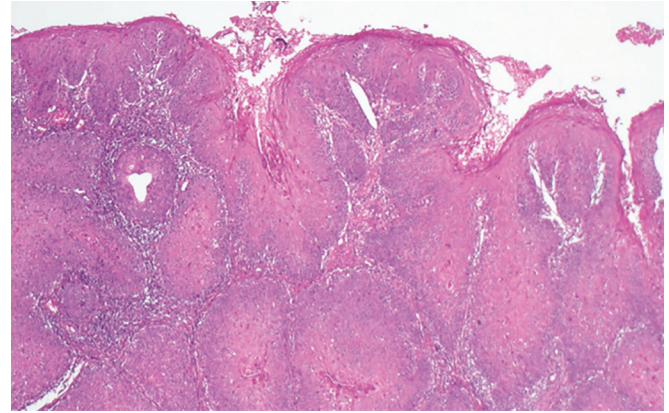


Fig. 3: Photomicrograph (hematoxylin and eosin, 4×) of connective tissue exhibiting keratin-filled crypts

sedimentation rate, and there were no palpable cervical lymph nodes. Provisionally, the lesion was diagnosed as verrucous hyperplasia, and an incisional biopsy of the lesion was done under local anesthesia (2% lignocaine with adrenaline). The gross specimen measured about 1.5×1 cm.

On histopathological examination, the section showed a well-differentiated stratified squamous epithelium exhibiting endophytic proliferations of keratin-filled crypts with minimal atypical features. The tumor cells lining the crypts demonstrated basilar hyperplasia, nuclear pleomorphism, hyperchromatism, and focal areas of keratin pearls. The invasive tumor front exhibited anastomosing burrowing strands and islands of squamous epithelium enclosing keratin-filled crypts with focal areas of microabscesses. The connective tissue exhibited diffuse mixed inflammatory cell infiltrate consisting predominantly of lymphocytes and plasma cells with few eosinophils (Figs 2 and 3). Based on the histopathologic features, a report of CC was given.

DISCUSSION

Oral CC is an uncommon subtype of SCC first reported by Flieger and Owiński in 1977.⁵ It presents over a wide age (9–87 years) with a mean age of 50 years and a male to female ratio of 3:1.⁶ Our case was seen in a 75-year-old female patient. Of the 57 cases of CC reported in the head and neck region, female patients constituted only 39% of the cases (Table 1).^{7,8}

Clinically it presents as pink to red exophytic growth with a cobblestone-like surface,⁹ as was the present case in the left buccal mucosa. Seventy-eight percent of cases of CC have been reported in the alveolar gingival or hard palate, where sinuous-burrowing pattern into the underlying bone is a consistent feature.¹⁰ In our case, the lesion was reported in the left buccal mucosa. To our knowledge,

only two cases have been reported in the buccal mucosa in the past 40 years.^{8,10,11}

Microscopically, CC has an endophytic, infiltrative growth pattern with short, blunt, burrowing, papillated cords in the invasive front. Areas of epithelial spongiosis, inflammatory cell exocytosis, and dyskeratosis are present to variable extent in every lesion.⁹ Our case exhibited a well-differentiated stratified squamous epithelium with keratin-filled crypts, microabscesses, and foci of eosinophils in the connective tissue.

Clinically and histopathologically, CC has to be distinguished from verrucous carcinoma (VC) as both these entities are distinct variants of SCC with locally aggressive growth and characteristic endophytic component. The CC presents clinically as sessile, pink, red, or white papillary growth with cobblestone-like surface, whereas VC shows white, warty lesion with prominent filiform surface projections.⁶ The CC is a slow-growing, locally destructive tumor with infiltrative growth pattern. It is also a slow-growing tumor exhibiting an exophytic growth pattern with pushing margins in the deeper portions. The VC may be associated with superficial bone erosion, but does not deeply penetrate into bone as does CC.^{12,13} The complex, branching network of keratinizing neoplastic squamous epithelium with cyst formation, “burrowing” invasive front in CC contrasts with the sharp church spire-like exophytic projections with pushing invasive front seen in VC.¹⁴

The CC and VC are locally aggressive, well-differentiated variants of SCC with endophytic and exophytic components. The CC may be clinically and histologically misdiagnosed as VC, especially in cases of superficial biopsies.

