



Carcinoma Cuniculatum of the Alveolar Mucosa: A Rare Variant of Squamous Cell Carcinoma

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Received: 5 April 2018 / Accepted: 23 May 2018 / Published online: 8 June 2018
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Abstract

Carcinoma cuniculatum is one of the variants of squamous cell carcinoma. It is significantly rare with an incidence rate <1% compared to other histological variants of squamous cell carcinoma. Various etiologic factors implicated are trauma, HPV, chronic inflammation and alcohol consumption but real causative agent still remains unclear. Initially it resembles plantar wart which slowly progress to bulky exophytic mass in the sole of the foot, where cases have been reported first. In the oral cavity it presents clinically as an exophytic growth and slowly invades the jaw and destroys the underlying bone. Microscopically it exhibits as both exophytic and endophytic epithelial masses along with well differentiated and pronounced hyperkeratosis. Treatment includes surgical resection alone unlike other variants which are treated by radiation with or without chemotherapy. Here we present a case of carcinoma cuniculatum occurred in alveolar mucosa of a 47 years old female. It presented as an exophytic growth in mandibular alveolar region, with histological features consistent with carcinoma cuniculatum.

Keywords Cuniculatum · Carcinoma · Rare variant of squamous cell carcinoma

Introduction

Carcinoma cuniculatum (CC) is one of the rare, low grade, clinicopathologic variants of squamous cell carcinoma. The latin term ‘cuniculus’ means rabbit warren or network of interconnecting rabbit burrows [1]. It was first described as ‘Epithelioma cuniculatum’ by Aird et al. in 1954, who reported two cases involving the foot [2]. In 1977, Fleiger and Owinski reported the first case of CC involving the oral cavity [3].

Clinically, it presents as a mucosal exophytic growth, whereas histologically it shows both papilliferous and verrucous growth patterns. It is a rare entity and till date only

50 cases involving the oral cavity have been reported in the literature [4]. We hereby report a case of CC involving the mandibular alveolar mucosa of a female patient.

History

A 47 year old female patient, presented with a chief complaint of a painless growth of 3 weeks duration in her right lower back tooth region.

Clinical Findings

On intraoral examination, a solitary, erythematous, nodular growth measuring about 2 × 1 cm² was seen in the mandibular alveolar mucosa of 46 region, 45 and 46 were clinically missing. The growth extended onto the lingual and buccal aspect of 47 partially overlapping the occlusal surface of 47 (Fig. 1). On palpation, the growth was soft in consistency and there was profuse bleeding.

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Fig. 1 Intraorally erythematous exophytic growth on alveolar mucosa in 46 and 47 region



Fig. 2 OPG shows slight marginal bone erosion seen in 47 region

Radiographic Findings

Radiographs showed edentulous radiolucent area in relation to 45, 46, and 47 regions with marginal bone erosion in relation to 47 (Fig. 2).

Diagnosis

Incisional biopsy was performed (Fig. 3). Microscopic examination of the Hematoxylin and Eosin stained soft tissue sections showed both exophytic and endophytic growth patterns. The surface epithelium was exophytic, papilliferous and verrucous with parakeratin filled crypts between the verrucous projections (Fig. 4). The endophytic growth pattern of the epithelium burrowed deep inside the connective tissue forming complex branching keratin filled tubules or canaliculi. These keratin lined canaliculi connected with one another forming a complicated network, resembling rabbit burrows (Fig. 5). Additionally,



