

Single Case

Carcinoma Cuniculatum of the Hand: A Case Report

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Keywords

Cutaneous squamous cell carcinoma · Low-grade carcinoma · Case report · Carcinoma cuniculatum

Abstract

Introduction: Cutaneous squamous cell carcinoma (cSCC) is a common malignant skin cancer arising from epidermal squamous cells, typically developing on chronically sun-exposed skin. The clinical diagnosis of cSCC is usually rather straightforward, although one should be aware of rare and atypical subtypes. **Case Presentation:** An 83-year-old woman, hospitalized for the workup of auricular fibrillation, presented a 10 × 5.5 cm, indolent, indurated, slightly purulent, tumoral mass on her left hand, that progressively increased in volume since around 2 years. There was no functional failure and no locoregional adenopathies. The first punch biopsy favored a keratoacanthoma. The culture of the purulent discharge revealed no microorganisms. MRI did not reveal any deep soft tissue or bone invasion. Excisional surgery was performed under local anesthesia. Histology revealed a well-differentiated cSCC-like exophytic tumor with an endophytic architecture composed of tortuous, keratin-filled, interconnected crypts, highly suggestive of cSCC of the cuniculatum type. **Conclusion:** Carcinoma cuniculatum is an exceptional subtype of cSCC, with an indolent clinical evolution and a well-differentiated histological presentation. Dermatologists and plastic surgeons should be aware of this rare type of cSCC that is to be differentiated from verrucous carcinoma, keratoacanthoma, cSCC and pseudo-epitheliomatous hyperplasia. Aggressive therapy must be avoided as deep invasion is exceptional, the growth is highly indolent and locoregional or systemic metastatic lesions are nearly never observed. Surgical excision is the cornerstone of treatment.

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Introduction

Carcinoma cuniculatum (CC) is a rare, low-grade, well-differentiated variant of cutaneous squamous cell carcinoma (cSCC), first described by Aird in 1954 on the sole of the foot [1, 2]. It is also referred to as epithelioma cuniculatum and is generally classified within the spectrum of verrucous carcinomas (VC) [3], although some authors consider it a distinct pathological entity [4].

Clinically, CC typically presents as a solitary, slowly enlarging tumor of variable size. Metastatic spread is uncommon, but extensive local invasion is not uncommon. The term cuniculatum derives from the Latin cuniculus, meaning “rabbit burrow,” reflecting the characteristic appearance of multiple small openings and channels on the tumor surface [5].

This neoplasm exhibits clinical and histopathological features that clearly distinguish it from conventional cSCC [6]. Clinically, CC evolves very slowly, is usually without pain, presents often purulent discharge, and manifests as a progressive exophytic verrucous-like mass, whereas cSCC is growing faster, maybe painful, tender, hyperkeratotic with or without ulceration. From a histological point of view, cSCC reveals an atypical, infiltrative squamous proliferation with cytologic atypia, whereas CC presents extremely well-differentiated squamous epithelium forming burrowing, keratin-filled sinuses with minimal cellular atypia. The aim of this case report was to raise awareness of this indolent yet potentially debilitating subtype of cSCC and to discuss its management, which differs from that of more common forms of cSCC.

Case Presentation

The CARE Checklist was completed and is provided as online supplementary material (for all online suppl. material, see <https://doi.org/10.1159/000553318>).

