

Carcinoma cuniculatum of the maxillary gingiva: a case report and review of literature

Case Report

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ABSTRACT

Introduction: this paper will report a case of carcinoma cuniculatum (CC) in maxillary gingiva along with a literature review related to the research topic which specifically focused on cases occurring exclusively in the oral cavity.

Observation: A 44-year-old man presented with an exophytic mass in maxillary alveolar region characterized by slow growth and the presence of bone erosion. The diagnosis of CC was established on the resected specimen. After surgery, the patient underwent adjunct radiotherapy and chemotherapy.

Discussion: Carcinoma cuniculatum (CC) is a rare variant of squamous cell carcinoma (SCC). Oral carcinoma cuniculatum is even rarer and is often initially misdiagnosed; it presents clinically as an exophytic growth and slowly penetrates the jaw, causing deterioration of the underlying bone. The primary treatment for carcinoma cuniculatum involves surgical resection.

Conclusion: this case report highlight the challenges involved in arriving at such an uncommon diagnosis while also discussing the diagnosis of CC based on the combination of clinical symptoms and the pathological findings.

Key Words: Carcinoma cuniculatum (CC); maxillary gingiva; squamous cell carcinoma (SCC); Clinicopathologic.

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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 marked by the presence of keratin-filled crypts enveloped by well-differentiated squamous epithelium. [3].

In 2005 and 2017, the World Health Organization (WHO) officially recognized oral carcinoma cuniculatum (OCC) as a distinct and well-differentiated subtype of oral squamous cell carcinoma (OSCC). It is crucial to establish a correlation between histological observations and clinical as well as radiographic characteristics in the diagnosis of oral carcinoma cuniculatum (CC). This correlation is essential for distinguishing it from other tumors, especially verrucous carcinoma (VC), well-differentiated squamous cell carcinoma (SCC), papillary squamous cell carcinoma (PSCC), and various other tumors listed in the histological differential diagnosis of oral CC. [4,5].

In this report, we present a case of carcinoma cuniculatum (CC) in the maxillary gingiva. We augment this case presentation with a review of the literature, emphasizing the unique characteristics, clinical behavior, and the inherent difficulties in the diagnosis and management of this rare and distinctive tumor.

Observation:

A 44-year-old man was referred to the Department of Maxillofacial and Oral Surgery of the Military Hospital Moulay Ismail by his dentist with a 6-years history of painless growth in the maxillary gingiva. His medical and family histories did not contribute to this problem and he had a 15-year history of heavy smoking. Because of the presence of mucosal fistulas secreting a purulent fluid, the patient had been treated by his dentist with antibiotics and mouthwashes for several weeks but without any improvement.

On intra-oral examination, a swelling in the maxillary gingiva was observed. It had a smooth, pebbly "cobblestone" appearance and measured approximately 3 cm × 2 cm. This swelling was present on both the buccal and palatal sides of the incisor region. Additionally, teeth 11, 12, 21, and 22 were clinically missing. The color of the lesion resembled that of the surrounding normal mucosa, with some areas showing a red-white mixture (Fig. 1).

On palpation, the growth was firm in consistency and there was bleeding.

No palpable draining lymph nodes were noted.

Orthopantomogram showed edentulous radiolucent area in relation to 11, 12, 21 and 22 regions with ill-defined

borders (Fig. 2). CBCT scan revealed an osteolytic lesion in the incisor region of the maxillary (Fig. 3). Cervico facial scan showed an osteolytic mass of the maxillary region extending from the incisors to the floor of nasal cavity enhanced by contrast injection with a maximal crosssection of 3.5 cm × 2.5, but no cervical lymph node swelling. Consequently, a malignant tumor was suspected.

An incisional biopsy specimen was obtained for histopathological analysis. Microscopically, the lesion displayed the growth of well-differentiated squamous epithelium but with little cytologic atypia and few mitoses, the initial diagnosis was high-grade intraepithelial neoplasia with suspected micro invasion.