Fig. 3 Incisional biopsy specimen. White soft tissue surrounding the tooth 47

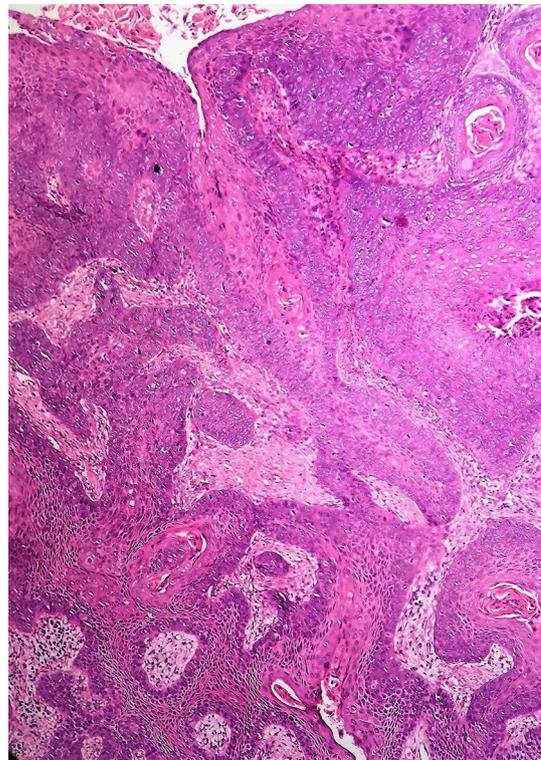


Fig. 4 Hematoxylin and Eosin stained soft tissue sections shows both exophytic and endophytic growth patterns with deep sinus tracts

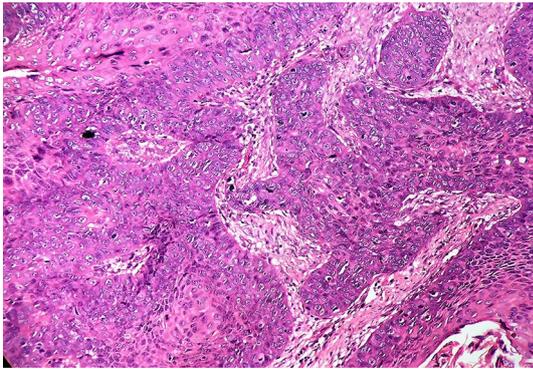


Fig. 5 Hematoxylin and Eosin stained soft tissue sections shows the endophytic growth pattern of the epithelium, burrowed deep inside the connective tissue

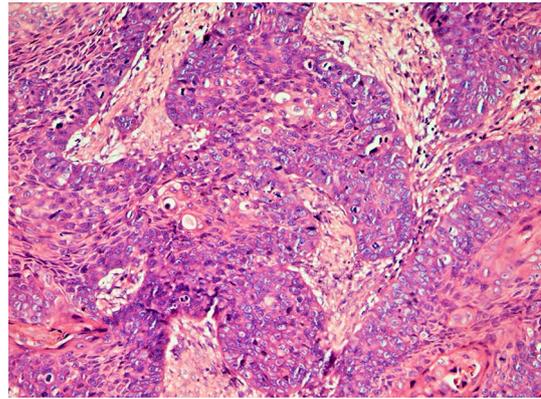


Fig. 7 Hematoxylin and Eosin stained soft tissue sections shows prominent dysplastic features with chronic inflammatory cells

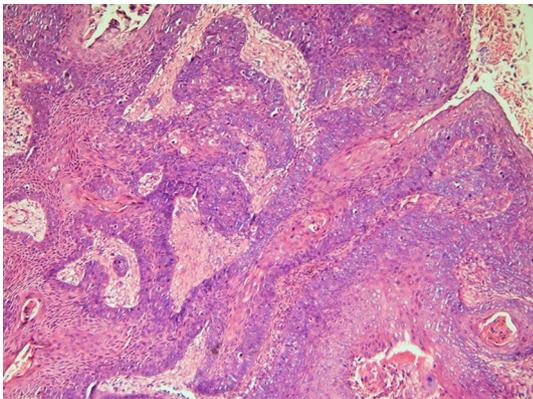


Fig. 6 Hematoxylin and Eosin stained soft tissue sections shows canaliculi connected with one another forming a complicated network, resembling rabbit burrows

epithelium exhibited dysplastic features such as nuclear hyperchromatism, cellular/nuclear pleomorphism, altered nuclear cytoplasmic ratio and numerous mitotic figures (Fig. 6). The surrounding connective tissue showed mixed inflammatory infiltrate of neutrophils, lymphocytes, plasma cells and mast cells (Fig. 7). These histopathological findings, favored the diagnosis of an unusual entity, the CC of alveolar mucosa in relation to 47.

Discussion

Oral CC is a rare uncommon variant of squamous cell carcinoma. CC accounts for only 1.9% of all squamous cell carcinomas [5]. The age of occurrence ranges from 23 to 84 years with a mean of 60 years. It shows male predominance and the male to female ratio is 14:5. Our case occurred in female patient which is comparatively rare. Etiological

factors include trauma, tobacco, alcohol and chronic inflammation [6]. Human papilloma virus (HPV; types 1–4, 6, 11, and 18) were also detected in certain cases but results were insignificant [7, 8]. Therefore, the exact etiology is not well established [6]. However, in the present case, the patient had no adverse oral habits. CC most commonly occurs on the lower extremities on plantar surface of foot [2]. Other sites include skin, genital mucosa, upper aerodigestive tract and rare in oral mucosa [9]. The present case, occurred in alveolar mucosa which is a rare.