Written informed consent was obtained from the patient for publication of clinical details and images. An 83-year-old woman, hospitalized for the workup of auricular fibrillation, presented a large (10 × 5.5 cm) indolent, indurated, slightly purulent tumoral mass on her left hand, present since around 2 years. No other significant medical or surgical prior history was present, particularly any form of immunosuppression. She did not take any immunosuppressive agents. She could not recall any prior traumatism or wound at the site. She never wore a wristwatch. The lesion progressively increased in size and presented multiple small holes and apertures on its surface (Fig. 1a, b). Because it remained painless, she had not sought medical attention earlier. She complained, however, from foul smell due to the keratin-filled apertures. Clinically, the lesion was rather spongy and moved freely on the underlying structures. No regional lymph nodes were identified on clinical examination. An initial clinical differential diagnosis included a keratoacanthoma, cSCC, pseudo-epitheliomatous hyperplasia, hypertrophic pyoderma gangrenosum (PG), or verrucous carcinoma. A 4-mm punch biopsy initially suggested a keratoacanthoma. No microorganisms were retrieved on culture of the purulent discharge. Due to the atypical aspect of the lesion, it was decided to use imaging techniques before deciding a therapeutic option. To evaluate whether there was any deep invasion a MRI examination was performed. T1-weighted MRI demonstrated a homogeneous subcutaneous mass with lobulated contours on inversion recovery sequences and contrast enhancement in the cubital region (Fig. 1c). Tendons were intact, and no bone involvement was detected. To exclude eventual metastatic lesions or adenopathy's a PET-CT was performed and demonstrated a focal hypermetabolism at the left thenar region without, however, any evidence of systemic involvement.

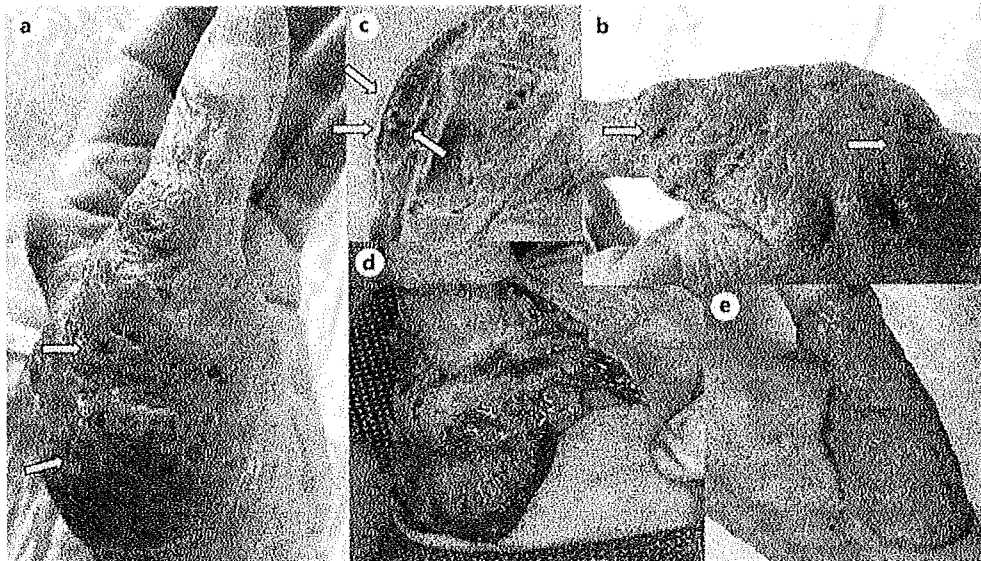


Fig. 1. **a, b.** Large 10 × 5.5 cm tumor mass on the left hand, at the thenar base of the thumb, indurated, with multiple openings (yellow arrows) sometimes with purulent discharge. **c** MRI image: homogeneous subcutaneous tumor mass, lobulated and with contrast enhancement in the tunnels (yellow arrows). **d** Intraoperative image of the surgical excision. **e** Healing by secondary intention (day 40).

The case was discussed at the multidisciplinary skin cancer board, and in agreement with the patient and her GP, a surgical excision was recommended. Surgical excision was performed under local anesthesia respecting a 0.5 cm margin (Fig. 1d). The wound was left to heal by secondary intention under an antiseptic dressing (Fig. 1e).

Histopathological examination showed a well-differentiated cSCC-like exophytic tumoral lesion with a deeply endophytic architecture composed of tortuous, keratin-filled, interconnected crypts or sinuses resembling “rabbit burrows,” highly suggestive of CC (Fig. 2). Ki-67 immunohistochemistry (IHC) demonstrated moderate proliferative activity. Immunohistochemical testing for syphilis, HSV-1, HSV-2, and HPV was negative. Grocott, PAS, and Ziehl-Neelsen stains excluded fungal or mycobacterial infection. Rare Gram-positive clusters were present. No perineural invasion or lymphovascular emboli were identified. No cytological atypia nor mitoses were detected. Correlation of clinical evolution and histology supported a final diagnosis of CC.