The excised specimen was sent for histopathological examination. The histopathological analysis revealed an endophytic growth characterized by a proliferative squamous epithelium, with notable keratinization in some areas (Fig. 5). This endophytic growth pattern of the epithelium extended deeply into the connective tissue, forming intricate branching structures filled with keratin, similar to tubules or canaliculi. These keratin-lined canaliculi interconnected, creating a complex network, resembling the burrows of a rabbit. Additionally, koilocytes were present in the specimen (Fig. 6). The resection specimen confirmed the diagnosis of carcinoma cuniculatum (CC), and the surgical margins were clear of any tumor. Following the surgery, the patient received adjunct radiotherapy and chemotherapy. As of the time of this report, the patient has been under follow-up for two years, and there have been no signs of a recurrence.



Figure 1: Photograph of the intraoral cavity showing a red-white colored lesion of the gingival maxillary mucosa with an exophytic “cobble-stone” surface.



Figure 2: OPG shows a radiolucent area in relation to 11, 12, 21 and 22 regions with ill-defined borders.

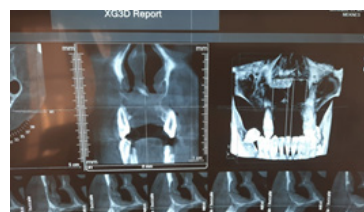


Figure 3 : CBCT scan showing an osteolytic lesion in the incisor region of the maxillary.



Figure 4 : A : Photograph of the intraoral cavity showing the palatal / maxillary post-surgical defect.
B : The patient rehabilitated by obturator prosthesis after maxillary resection.

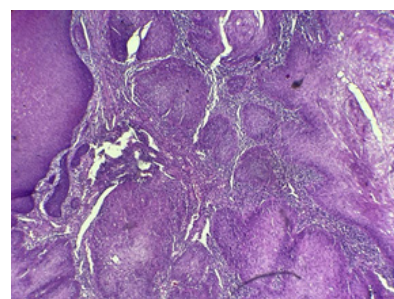


Figure 5: histologic section showing endophytic growth pattern of the epithelium, burrowed deep inside the connective tissue (× 10), The architecture resembled rabbit burrows, from which the Latin term “cuniculatum” is derived and comprised branching crypts.

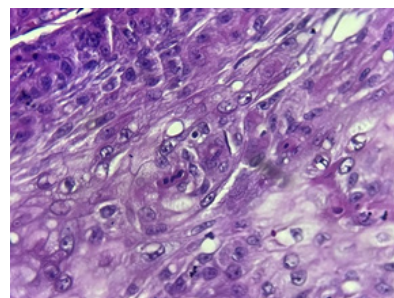


Figure 6: histologic section showing koilocytes (× 40).

DISCUSSION:

Oral carcinoma cuniculatum is a very rare subtype of squamous cell carcinoma first described by Flieger and Owinski in 1977 [6]. The rarity of this subtype and the limited understanding of its pathological and clinical characteristics have resulted in a lack of recognition of CC among both pathologists and oncologists, even after five decades since its initial description in the head and neck area. Except for two exceptional pediatric cases documented by Hutton et al. (7 years old) and Flieger et al. (9 years old), oral carcinoma cuniculatum predominantly occurs in adults during their sixth and seventh decades of life (average age ; 50 years , range ; 7–87 years) with a male preponderance (M: F = 3:1) [6,7,8,4,9,10]. Multiple potential causes for carcinoma cuniculatum (CC) have been suggested, such as tobacco and alcohol use, human papillomavirus (HPV) infection, traumatic event, chronic inflammation, radiation, and arsenic ingestion. However, the exact underlying cause remains uncertain [11]. While some studies have indicated an HPV link to nonoral CC, this association hasn't been confirmed in all cases of oral CC. [11, 12]. Oral CC represents 2.7% of oral squamous cell carcinomas [13]. Intraoral sites include attached gingiva, palatal mucosa, tongue, edentulous alveolus and mandible [14]. Clinically, it appears as a slowly expanding, painful, and persistent verrucous exophytic mass the surface of which may be papillary, nodular, cobble stone and/or ulcerated [14, 15, 5]. Similar to its occurrence in the skin and other anatomical sites, oral carcinoma cuniculatum is characterized by its gradual growth but local invasiveness. It infiltrates the underlying connective tissue and bone, and this progression may or may not be preceded by an area of leukoplakia [4, 8]. It can also lead to tooth mobility and mimic the symptoms of an abscess.

