Carcinoma Cuniculatum in the Tongue of a Patient with Oral Lichen Planus: Unusual Presentation

Abstract
Carcinoma cuniculatum (CC) is a rare variant of squamous cell carcinoma (SCC). Only 27 cases have been published in English. A 50-year-old male, who presented a white nodule with erythematous areas, localized in the lateral border of the tongue with 2 months of duration. The patient presents oral lichen planus lesions on the tongue, commissure, and buccal mucosa. The microscopy evaluation of the nodular lesion of the tongue revealed a malignant epithelial neoplasia characterized by cuniculatum architecture, similar in appearance to “rabbit burrows” and the final diagnosis was of CC. The management of CC needs cooperation between surgeons and pathologists to establish a correct diagnosis and treatment. CC is a rare entity and must be recognized by oral pathologist so that it is not misdiagnosed as verrucous carcinoma or oral SCC (OSCC). Regarding prognosis, CC must be evaluated and distinguished from other variants of OSCC.

Keywords: Carcinoma cuniculatum, oral, squamous cell carcinoma

Introduction
Carcinoma cuniculatum (CC) is a rare variant of squamous cell carcinoma (SCC). It was first described in 1954 by Aird et al., who reported three planar cases of this lesion. Only 27 cases affecting the oral cavity have been published in the English literature. In the oral cavity, most cases are situated in the alveolar mucosa or hard palate, in male patients, mainly in their sixth and seventh decades of life. The etiology remains unclear; however, several studies have suggested that CC may be associated with human papillomavirus, inflammation, chronic trauma, irradiation, or arsenic ingestion. CC is clinically characterized by slow-growing exophytic or endophytic lesions with verrucous or papillary surfaces, showing locally aggressive behavior.

Histopathological features of CC revealed a cuniculatum architecture, similar in appearance to “rabbit burrows.” Papillomatous surfaces penetrate deeply into the underlying tissues, resulting in a number of ramified crypts and lumen formations filled by keratin that look like rabbit burrows or cuniculus. CC is a well-differentiated lesion, with no significant cytologic atypia. The mitosis rate is normal or slightly increased. Microabscesses filled with neutrophils were also frequently observed.

The aim of this study was to describe a case of CC that occurred in the lateral border of the tongue and to conduct a literature review about this rare disease.

Case Report
A 50-year-old white male, presented with a nodular lesion localized in the right side of the lateral border of the tongue with 2 months of duration. The patient’s previous medical and family histories did not contribute to this problem, and he had no history of smoking or alcohol abuse.

The patient has been treated for oral lichen planus (OLP) for the past 10 years. The treatment started in 2003 when he presented a white plaque in the tongue, bilateral buccal mucosa, and commissure diagnosed as OLP; in the palate, he presented red patches that were diagnosed as oral candidiasis. Hematological examinations were performed, but there were no changes. The patient was treated with nystatin 100,000 IU for 14 days. After the improvement of the lesion, the patient did not show any signs of recurrence.

Address for correspondence: Prof. Marcia Gaiger Oliveira, Department of Oral Pathology, School of Dentistry, Federal University of Rio Grande do Sul, Porto Alegre, Brazil.

E-mail: marciago@gmail.com

Access this article online
Website: www.ijdr.in
DOI: 10.4103/ijdr.IJDR_185_16
Quick Response Code:
How to cite this article: Ramos GO, Meyer Gd, Visioli F, Manoela MD, Oliveira MG. Carcinoma cuniculatum in the tongue of a patient with oral lichen planus: Unusual presentation. Indian J Dent Res 2018;29:525-8.
Table 1: Clinical features of oral cuniculatum carcinoma

