Carcinoma cuniculatum in maxillary gingiva mimicking verruciform xanthoma: a case report

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Abstract: Carcinoma cuniculatum (CC) is a rare and well-differentiated clinicopathological variant of squamous cell carcinoma (SCC) that is not common in head and neck. It is defined histologically by the infiltrative pattern of a deep, broad, and complex proliferation of stratified squamous epithelium with keratin cores and keratin-filled crypts. It has a propensity for local invasion and rare metastasis. This case report describes a 39-year-old man who was referred to our hospital with painful swelling in the right maxillary gingiva for 1 month and restriction of mouth opening for 1 week. Two biopsy examinations were negative for the diagnosis of malignancy, and the patient was misdiagnosed with verruciform xanthoma before an accurate diagnosis of CC. The biopsy reports were not in line with the imaging findings and clinical manifestations. Finally, he was diagnosed based on the combination of clinical manifestations and the pathological findings. Our case report provided a thorough clinical and histopathologic case of CC in maxillary gingiva, together with a brief review of the literature. In addition, we highlighted the difficulties in arriving at this uncommon diagnosis, and discussed the diagnosis of CC based on the combination of clinical manifestations and the pathological findings. To our knowledge, this is a very rare case of CC of the gingiva mimicking verruciform xanthoma.

Keywords: Carcinoma cuniculatum (CC); maxillary gingiva; squamous cell carcinoma (SCC); verruciform xanthoma; case report

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Introduction

Carcinoma cuniculatum (CC), a rare, well-differentiated distinct clinicopathological variant of squamous cell carcinoma (SCC) (1), is first described by Aird on the sole of the foot in 1954 (2). Histologically, it is featured by infiltrative pattern of a deep, broad, and complex proliferation of stratified squamous epithelium with keratin cores and keratin-filled crypts, which results in information of tumor with a cuniculatum architecture similar to rabbit burrows. Nowadays, the diagnosis of CC is still a challenge in clinical practice as it usually mimics a variety of other lesions with an insidious onset and a benign course. To our best knowledge, rare CC cases showed features of verruciform xanthoma (3). Herein, we present a case of CC in the maxillary gingiva mimicking verruciform xanthoma, who was misdiagnosed in the preoperative biopsies at first. We present the following article in accordance with the CARE reporting checklist (available at https://dx.doi.org/10.21037/tcr-21-552).

Case presentation

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal. The study protocols were approved by the Ethical Committee of the Qingdao
A 39-year-old male presented to our department with painful swelling in the right maxillary gingiva for 1 month and restriction of mouth opening for 1 week. He received no treatment within 1 month. On intra-oral examination, there was a red, ill-defined mass (3.0 cm × 2.0 cm) with overlying superficial mucosal erosion between the right maxillary #15 and #17. Obvious touch pain was reported by the patient.

CT and MRI revealed an osteolytic lesion in the right maxillary region, hard palate and pterygoid process (Figure 1), as well as a soft tissue mass with a maximal cross-section of 4.8 cm × 4.2 cm. Thus, malignant tumor was considered. Initial biopsy was performed 4 weeks upon the presence of clinical presentations, which showed papillary surfaces and parakeratinized squamous epithelia with elongated epithelia rete ridges. This was characterized by the presence of foam cells in the connective tissue papillae. Then the patient was diagnosed with verruciform xanthoma. After taking the clinical presentation and radiographic evidence of bone invasion into consideration, the lesion was considered to be highly malignant.

The patient received subtotal maxillectomy. The findings of the intraoperative freezing section analysis were in line with the first biopsy. There was no radiographic evidence of cervical lymph node involvement. No cervical lymph nodes dissection was performed.

The resected specimen was sent for histopathological analysis. For the macroscopic observation on the surface, an irregular mass was seen to infiltrate the tissues from Municipal Hospital (approval No. 2021-051).