Differential diagnoses of CC have encompassed verrucous carcinoma (VC), papillary squamous cell carcinoma (PSCC), well-differentiated SCC, and chronic infection [3,4]. Upon analyzing all cases of oral carcinoma cuniculatum in the English literature, it can be seen that roughly one-third of these cases were initially misdiagnosed, leading to a delay in the appropriate treatment of these patients. Consequently, obtaining sufficient tissue samples for microscopic analysis is critically important for an accurate diagnosis, and establishing a proper clinicopathologic correlation is essential to minimize the risk of misdiagnosis [16]. Imaging radiology can help assess the possible locoregional invasion of adjacent tissues particularly bone and explore the cervical lymph nodes. The histological features of CC involve an endophytic growth pattern which includes several expansive and branching keratin-filled cysts; this is why it's referred to as "cuniculatum," drawing a comparison to a rabbit burrow. These cysts are surrounded by a well-differentiated epithelium that generally exhibits little to no significant cytologic atypia and few cell divisions (mitosis) [12].

These features were present in this case, which was intended to represent a typical example of CC. There is a limited diagnostic utility of immunohistochemistry. A few investigations have examined the protein Ki-67, which is expressed during cell division, as a measure of proliferation; low Ki67 expression (<5–15%) has been observed in the basal and suprabasal cell layers of the tumor [7, 17, 18]. The role of HPV has not been thoroughly explored. In the limited number of studies that have utilized p16 or HPV testing, the presence of HPV has not been detected in oral CC. [7, 18]. In our case, the histopathological analysis identified koilocytes which occur as a result of infection of the cell by human papillomavirus (HPV).

Surgery is the primary treatment for CC [3, 11]. It is imperative to perform a complete excision with a safety margin because of the tendency for local invasion. When lymph nodes are radiologically suspicious or clinically enlarged, nodal dissection is advised [19]. The frequency of lymph node metastasis ranges between 14% and 24% [7, 8, 4, 19]. In a recent literature review, there is a limited number of reviews discussing the use of chemotherapy and radiotherapy in the treatment of CC. Its locally aggressive behavior makes the benefits of chemotherapy and/or radiotherapy debatable. The role of radiotherapy, which some contend might induce anaplastic transformation, remains a subject of ongoing discussion [20].

Although its local aggressive activity, the prognosis is generally favorable and distant metastases is uncommon (~2%) [13, 4, 19].

CONCLUSION

In conclusion, oral CC is an uncommon variant of oral SCC characterized by distinctive clinical and histopathological features. Given its aggressive and invasive characteristics, it is advisable to conduct multiple deep biopsies of the suspected lesions and ensure a comprehensive sampling of these biopsies to prevent potential underdiagnosis.

Conflict of Interest:

There are no conflicts of interest.

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Ethical approval:

The authors declare that ethical approval was not required.

Informed Consent:

Patient's consent was taken before presenting the case report and intraoral pictures.

Authors contribution

H.Boukaaba: the literature search, Methodology, data collection, preparation of the manuscript and writing.
 A.Kessab, A.Boudhas: Supervision and reviewing.
 M.Y.Naji: methodology and design. M.Moumine: Supervision, reviewing and approval of the final manuscript.

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