

CASE REPORT

Carcinoma Cuniculatum of the Foot Invading the Bone Mimicking a Pseudo-Epitheliomatous Reaction to an Acute Osteomyelitis

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ABSTRACT

Carcinoma cuniculatum is a rare variant of squamous cell carcinoma. The clinical presentation is usually a non-verrucous exophytic plaque or tumor of the plantar region with a penetration in the deep tissues. Histological examination shows a proliferation of well-differentiated keratinocytes. We describe a patient affected by a slowly enlarging tumoral lesion overlying the fifth metatarsum of the left foot. Clinical examination and radiological investigations suggested a chronic osteomyelitis and a first histological examination of a punch biopsy was suggestive of a pseudo-epitheliomatous hyperplasia. The patient underwent several cycles with systemic

antibiotics without improvement. Finally, the fifth metatarso was amputated and the skin lesion was completely removed. The histological examination of the whole operatory mass allowed a diagnosis of carcinoma cuniculatum invading the bone.

Keywords: Carcinoma cuniculatum; Osteomyelitis; Squamous cell carcinoma

INTRODUCTION

Carcinoma cuniculatum is a rare form of squamous cell carcinoma with well-differentiated tumoral keratinocytes [1, 2]. The clinical presentation is variable and usually patients show a non-verrucous exophytic tumoral mass of the plantar region. The tumor rarely metastatizes but it is capable of a slow and progressive invasion of the deeper tissues, i.e., subcutaneous fat and bone [3]. Herein, we report a patient with a long history of a tumoral lesion of the skin overlying the fifth metatarsum of the left foot that was not diagnosed correctly until the bone and the skin mass were surgically completely removed.

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CASE REPORT

A 55-year-old white man came to the outpatient clinic of the Dermatology Department of the University of Brescia with 2-year history of a slowly growing tumor of the plantar region of the left forefoot. The lesion was always painful and pain was deeper during walking. Two years before, the lesion had been previously diagnosed as a wart and treated with topic keratolytics without any benefits and referred progressive growth of the lesion itself.

The patient had been previously hospitalized and underwent a magnetic resonance and cultural exam of bone biopsy of the lesion of the foot that had highlighted an acute osteomyelitis by *Staphylococcus lugdunensis*. For this reason, he had been treated with oxacillin 2 g intravenous (IV) every 4 h for 4 weeks with benefit.

Two months after discharge, the patient had referred a new worsening of the pain symptoms. A new bone biopsy had shown only fibrous rehash and a preventive systemic therapy with 4.5 g IV every 8 h piperacillin/tazobactam for 4 weeks was performed.

The inspection at our first visit revealed the presence of a nodular lesion of the fifth metatarsum of the plantar and lateral surface of the left foot, with a draining sinus tract that was malodorous (Fig. 1a, b). The lesion partially involved the dorsum of the foot that was erythematous and edematous over the fifth digit. The nodule was firm with a hyperkeratotic consistency and it was associated with strong local pain. Neurologic and peripheral vascular examination elicited no deficits and inguinal lymph nodes palpation was negative. The patient was otherwise in good health and he denied any history of trauma or prior foot pathologies.



Fig. 1 Nodular lesion of the fifth metatarsum of the plantar (a) and lateral (b) surface of the left foot

Incision biopsy of the lesion was performed. The diagnosis was pseudo-epitheliomatous hyperplasia. Because of the worrisome clinical aspect of the lesion, a new biopsy was planned. Multiple sections at different levels were examined, but only focal atypia was seen. The second diagnosis was squamous atypical proliferation; a well-differentiated squamous cell carcinoma cannot be excluded.

After the diagnosis, the patient was sent for an orthopedic consult which suggested a fifth metatarsal amputation of the left foot. Histopathological examination of the operatory specimen showed a well-differentiated squamous cell carcinoma with endophytic growth in the form of complex and burrowing sinus tracts, extending from the surface until the deep subcutaneous adipose tissue. Wide tracts were sometimes filled with keratin material and neutrophilic exudate. Metatarsal bone was focally involved, both cortical and medullary; a quite dense inflammatory reaction was associated. Excisional margins were not involved. The final diagnosis was well-differentiated squamous cell carcinoma, cuniculatum type (Fig. 2a, b).

