Case Report

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

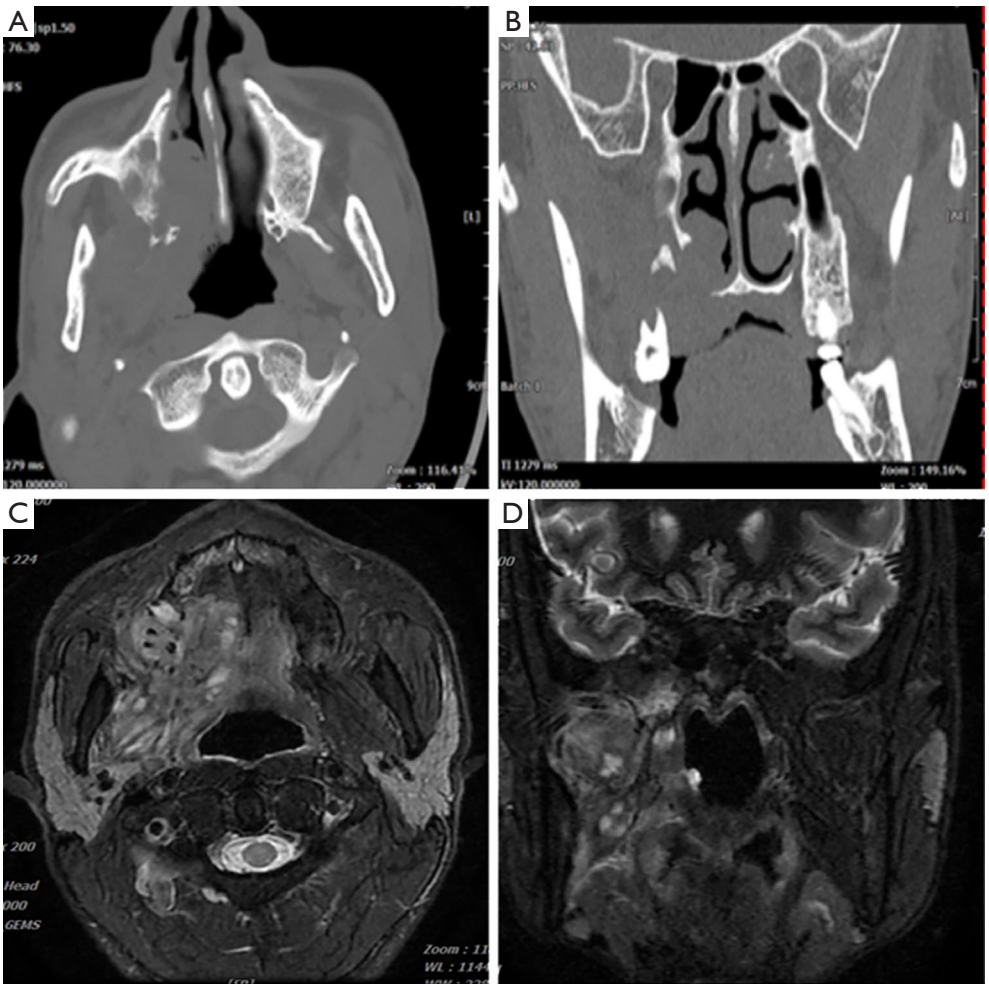

Figure 1 CT and MRI imaging showed an osteolytic lesion of the right maxillary, hard palate and pterygoid process. (A) CT scan, axial view; (B) CT scan, coronal view; (C) axial T2-weighted MRI; (D) coronal T2-weighted MRI.

Municipal Hospital (approval No. 2021-051).

