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Carcinoma Cuniculatum: A Review

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Abstract
Carcinoma cuniculatum (CC) is a low grade variant of squamous cell carcinoma (SCC) showing features of both SCC and verrucous carcinoma (VC). It may present as a keratinized or condylomatous lesion that may become ulcerated. The etiology is unknown. Histologically the tumour shows both endophytic and exophytic growth, having papillomatous surface from which well-differentiated squamous cells penetrate deep into the underlying tissue, forming a burrowing pattern like a rabbit. It shows local invasion but not metastasis. Treatment is surgical excision with free surgical margins. To the best of our knowledge, only 19 cases have been reported in the maxillofacial region so far; hence it is an extremely rare lesion of the oral cavity.

Key Words
Carcinoma cuniculatum, exophytic, endophytic, papillomatous, verrucous.

Introduction:

Carcinoma cuniculatum (CC) is a rare variant of squamous cell carcinoma (SCC), which may show histopathological features of both SCC and Verrucous carcinoma.[1],[2],[3] However, some authors are of the view that it is just another form of verrrucous carcinoma found in the extremities. [4],[5] It is a low grade tumor, with sinus-like endophytic burrowing growth pattern and penetration deep into the lamina propria.[6],[7] It may present as a keratinized or condylomatous lesion that may become ulcerated. The etiology is not known. The name 'cuniculatum' derives from the appearance of the network of epithelial strands that resembles a rabbit warren (Latin- cuniculatum). The lesion was first described by Aird et al in 1954, in the foot,[7],[8] which is the most common location for this lesion.[9],[10] A few lesions have also been described in the hand, wrist, finger, knee, buttock, nasal cavity, larynx, pharynx, oesophagus, penis, face and oral cavity.[1],[6], [7], [8], [9], [11], [12], [13], [14] Intraoral presentation of the CC is usually a mucosal exophytic lesion or an ulcerated proliferation that invades in a burrowing pattern into the surrounding tissues. The tumor is slow growing, locally invasive and metastasis to the lymph nodes is rare. Chronic suppuration, local abscess formation and sequestration are common when the tumor invades bone, and may be mistaken for osteomyelitis. Treatment is usually radical surgical excision.[1].

Pathogenesis: The pathogenesis of CC is unknown. Possible etiologic factors may be HPV, traumatic event, chronic infiammation, radiation or arsenic ingestion. In some reports, alcohol and tobacco consumption were proposed as the predisposing factors, in cases of oral CC, but the real etiology remains unclear.[8]

Typical features of oral CC:

- Age of onset around 50 years.
- Presentation as a mucosal or gingival lesion.
- Smoking as a potential causative factor.
- Unusual features and slow growth that may complicate the diagnosis.
- Destruction of local anatomical features.
- Radiographic features indicative of an infectious rather than a neoplastic condition.
- Inevitable need for surgical resection of the lesion, but the benefit of radio- and or chemotherapy is controversial.[1]

The lesion begins as a condylomatous or keratinized lesion which eventually ulcerates and develops sinuses that exhibit foul smelling keratinaceous material.[6],[7]

Histopathological Features:

Grossly, carcinoma cuniculatum is bulky and white / gray in color, with a granular, multilobulated, verrucous/ papillary surface. Multiple sinuses typically form on the surface of the lesion, and they may produce a foul-smelling keratinaceous discharge. [6]

Histologically, the tumour shows both, endophytic and exophytic growth, having papillomatous surface from which well-differentiated squamous cells penetrate deeply to the underlying tissue. The cellular elements are organized in ramified sinuses, tunnels and/or crypts, which look like rabbit burrows and are full of keratotic debris. However, the basal membrane is intact with a single basal layer; the apparition of little zones of invasion defines the transformation into epidermoid carcinoma. There are layers with ortho- and parakeratotic horn formations looking like onion rings and many foci of microabscesses. The tumour

has pushing borders. Other areas exhibit jagged epithelial stromal interfaces surrounded by lymphoplasmacytic inflammatory infiltrate. There may be only mild cytologic atypia but frequent mitosis and lymphocytic infiltration are seen. Koilocytic changes are absent.[6],[8],[12],[16], [17], [18], [19], [20] **(Fig. 1)**