Oral CC represents 2.7% of oral squamous cell carcinomas [10]. Intraoral sites include attached gingiva, palatal mucosa, tongue, edentulous alveolus and mandible [4]. Our patient had exophytic growth involving buccal and lingual aspect of 47 and also extended over edentulous area adjacent to it.

Clinically it presents as a slow growing, painful and non healing verrucous exophytic mass the surface of which may be papillary, nodular, cobble stone and/or ulcerated [4, 9, 11]. It appears like an over ripened orange with squashy mass [2]. It is usually associated with yellowish keratin secretion with foul odor [11]. Similarly the present case had an exophytic, erythematous, nodular, asymptomatic growth in relation to right mandibular second molar, but without any discharge or foul odour.

Histopathologically, CC shows exophytic and endophytic pattern. It shows deep, broad, complex proliferation of stratified squamous epithelium with keratin cores and keratin filled crypts resembling rabbit warren appearance [1, 12]. The pattern of hyperplasia is in the form of canaliculi. Lack of obvious cytological features of malignancy, despite its destructive growth pattern with variable mitotic activity along with neutrophil micro abscess formation is seen [13]. Similar features but with prominent dysplastic changes were observed in the biopsied specimen obtained from the present case.

In earlier days, CC was thought to be other name of verrucous carcinoma [14]. Few authors considered CC to be a variant of verrucous carcinoma, even the terms were used synonymously and lead to misconception. It has even been described as an inverted verrucous carcinoma [16]. CC should be differentiated from verrucous carcinoma, both of which may be similar clinically but can be differentiated histologically by the presence of broad rete ridges with pushing margins, intact basement membrane, minimal cytological atypia and prominent vertical fronds with surface projections mimicking church spires in verrucous carcinoma [15, 16]. Later, both terms were distinguished by few authors, thereby CC was considered to be a separate variant of squamous cell carcinoma [15] and distinct from verrucous carcinoma.

Other differential diagnosis of CC is papillary squamous cell carcinoma in which HPV has been suggested as an etiologic factor, with prevalence rate of 0–48% [13]. It always presents as a characteristic papillary finger-like pattern of growth with narrow fibrovascular stroma histologically, with clear invasive growth pattern, along with regional metastasis [9, 13]. CC is totally different from papillary squamous cell carcinoma which has rare metastasis.

Immunohistochemical studies by few authors showed varied (both minimal and over expression) expressions of p53, p63 and ki67 [14]. In this present case lesser staining expressions were observed with p53 and Ki67. Fifty CC cases were reported till date in oral cavity, with low recurrence despite rare metastasis and CC has got better prognosis than oral squamous cell carcinoma and aggressive when compared to verrucous carcinoma [4].

Summary

A case of CC, a rare oral entity, in a 47 years old female, who is not having any tobacco habits is reported here. It presented as an exophytic growth on right mandibular alveolus in 47 tooth region of 3 weeks duration. On intraoral examination, we found a nodular growth surrounding the tooth along with partial overlap of occlusal surface of crown and it was soft, profusely bleeding on palpation. Radiographically, slight marginal erosion on alveolar bone of 47 was evident. Provisional diagnosis of oral squamous cell carcinoma was made. Histologic sections showed both exophytic and endophytic growth patterns. Exophytic growth is in the form of papilliferous and verrucous patterns with formation of crypts lined by parakeratin between the verrucous projections. And the endophytic growth pattern with epithelium burrows deep inside the connective tissue and forms complex branching keratin filled tubules or canaliculi forming complicated network, resembling rabbit burrows. Additionally, epithelium exhibited dysplastic features such as, nuclear hyperchromatism, cellular/nuclear pleomorphism, altered

nuclear cytoplasmic ratio and numerous mitotic figures. The surrounding connective tissue showed mixed inflammatory infiltrate. With these histopathological findings, CC, a variant of squamous cell carcinoma, of alveolar mucosa in relation to 47 was diagnosed.

CC has overlapping features with verrucous carcinoma, oral squamous cell carcinoma and its variants. By correlating clinical and histopathological findings, appropriate diagnosis of CC can be rendered for efficient treatment.

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