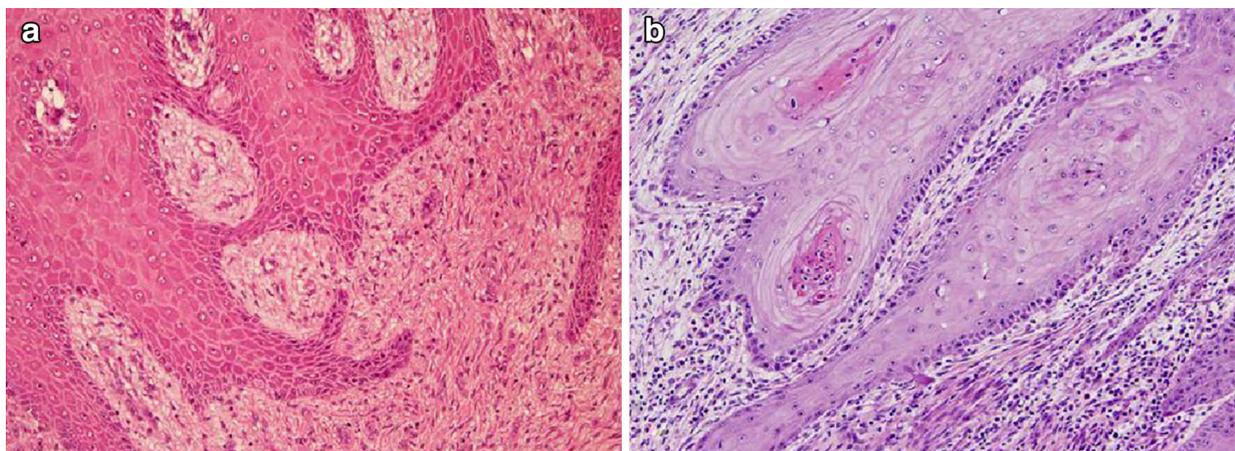


Fig. 2 **a** Squamous intradermal growth from a non-verrucous epidermal surface (10×). **b** Deep infiltrating margins with mild cytological atypia (20×)

After 6-month follow-up, the patient was able to ambulate with the assistance of orthotics and no recurrence of disease at the site of the amputation or metastases was detected.

Informed consent was received from the patient for publication of this case report.

DISCUSSION

We have reported a case of carcinoma cuniculatum in which a late diagnosis and inappropriate therapeutic approaches led to invasion of the underlying bone and the partial amputation of the foot.

Carcinoma cuniculatum is a rare, locally invasive squamous cell carcinoma with a low grade of malignancy [1]. It is rare with only about 100 cases reported so far, with the first report by Aird et al. [1] in 1954 [4]. It occurs in older patients, with an average age at diagnosis of about 60 years, and with a higher prevalence in men as compared to women.

Clinical presentation is most often reported as a painful warty exophytic tumor with crypts and sinuses that drain a malodorous exudate. The lesion is almost always single and bilateral lesions have been described only in two patients

[3, 5]. The tumor mass enlarges slowly progressively infiltrating the underlying tissues, i.e., subcutaneous fat and bone.

Early diagnosis is quite uncommon and the lesion is very often misdiagnosed at first as a wart or corn, which grows progressively despite topical treatments [6]. The delay in diagnosis allows the invasion to the underlying bones. Fortunately, the tumor rarely metastasizes with only five reports of metastatic epithelioma cuniculatum, all to draining lymph nodes and one also to the lung [7, 8].

On pathological examination, carcinoma cuniculatum looks as a well-differentiated squamous cell carcinoma with low-grade cytological atypia and burrowing sinus tracts, often filled with keratinous debris, descending to the subcutaneous fat and sometimes infiltrating the bone. This pattern of growth is difficult to be identified with histology of incisional punch biopsies and therefore the correct diagnosis is often allowed only by the histological examination of the whole lesion after surgical removal.

Unlike squamous cell carcinoma of the other body districts, carcinoma cuniculatum is clearly unrelated to chronic sun exposure whereas

chronic and repeated plantar traumatism, unrepaired or slowly repairing bone fracture or osteomyelitis, local infiltration of corticosteroids, chronic decubitus ulcer and chronic inflammatory diseases (e.g., plantar keratoderma or plantar intertrigo) could play a role in the pathogenesis [8–12]. Recently, a chronic infection by human papillomaviruses (HPV; types 1–4, 6, 11, and 18) has been suggested to have a role in the pathogenesis because they have a weak oncogenic potential [13].

The differential diagnosis of carcinoma cuniculatum entails, in first place, verrucous squamous cell carcinoma. This tumor was originally described in 1948 by Lauren Ackerman in the mouth and afterward also at various skin and mucosal sites [14]. Both lesions are very well-differentiated variants of squamous cell carcinoma with burrowing sinus tracts but the skin surface is smooth in carcinoma cuniculatum whereas it is verrucous and papillomatous in verrucous carcinoma [15].

Other clinical differential diagnoses for carcinoma cuniculatum include viral wart, eccrine poroma, reactive epidermal hyperplasia, adnexal tumors, giant keratoacanthoma verruciform xanthoma, and verrucous melanoma [16].

From a histological point of view, pseudocarcinomatous hyperplasia is a most difficult differential diagnosis because both lesions show well-differentiated keratinocytes, and often, only the investigation of the morphology of the whole lesion and a correct clinical pathological correlation allows the correct diagnosis [15].

The current mainstay of treatment is a surgical excision. Several authors have recommended aggressive excision or even amputation of the affected foot, but at present, a complete excision with tumor-free

margins of at least 5 mm is considered the treatment of choice. After excision, reconstruction of the surgical wound is often a challenge because of the extent and location of the tumor. Primary, secondary, and delayed closure techniques, skin grafts, and flaps have been suggested for larger skin defects [4, 6]. Other conservative therapeutic approaches, for example, electrodesiccation, cryotherapy, and laser ablation, are not always effective and often result in tumor recurrence [3].

In conclusion, epithelioma cuniculatum is a well-differentiated squamous cell carcinoma with low intrinsic aggressive potential. However, it is often misdiagnosed and, like in the present patient, the late diagnosis and inappropriate therapeutic approaches allow the invasion of the underlying bone and the following need of amputation leads to a substantial morbidity. Therefore, it is important that dermatologists have a better knowledge of this uncommon variant of squamous cell carcinoma.

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Compliance with ethics guidelines. Informed consent was received from the patient for publication of this case report.

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