Figure 1 CT and MRI imaging showed an osteolytic lesion of the right maxillary, hard palate and pterygoid process. (A) CT scan, axial view; (B) CT scan, coronal view; (C) axial T2-weighted MRI; (D) coronal T2-weighted MRI.
surface to deep (Figure 2A). Histopathologic analysis indicated papillary surfaces and parakeratinized squamous epithelia, which was featured by the presence of massive foam cells in the connective tissue papillae between the epithelial rete ridges (Figure 2B) and multiple cysts formation of burrowing structures with various size and shape that deeply penetrated in the underlying tissues (Figure 2C,2D). The cysts were lined by well-differentiated keratinizing squamous epithelium, which showed mild to moderate cytologic atypia and few mitoses. The cavity was filled with hyperkeratotic and parakeratotic cornified cells combined with neutrophils (Figure 2D). Immunohistochemistry revealed that the tumour was negative for P16 and immunoreactive for P40 (Figure 3A) and CK. Immunohistochemical staining indicated a Ki-67 positivity in 10% of cells (Figure 3B). The foam cells were immunoreactive for CD68. Immunohistochemistry for p53 indicated a wild type. Finally, the patient was diagnosed with oral CC mimicking verruciform xanthoma. After surgery, the patient was followed up for two months, and he was confirmed to be clinically and radiographically disease free.

**Discussion**

Based on the literature review, a total of 57 cases (4-25) with oral CC were obtained in Table 1 Oral CC has been reported in the English articles (Table 1). For the patient characteristics, there seemed to be a slight male preponderance (male: 35; female: 23). In addition, the patients diagnosed with oral CC were predominantly aged population (60 to 70 years old). For the treatment, surgery was the preferred treatment option as almost all the cases received surgery except one with no information on the
Figure 3 Immunohistochemical staining of p40 (A), Ki-67 (B) under a magnification 10×.

Table 1 Review of 57 published cases and the present case of Oral carcinoma cuniculatum

| Authors, year                  | Number | Age/gender | Site                                           | Preoperative diagnosis       | Treatment of cases |
|--------------------------------|--------|------------|------------------------------------------------|-------------------------------|-------------------|
| Flieger et al. (1977) (4)      | 4      | 50/M       | Maxillary molar region and sinus               | Osteomyelitis                 | Surgery           |
|                                |        | 60/M       | Maxillary molar region                         | Tuberculosis                  | Surgery           |
|                                |        | 9/M        | Maxillary premolar region                      | N/A                           | Radiotherapy       |
|                                |        | 69/F       | Hard palate                                    | N/A                           | Surgery           |
| Kahn et al. (1991) (5)         | 3      | 62/M       | Maxillary alveolus and sinus                   | Cystic lesion                 | Surgery           |
|                                |        | 49/M       | Submandibular space                            | N/A                           | Surgery, ND       |
|                                |        | 52/M       | Anterior floor of mouth                        | N/A                           | Surgery, ND       |
| Delahaye et al. (1994) (17)    | 5      | 51/M       | Retromolar triangle                            | SCC                           | Surgery           |
|                                |        | 55/M       | Tonsil, floor of mouth                         | Verrucous carcinoma           | Surgery, ND       |
|                                |        | 63/M       | Subglottic larynx                              | N/A                           | ND                |
|                                |        | 31/M       | Hard palate                                    | N/A                           | Surgery           |
|                                |        | 52/M       | Buccal mucosa                                  | N/A                           | Surgery, ND       |
| Huault et al. (1998) (6)       | 1      | 55/M       | Mandibular alveolus                            | Hyperkeratotic papilloma      | Surgery           |
| Allon et al. (2002) (18)       | 1      | 56/M       | Maxillary gingiva                              | N/A                           | Surgery           |
| Raguse et al. (2006) (7)       | 1      | 81/F       | Mandibular symphysis                           | Osteomyelitis                 | Surgery           |
| Kruse and Graetz (2009) (19)   | 1      | 74/F       | Maxillary alveolus                             | SCC                           | Surgery, ND       |
| Pons et al. (2012) (8)         | 3      | 72/M       | Mandibular molar region                        | Inflammatory granuloma        | Surgery, ND       |
|                                |        | 82/M       | Mandibular molar region                        | N/A                           | Surgery, ND       |
|                                |        | 43/M       | Mandibular retromolar region                   | Keratocyst                    | Surgery           |
| Hutton et al. (2010) (9)       | 1      | 7/M        | Maxillary gingiva                              | Dental abscess                | Surgery           |
| Suzuki et al. (2012) (10)      | 1      | 68/M       | Mandibular gingiva                             | Osteomyelitis with leukoplakia| Surgery           |
| Thavaraj et al. (2012) (20)    | 1      | 61/M       | Tongue                                         | N/A                           | Surgery           |
Radiotherapy and chemotherapy are also utilized for some patients, but further investigations are required to validate its efficiency.