The surgical wound healed over around 5 weeks and no postoperative functional impairment was observed. No recurrence was observed at the 1-year follow-up visit.

Discussion

cSCC is the second most common type of keratinocyte cancer worldwide, following basal cell carcinoma. UV-exposure, HPV infection, chronic inflammation, immunosuppression, radiation, smoking, genetic immune diseases, and chemical carcinogens are among the most important causal agents. Risk stratification is based on differentiation and ranges from low- to moderate-risk variants (keratoacanthoma, VC, clear-cell cSCC) to high-risk subtypes (spindle-cell SCC, adenosquamous carcinoma, adenoid cSCC).

CC represents an exceptionally rare and low-risk variant of cSCC. CC is considered a type of VC and is typically located on the plantar aspect of the foot [7]. It has also been reported in

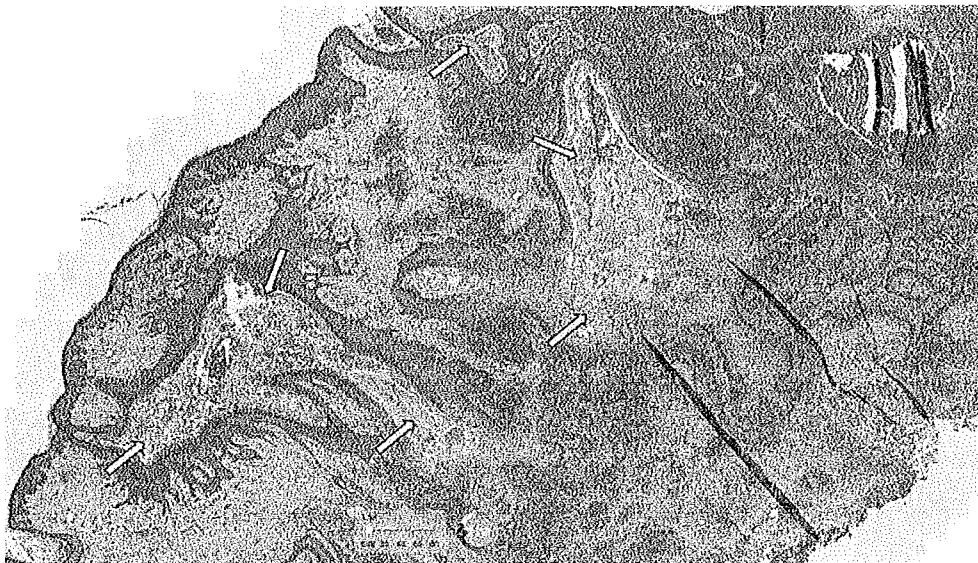


Fig. 2. Typical histologic appearance of CC, with an endophytic architecture of well-differentiated squamous epithelium forming deep, tortuous, keratin-filled interconnected crypts ("rabbit burrow") (yellow arrows) (H/E, $\times 15$).

the oral cavity (gingiva, mandible, tongue), esophagus, nail apparatus, and other cutaneous sites [8].

Chronic irritation or inflammation is thought to predispose to CC. It typically affects individuals between 30 and 80 years of age.

Clinically, CC is a slowly progressive, exophytic lesion that may take months to years to develop. A hallmark feature is the presence of multiple keratin-filled openings resembling rabbit burrows, often associated with foul-smelling purulent discharge. Although CC rarely metastasizes beyond the locoregional lymph nodes, it may be locally aggressive, invading soft tissue and especially bone, particularly in immunocompromised patients.