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

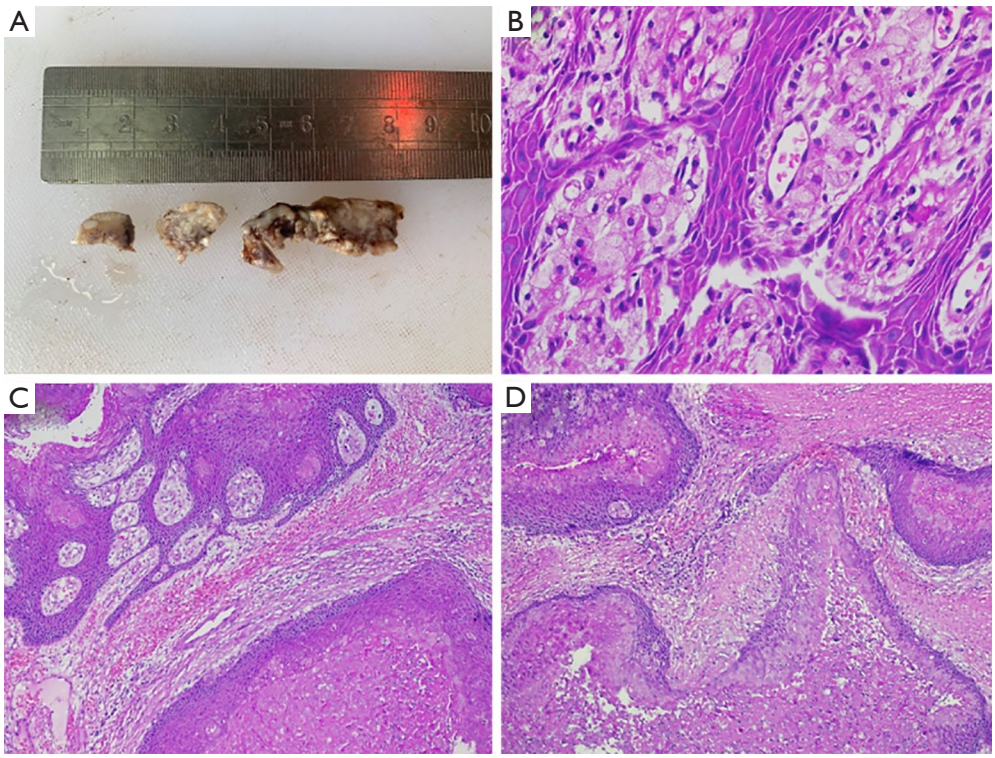

Figure 2 Macroscopic observation and histological staining of carcinoma cuniculatum. (A) The gross specimen showed a lumpy mass in the right maxillary. The incisal surface revealed irregular sinuses of tumor invaginations that went from surface-to-deep structure penetration. (B) The presence of foam cells in the connective tissue papillae between the epithelial rete ridges by H&E staining. The images were observed under a magnification of 40×. (C) Histologic sections showed a prominent papillary growth pattern in the surface and a complex, branching networks of mostly bland, keratinizing squamous epithelium with cyst formation "burrowing into bone". The H&E staining results were observed under a magnification of 10×. (D) The cysts were lined by benign-looking keratinizing squamous epithelium and filled with hyperkeratotic and parakeratotic cornified cells by H&E staining under a magnification 10×.

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

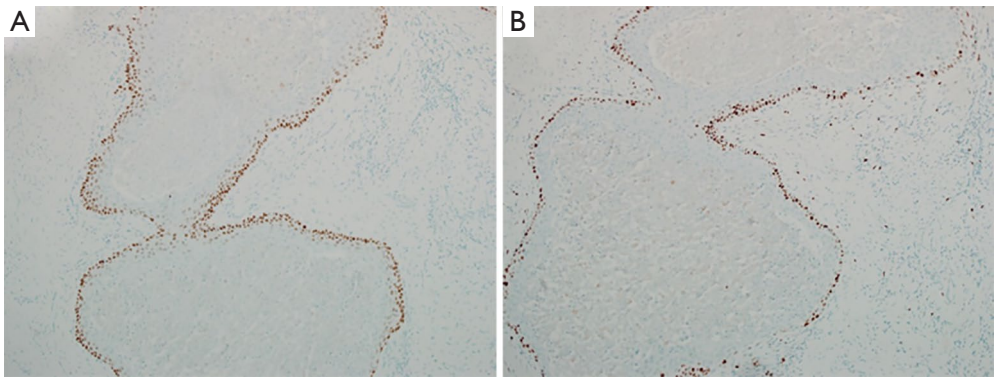

Figure 3 Immunohistochemical staining of p40 (A), Ki-67 (B) under a magnification 10×.

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

Table 1 (*continued*)

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Authors, year	Number	Age/gender	Site	Preoperative diagnosis	Treatment of cases
Sun Y *et al.* (2012) (21)	15	44-92/7M,8 F	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.

treatment. 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

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

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://dx.doi.org/10.21037/tcr-21-552

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.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. 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 Municipal Hospital (approval No. 2021-051).

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