| Case report (year)            | Number of cases | Sex | Age Mean (Range) | Anatomic localization | Tobacco use | Alcohol use | Metastasis regional/distant | Treatment             |
|-------------------------------|-----------------|-----|------------------|-----------------------|-------------|------------|-----------------------------|-----------------------|
| Allon et al., 2002[7]         | 1               | Male| 56               | Anterior maxilla      | Yes         | No         | No/no                       | Surgery               |
| Raguse et al., 2006[8]        | 1               | Female| 81              | Mandible              | No          | No         | No/no                       | Surgery               |
| Kruse et al., 2009[9]         | 1               | Female| 74              | Maxilla               | No          | No         | No/no                       | Surgery               |
| Hutton et al., 2010[10]       | 1               | Female| 7               | Maxilla               | No          | No         | No/no                       | Surgery               |
| Suzuki et al., 2012[5]        | 1               | Male | 68               | Mandibular gingiva    | Yes         | Yes        | No/no                       | Surgery               |
| Pons et al., 2012[6]          | 3               | Male | 72               | Posterior mandible    | No          | No         | No/no                       | Surgery               |
|                              |                 | Male | 82               | Anterior Mandible     | No          | No         | No/no                       | Surgery               |
| Thavaraj et al., 2012[3]      | 1               | Male | 42               | Tongue                | No          | No         | No/no                       | Surgery               |
| Sun et al., 2012[2]           | 15              | Female (8) | Mean age 67 (44-92) | Tongue (8) Mandible (6) Vestibule (1) | Yes (5) | Yes (5) | Yes (3) | Surgery |
| Fonseca et al., 2013[4]       | 2               | Female (7) | Male | Anterior mandible Maxillary gingiva | No | No | No/no | Surgery |
| Goh et al., 2014[11]          | 1               | Male | 62               | Tongue                | Yes        | No         | No/no                       | Surgery               |
| Padilla and Murrah, 2014[2]   | 10              | Female (7) | Male (3) | Mean age 71.9 (38-88) Mandible (9) Vestibule (1) | Yes (2) | No | No/no | Surgery |
| Present case                  | 1               | Male | 50               | Tongue                | No          | No         | No/no                       | Surgery               |

not return for a follow-up. In 2005, the patient returned with painful symptoms in the tongue and buccal mucosa and was treated with dexamethasone mouthwash for 14 days, but the patient did not return for a follow-up. After that, the patient returned only in 2013 reporting pain and esthetics discomfort by lichen planus lesions in the tongue.

The intraoral examination revealed white and red plaques in the commissure, the bilateral buccal mucosa [Figure 1a and b], and the tongue [Figure 1c], which were diagnosed clinically as lichen planus. The lateral border of the tongue presented a white nodule with erythematous areas, measuring approximately 1 cm in diameter [Figure 1d]. The lesion was clinically diagnosed as pyogenic granuloma due to its clinical appearance. Biopsies were carried out in two regions, in the nodular area and in a white plaque. There were no pathological findings in the extraoral examination.

The incisional biopsy of the white plaque was also performed. The microscopy evaluation showed a parakeratotic stratified squamous epithelium, with the formation of saw-tooth rete ridges and a dense band-like infiltrate of lymphocytes immediately subjacent to the epithelium; with degeneration of the basal cell layer. These features confirmed the clinical diagnosis of OLP [Figure 2a].

The excisional biopsy of the nodule was performed, and the microscopy evaluation showed a malignant epithelial neoplasia characterized by endophytic proliferation with surface penetrates deep into the underlying tissues, resulting in ramified crypts filled by keratin-like “rabbit burrows” [Figure 2b and c]. Microabscesses were also observed [Figure 2d]. Cytological atypia and mitosis were absent [Figure 2c and d]. According to these characteristics, we established the diagnosis of CC.

The OLP treatment was done with clobetasol propionate 0.05% in association with nystatin for 2 weeks. The patient was referred to a head and neck service to perform the treatment of CC. The definitive treatment was performed with surgery; there was not regional or distant metastasis. The patient remained under clinical monitoring for the OLP in the pathology clinic of the Universidade Federal do
Rio Grande do Sul, without recurrence after 10 months of follow-up [Figure 3].

Discussion

The World Health Organization included CC in the 2005 classification of head and neck tumors as a rare variant of SCC that can be distinguished from verrucous carcinoma (VC). According to Sun et al., the incidence rate of CC was 2.7% of all oral SCC (OSCC) cases, but this rate could be lower because this is the only study that calculated the incidence; all other studies were case reports. CC was originally called epithelioma cuniculatum and it was believed to occur only in cutaneous tissue, mainly in the plantar surface of the foot. However, it has been reported in other anatomical locations such as esophagus, larynx, penis, and oral mucosa. CC is characterized by a cuniculatum architecture, organized into ramified sinuses and keratin-filled crypts, and has an appearance similar to “rabbit burrows” or cuniculatum in Latin.

Several studies suggest that CC etiology may be associated with human papillomavirus, inflammation, chronic trauma, irradiation, or arsenic ingestion. Although alcohol and tobacco use have been associated with the development of OSCC, their role in CC etiology remains unclear.