Histologically, CC is characterized the presence of multiple, deep, endophytic, burrowing, tortuous, keratin-filled sinuses and crypts ("rabbit burrow"), marked hyperkeratosis, parakeratosis, acanthosis, and expansile nests of very well-differentiated squamous epithelium with only slight cytologic atypia or even no atypia, often accompanied by a chronic lymphohistiocytic inflammatory infiltrate [8].

The histological differential diagnosis includes: VC (more pronounced exophytic wart-like surface with broad, pushing verruciform growth with minimal atypia), viral warts, conventional cSCC (more pronounced cytological atypia, less organized architecture, and more irregular invasion pattern with infiltrating cords), pseudo-epitheliomatous hyperplasia (absence of deep crypts filled with keratin) [9], or keratoacanthoma (rapidly growing tumor unlike CC, central characteristic keratinized crater and epidermal lipping). An actinic comedonal plaque can also be discussed (solitary plaque with multiple open comedones on photo-damaged skin). The pustular discharge could also evoke a PG, but histologically PG is not a neoplastic skin disease, but a neutrophilic dermatosis with ulceration with dense neutrophilic infiltrates, dermal edema, necrosis and on occasion, a leukocytoclastic vasculitis.

IHC may help differentiate keratoacanthoma from other cSCC variants by a distinctive IHC profile of mosaic p16, peripheral p53 and low Ki-67 expression. Furthermore, Wnt5a

and β -catenin may help distinguish keratoacanthoma from VC and cSCC, but VC and CC are not separable by these markers. In sum, CC and VC share similar IHC profiles and often resemble well-differentiated cSCC, making the morphological features more decisive than IHC [10]. To reach a final diagnosis of CC, a thorough clinico-pathological correlation should be made and often requires multiple deep biopsies but preferably the histological examination of the entire excision specimen.

The mainstay of treatment is surgical excision with a recommended 1-cm margin, using either conventional surgery or Mohs micrographic surgery. The excision margin in our case was less than recommended due to the absence of deep infiltration and the mobile character of the lesion. Radiotherapy may be considered for unresectable tumors or positive margins. The role of systemic therapy remains unclear, and it is unknown whether PD-1 inhibitors such as cemiplimab [11] may be beneficial in selected cases. Given the complex anatomy of the hand, a prior MRI examination to exclude deep soft tissue or bone infiltration was performed. In our patient, wide local excision without amputation was feasible due to the absence of fascia bone involvement, and healing by secondary intention was successful. A sentinel lymph node examination, lymphadenectomy or other imaging techniques are not systematically indicated and should be decided on a case-to-case base by the multidisciplinary skin cancer board.

The present case is notable for its unusual location and large size. Indeed, only a small number of cases involving the hand have been described: back of the hand [12], palmar surface [8], the thumb [13], finger and wrist [2], 3 cases of the nail apparatus [14]. More recently, a case of CC of the right thenar region with bone and lymph node involvement has been described for which palliative radiotherapy was performed [15].

In summary, this case of CC is atypical due to its localization, the absence of deep invasion and locoregional lymph node involvement despite its large size and longstanding clinical evolution, and the absence of chronic local irritation as potential triggering factor. The clinical implication of this case report is to increase awareness of the clinical features, the imaging and the management particularities of CC. It also stresses out that the final diagnosis can only be made on the clinical evolution of the lesion and on the histological examination of the entire lesion, to avoid misdiagnosis and erroneous therapeutic decisions.

Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images. In addition, this study was reviewed and the need for approval was waived by (EC CHU Liège, Accreditation number: 707, Liège, BELGIUM).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Category 1: conception and design of study: Mathilde Longrée, and Arjen F. Nikkels, acquisition of data: Mathilde Longrée. analysis and/or interpretation of data: Mathilde Longrée, Marie-Annick Réginster, Jorge E. Arrese, and Arjen F. Nikkels. Category 2: drafting the manuscript: Mathilde Longrée, and Arjen F. Nikkels. Category 3: approval of the version of the manuscript to be published: Mathilde Longrée, Marie-Annick Réginster, Jorge A. Arrese, and Arjen F. Nikkels.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further enquiries can be directed to the corresponding author.

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