Differential Diagnoses:

The differential diagnoses for carcinoma cuniculatum of the oral cavity include verrucous carcinoma (VC) and squamous cell carcinoma (SCC). The nomenclature and morphologic definition of CC is not uniform, and some authors have even equated it with VC. However, it should be distinguished as a distinct entity for both therapeutic and academic reasons. CC displays hybrid features of SCC not otherwise specified (SCC NOS) and VC. VC shows broad pushing borders **(Fig 2)** while CC has a branching pattern of epithelial invasion, focally jagged borders and a propensity to invade more deeply. In contrast to SCC NOS, CC has not been associated with lymphatic or distant metastases despite deep invasion. The most important differentiating feature, however, remains the characteristic deep burrowing pattern displayed by the tumor.[1],[6] Sometimes CC can also be confused with Basal cell carcinoma (BCC), if it presents on sun-exposed skin as an ulcerated mass. Histologically, however, BCC presents with nests, islands, cords or irregular tumour tongues of variable size and shape, composed of basaloid cells having large hyperchromatic nuclei, scant cytoplasm, and indistinct cell membranes, with classical palisading of nuclei on the periphery of the islands. Moreover, the tumour cells show a cleft-like stromal retraction at the interface, absent in CC.[21], [22], [23], [24], [25] **(Fig 3)**

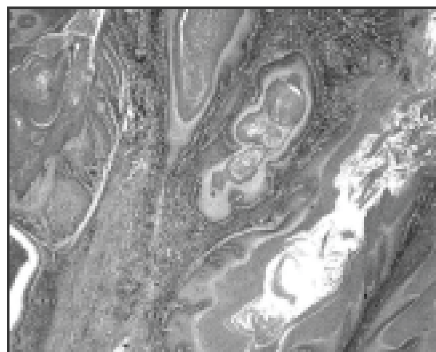

FIG - 1, H&E stained section exhibits a CC with well-differentiated neoplastic cells forming sinuses and tracts, filled with hyperkeratotic material, having irregular jagged borders, burrowing into the underlying connective tissue.

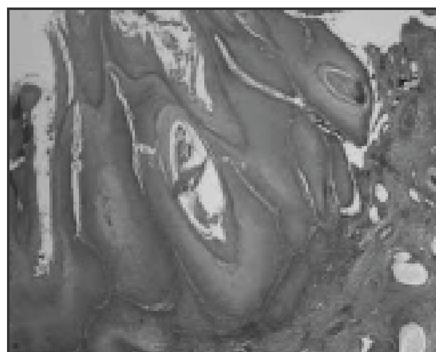

Fig 2. H&E stained section exhibits a VC with marked exophytic growth showing keratinization, and broad rounded rete pegs extending into the underlying collagen.

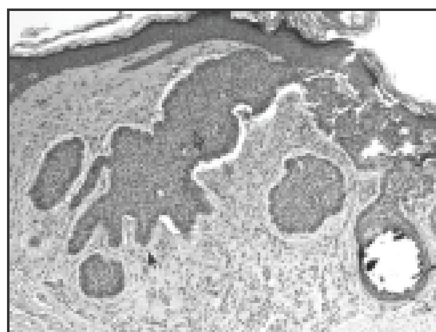

Fig 3. H&E stained section shows a BCC with nests and irregular tumour tongues of basaloid cells (green arrow), showing peripheral palisading of nuclei, slit-like stromal retraction (red arrow) and myxoid stroma containing mucin (blue arrow).

Conclusion:

CC predominantly affects older men, mean age 77 years (73-83 years)[7],[26] but there are no definitive statements about etiology and pathology and only few data about recurrence rate or metastatic behavior exist. Due to its local aggressive behavior, surgical excision with free margins is demanded as therapy of choice, but the benefit of radio- and/ or chemotherapy is controversial. [6],[12],[27] Typical localization of CC is the lower extremity, especially the plantar region and some lesions on the sacral or genital region are described.[6],[7] To the best of our knowledge, involvement of the oral cavity is extremely rare, as only 19 cases have been reported in the literature so far.[13] The long term prognosis of the lesion appears very favourable as no case of recurrence following resection has been reported so far.[1],[16],[27].

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