Regarding incidences in oral cavities, only 37 cases have been published in the English language literature, and these cases occurred mostly in the alveolar mucosa, the hard palate, and the tongue. Other sites of the oral cavity affected by CC have been reported in French and German literature such as the floor of the mouth and the buccal mucosa. CC affects more women than men (17 males/21 females) and occurs in patients with a mean age of 49.5 years, varying between 7 and 92 years.

The additional case presented here occurred in a 50-year-old male patient, in the lateral border of the tongue, showing similar features to the cases reported in the literature.

Differential diagnosis between CC and VC must be established. Microscopically, CC is a well-differentiated lesion, with an absence of any significant cytological atypia. It can show both exophytic and endophytic growth. The papillomatous surface penetrates deeply into the underlying tissues, differently from VC. CC is characterized by the formation of keratin-filled crypts, creating branching sinuses that look like rabbit burrows. The keratin-filled crypts tend to discharge a yellowish, foul-smelling secretion, which has not been described for VC. Microscopic studies found a hyperkeratinized, well-defined tumor. The mitosis rate is normal or slightly increased, and microabscesses filled with neutrophils were also frequently observed. An inflammatory reaction, mainly comprised lymphocytes, was observed in the stroma. The main features which characterize a CC are the keratin-filled crypts and typical ramified sinuses which should be distinguished from OSCC and VC.

Several authors believe that CC is a variant of VC, considering that they are the same lesion; however, the WHO defined that CC is different from VC, and both are variants of OSCC. The differences between CC and VC are resumed. The differential diagnosis can be difficult because CC can mimic reactive or benign lesions such as abscesses, keratin-forming cysts, leukoplakia, true viral verruca, verrucous hyperplasia, and squamous papillomas. In skin lesions, the CC differential diagnosis is made with viral warts, reactive epidermal hyperplasia associated with deep fungal infection (blastomycosis and coccidioidomycosis), chronic ulcer, abscesses, certain drug eruptions (such as bromoderma and iodoferma), epidermal cysts, giant seborrhic keratosis, and pyogenic granuloma. In our case, the clinical diagnosis was a pyogenic granuloma because clinically the lesion was a white nodule with erythematous areas and history of trauma.
One interesting finding of our case is that the patient also presents OLP and this feature was also observed in three patients of Sun et al.[12] and in one of Padilla and Murrah.[12] Several studies have documented a relationship between OLP and OSCC,[19,20] which have led the WHO[10] to classify OLP as a potentially malignant disorder. The literature reported the occurrence of VC in patients with OLP.[21‑24] The risk of a malignant transformation varies between 0.4% and 5%.[19] However, there is no evidence to confirm this association.[20] Furthermore, some authors have shown an association between OLP and many systemic diseases such as infection by hepatitis C virus.[19]

The main therapeutic approach for oral CC is a complete surgical excision with a minimum free margin of 5 cm.[2,3] Chemotherapy and radiotherapy are not the first choices of treatment because their efficiency is controversial for CC and need to be further investigated.[2,4‑5,9] According to the literature, all cases underwent surgical treatment, and only one received both surgery and radiotherapy [Table 1]. The prognosis of CC is good because it rarely presents regional and distant metastasis, although CC may be locally aggressive. According to Table 1, only three cases developed regional metastasis and one had distant metastasis.