Unlike CC and VC, papillary variant of SCC (PSCC) is an invasive SCC with an exophytic papillary component. The PSCC exhibits cytologic signs of malignancy, a higher mitotic rate, and variable number of atypical mitotic figures. Keratinization is a prominent feature of

Table 1: List of CC cases reported in the head and neck region from 1977 to 2017

| <i>Authors/References</i> | <i>Number of cases</i> | <i>Age/Gender</i> | <i>Site</i> |
|----------------------------------|------------------------|---------------------------------|---|
| Flieger and Owinski ⁵ | 4 | 50/M | Maxillary molar and sinus |
| | | 60/M | Maxillary molar region |
| | | 9/M | Maxillary premolar region |
| | | 69/F | Hard palate |
| Kahn et al | 4 | 62/M | Submandibular space |
| | | 49/M | Anterior floor of the mouth |
| | | 52/M | Mandibular molar region |
| | | 54/F | Larynx, subglottic |
| Delahaye et al ¹⁰ | 5 | 51/M | Retromolar trigone |
| | | 55/M | Tonsil, floor of the mouth |
| | | 63/M | Subglottic larynx |
| | | 31/M | Hard palate |
| | | 52/M | Buccal mucosa |
| Szmeja et al | 1 | Not stated | Nasal cavity and paranasal sinuses |
| Huault et al | 1 | 55/M | Mandibular alveolus |
| Allon et al | 1 | 56/M | Maxillary gingiva |
| Gassler et al ¹¹ | 1 | Not stated | Buccal mucosa |
| Raguse et al | 1 | 81/F | Mandible |
| Puxeddu et al | 1 | 72/M | Larynx |
| Kruse and Graetz ¹⁶ | 1 | 74/F | Anterior maxillary alveolus |
| Hutton et al | 1 | 7/M | Maxilla |
| Pons et al ⁴ | 3 | 72/M | Mandibular molar region |
| | | 82/M | Mandibular molar region |
| | | 43/M | Mandibular retromolar region |
| Sun et al ¹⁴ | 15 | 44–92 years 7 Male and 8 Female | Tongue—8 Cases Mandible—6 Cases Oral vestibule—1 Case |
| Suzuki et al | 1 | 68/M | Mandibular gingiva |
| Thavaraj et al ⁶ | 1 | 61/M | Tongue |
| Fonseca et al | 1 | 62/F | Anterior mandible |
| Padilla and Murrah ⁹ | 10 | 65/M | Mandibular attached gingiva |
| | | 38/F | Mandibular gingiva |
| | | 72/M | Mandibular gingiva |
| | | 81/F | Anterior maxillary gingiva |
| | | 67/F | Mandible and buccal mucosa |
| | | 79/M | Oral vestibule |
| | | 88/F | Maxillary gingiva/ridge |
| | | 75/F | Mandibular gingiva and buccal mucosa |
| | | 69/F | Mandibular gingiva |
| 85/F | Mandibular gingiva | | |
| Goh et al | 1 | 62/M | Tongue |
| Shakil et al | 1 | 63/F | Not stated |
| Griffith et al ⁸ | 1 | 49/M | Larynx |
| Shapiro et al | 1 | 71/M | Anterior mandible |
| Uma Vasant et al | 1 | 58/F | Mandibular gingiva |
| *Present case | 1 | 75/F | Buccal mucosa |

*Inclusive of the present case there are totally 58 cases in head and neck region, with 51 cases in oral cavity; 4 cases previously reported in buccal mucosa as in our case (totally 5 cases reported till date in buccal mucosa inclusive of the present case)

VC and CC, whereas it is slight to minimal in PSCC. In PSCC, metastasis to the local lymph nodes is common.¹⁵ The VC and CC have a better prognosis with surgical excision than PSCC.¹⁷⁻¹⁹

The diagnosis of CC, a well-differentiated, uncommon variant of SCC, sharing clinical and histological similarities with VC, is challenging. A histopathological

examination of the representative site will enable the identification of extensive growth pattern.

CONCLUSION

The CC is a locally aggressive lesion that predominantly occurs in the elderly, with low recurrence rates. Considering its invasive growth pattern, surgical excision

with tumor-free margins is the therapy of choice. Biopsy and meticulous histopathologic examination become exigent for the proper diagnosis and treatment planning of oral CC.

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