In this case, the patient received subtotal maxillectomy. After surgery, he was followed up for two months, and was confirmed to be disease free. This indicated that surgery was feasible for treating oral CC.

The diagnosis of oral CC is still very difficult as it usually exhibits an insidious course mimicking benign lesion. In clinical practice, patients with oral CC often show similar manifestations with osteomyelitis, cystic lesion, lichen planus, papilloma or a dental abscess (4-16). The lesions were misdiagnosed with reactive or hyperplastic lesions in cases of a superficial or limited biopsy specimen of CC, a lack of cytologic atypia or combination of clinical manifestations. To our best knowledge, this is the first oral CC case mimicking pathological features of verruciform xanthoma. Based on the prognosis, CC must be distinguished from other clinical and microscopic

Table 1 (continued)

| Authors, year | Number | Age/gender | Site | Preoperative diagnosis | Treatment of cases |
|---------------|--------|------------|------|------------------------|--------------------|
| Sun Y et al. (2012) (21) | 15 | 44-92/7M,8F | Tongue (n=8), Mandible (n=6), vestibule (n=1) | N/A | Surgery |
| Fonseca et al. (2013) (11) | 2 | 62/F | Mandibular gingiva | Keratocyst | Surgery |
| | | 47/F | Maxillary gingiva | Osteomyelitis | Surgery/radiotherapy |
| Padilla et al. (2014) (12) | 10 | 65/M | Mandibular gingiva | Malignant tumor | Surgery |
| | | 38/F | Mandibular gingiva | Benign proliferation | Surgery |
| | | 72/M | Maxillary gingiva | N/A | Surgery |
| | | 81/F | Palate | N/A | Surgery |
| | | 67/F | Mandibular gingiva | Lichen planus vs. carcinoma | Surgery |
| | | 76/M | Mandibular gingiva | N/A | Surgery |
| | | 88/F | Maxillary gingiva | N/A | Surgery |
| | | 75/F | Edentulous ridge of mandible | Hyperkeratosis, epithelial atrophy, and dyskeratosis | Surgery |
| | | 69/F | Mandibular gingiva | N/A | Surgery |
| | | 85/F | Maxillary gingiva | N/A | Biopsy |
| Goh et al. (2014) (22) | 1 | 62/M | Tongue | Malignant tumor | Surgery |
| Shay et al. (2015) (13) | 1 | 58/M | Mandible | Oral and facial abscesses | Surgery |
| Shapiro et al. (2015) (14) | 1 | 71/F | Mand gingiva | Osteomyelitis and dental abscess | Surgery |
| Shakil et al. (2014) (23) | 1 | 63/F | Buccal mucosa | N/A | Surgery/radiotherapy |
| Datar et al. (2017) (24) | 1 | 58/F | Mandibular gingiva | N/A | Surgery |
| Zhang et al. (2018) (25) | 1 | 39/M | Mandibular gingiva | Malignant tumor | Surgery |
| Ramos et al. (2018) (15) | 1 | 50/M | Tongue | Oral lichen planus | Surgery |
| Lee et al. (2020) (16) | 1 | 5/M | Anterior maxillary gingival | Pseudoepi the liomatous hyperplasia | Surgery |
| Present case | 1 | 39/M | Maxillary gingiva | Verruciform xanthoma | Surgery |

F, female; M, male; N/A, not available; ND, neck dissection.
overlapping tumors (e.g., well-differentiated SCC, verrucous carcinoma and solid variant of keratocystic odontogenic tumor) (17).

In summary, attention should be paid to its clinic-pathologic characteristics for the accurate diagnosis in clinical practice. In this case report, we emphasized the importance of the combination of clinical and pathological findings in the diagnosis of the oral CC.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/tcr-21-552). The authors have no conflicts of interest to declare.

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