In summary, oral CC is a variant of OSCC. It is typically a mucosal exophytic lesion located mostly in the hard palate or the tongue area. Furthermore, the tumor grows slowly, and it is locally aggressive. The management of CC needs close cooperation between surgeons and pathologists to establish a correct diagnosis and treatment. CC is considered a rare entity; therefore, it could be unrecognized by oral pathologist and misdiagnosed as a VC or OSCC. Regarding the prognosis, CC must be evaluated and distinguished from other variants of OSCC.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Aird I, Johnson HD, Lennox B, Stansfeld AG. Epithelioma cuniculatum: A variety of squamous carcinoma peculiar to the foot. Br J Surg 1954;42:245‑50.
2. Sun Y, Kuyama K, Burkhardt A, Yamamoto H. Clinicopathological evaluation of carcinoma cuniculatum: A variant of oral squamous cell carcinoma. J Oral Pathol Med 2012;41:303‑8.
3. Thavaraj S, Cobb A, Kalavrezos N, Beale T, Walker DM, Jay A. Carcinoma cuniculatum arising in the tongue. Head Neck Pathol 2012;6:130‑4.
4. Fonseca FP, Pontes FA, Pontes FS, de Carvalho PL, Sena‑Filho M, Jorge J, et al. Oral carcinoma cuniculatum: Two cases illustrative of a diagnostic challenge. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:457‑63.
5. Suzuki J, Hashimoto S, Watanabe K, Takahashi K, Usubuchi H, Suzuki H. Carcinoma cuniculatum mimicking leukoplakia of the mandibular gingiva. Auris Nasus Larynx 2012;39:321‑5.
6. Pons Y, Kerrary S, Cox A, Guerre A, Bertolus C, Gruffaz F, et al. Mandibular carcinoma cuniculatum: Apropos of 3 cases and literature review. Head Neck 2012;34:291‑5.
7. Allon D, Kaplan I, Manor R, Calderon S. Carcinoma cuniculatum of the jaw: A rare variant of oral carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002;94:601‑8.
8. Raguse JD, Menneking H, Scholmenn HJ, Bier J. Manifestation of carcinoma cuniculatum in the mandible. Oral Oncol Extra 2006;42:173‑5.
9. Kruse AL, Graetz KW. Carcinoma cuniculatum: A rare entity in the oral cavity. J Craniofac Surg 2009;20:1270‑2.
10. Barnes L, Everson JW, Reichart P, Sidransky D. Pathology and Genetics of Head and Neck Tumours. World Health Organization Classification of Tumours. 3rd ed. Lyon: IARC Press; 2005.
11. Goh GH, Venkateswaran K, Leow PC, Lol KS, Thamboo TP, Petersson F. Carcinoma Cuniculatum of esophagus and tongue: report of two cases, including TP53 mutation analysis. Head Neck Pathol 2014;8:261‑8.
12. Padilla RJ, Murrah VA. Carcinoma cuniculatum of the oral mucosa: A potentially underdiagnosed entity in the absence of clinical correlation. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2014;118:684‑93.
13. Hutton A, McKaig S, Bardsley P, Monaghan A, Parmar S. Oral carcinoma cuniculatum in a young child. J Clin Pediatr Dent 2010;35:89‑94.
14. Arefi M, Philpine E, Caprioli R, Haight J, Richardson H, Sheng C. A case of verrucous carcinoma (epithelioma cuniculatum) of the heel mimicking infected epidermal cyst and gout. Foot Ankle Spec 2008;1:297‑9.
15. Devaney KO, Ferlito A, Rinaldo A, El‑Naggar AK, Barnes L. Verrucous carcinoma (carcinoma cuniculatum) of the head and neck: What do we know now that we did not know a decade ago? Eur Arch Otorhinolaryngol 2011;268:477‑80.
16. Steffen C. Dermatopathology in historical perspective: Epithelioma cuniculatum (Aird). Am J Dermatopathol 2006;28:451‑61.
17. Kubik MJ, Rhatigan RM. Carcinoma cuniculatum: Not a verrucous carcinoma. J Cutan Pathol 2012;39:1083‑7.
18. Jafarzadeh H, Sanatkhanl M, Mohtasham N. Oral pyogenic granuloma: A review. J Oral Sci 2006;48:167‑75.
19. Scully C, Carrozzo M. Oral mucosal disease: Lichen planus. Br J Oral Maxillofac Surg 2008;46:15‑21.
20. Munde AD, Karle RR, Wankhede PK, Shaikh SS, Kulkurni M. Demographic and clinical profile of oral lichen planus: A retrospective study. Contemp Clin Dent 2013;4:181‑5.
21. Carrozzo M, Carbone M, Gandolfo S, Valente G, Colombatto P, Ghisetti V. An atypical verrucous carcinoma of the tongue arising in a patient with oral lichen planus associated with hepatitis C virus infection. Oral Oncol 1997;33:220‑5.
22. Castaño E, López‑Rios F, Alvarez‑Fernández JG, Rodríguez‑Peralto JL, Iglesias L. Verrucous carcinoma in association with hypertrophic lichen planus. Clin Exp Dermatol 1997;22:23‑5.
23. Nagao Y, Sata M. Oral verrucous carcinoma arising from lichen planus and esophageal squamous cell carcinoma in a patient with hepatitis C virus‑related liver cirrhosis‑hyperinsulinemia and malignant transformation: A case report. Biomed Rep 2013;1:53‑6.
24. Warshaw EM, Templeton SF, Washington CV. Verrucous carcinoma occurring in a lesion of oral lichen planus. Cutis 2000;65:219‑22.