Letter to the Editor
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A case of giant cutaneous squamous cell carcinoma mimicking a chronic leg ulcer
Kronik bacak ülserini taklit eden dev kutanöz skuamöz hücreli karsinom olgusu

Erol Mart et al. A giant cutaneous squamous cell carcinoma

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To Editor,
Cutaneous squamous cell carcinoma (cSCC) is the second most common skin cancer, constituting 20% of cases, with its incidence is rising due to aging populations. Advances in dermatoscopy and screening programs aid in early diagnosis. Without treatment, cSCC can pose significant health risks, with rare occurrences of regional lymph node invasion, distant metastasis or death. Tumor diameter >2 cm, localization on temple/ear/lip, thickness >6 mm, poor differentiation, desmoplasia, perineural invasion, bone erosion and immunosuppression are prognostic factors to consider a common primary cSCC as high-risk [1, 2]. This case report aims to highlight the importance of considering malignancy in the context of chronic leg ulcers.

A 71-year-old woman presented with a cutaneous mass on her left lower leg, which had been present for years but grew rapidly after a thorn prick 5 months ago. She had no systemic symptoms. Her past medical history included diabetes mellitus, hypertension and hyperlipidemia. She belonged to a socio-economically disadvantaged group and was illiterate. Dermatological examination revealed a 9x7 cm ulcerated tumor on the anterior aspect of the left tibia, with an accumulation of malodorous purulent exudate between the verrucous projections (Figure 1a). Laboratory findings included anemia, minimal CRP elevation, and anti-HCV antibody positivity. Initial differential diagnoses included deep fungal infection, lupus vulgaris, atypical mycobacterial infection, cutaneous leishmaniasis, neutrophilic dermatosis, pyoderma vegetans, and cSCC. Enterococcus avium was grown in tissue culture and ampicillin sulbactam was started. There was no growth in fungal culture. Mycobacterium tuberculosis PCR and QuantiFERON test were negative. The initial skin biopsy was nonspecific. A more detailed examination was performed as the lesion grew to 10x8 cm, including deeper and wider incisional skin biopsy and ultrasonography of the inguinal lymph nodes, revealing lymph nodes with a pathologic appearance. An excisional biopsy from the left inguinal lymph node was performed and the histopathology showed reactive changes with no evidence of tumor metastasis. Another skin biopsy was reported as ‘severe squamous hyperplasia characterized by areas of dermal invagination and accompanying inflammation findings, leading to suspicion of well-differentiated SCC’. The lesion was re-excised by plastic surgery to clarify the diagnosis of SCC. The pathology result was reported as grade 1 well-differentiated SCC, tumor thickness 5.5 mm, Clark level 4, no lymphovascular or perineural invasion, low and high-risk HPV negative (Figure 2). MRI and PET-CT scan were performed for staging (Figure 3). According to the Union for International Cancer Control TNM staging system 8th edition, the lesion was classified as stage III (T3N0M0-locally advanced SCC). Amputation was recommended, but the patient refused due to psychosocial reasons. Treatment with radiotherapy and cisplatin was initiated, resulting in partial response initially (Figure 1b), but the patient died of septic shock due to wound site infection.

Giant cSCCs with a diameter over 5 cm pose higher risks of complications, morbidity, and mortality [3]. Delayed diagnosis often stems from neglect, low socioeconomic status, old age, poor hygiene, and fear of diagnosis consequences , as observed in our patient [4].

Malignant skin lesions on the lower leg can mimic chronic ulcers, leading to misdiagnosis and treatment delays. There's controversy regarding when to biopsy chronic leg ulcers, with recommendations varying from 4-6 weeks to 4 months of non-healing wounds [5]. Standard surgical excision with 4-6 mm margins is preferred for low-risk cSCCs, while high-risk lesions may require wider margins or Mohs surgery. Wide surgical resections may not always be feasible due to aesthetic and functional concerns. In these cases, radiotherapy should be considered as the primary treatment. Radiaotherapy can also help reduce tumor size, control bleeding, and alleviate discomfort for locally advanced cSCCs. Conventional chemotherapy yields moderate results, leading to the exploration of innovative therapies. For patients with metastatic or locally advanced cSCC who are not candidates for curative surgery or radiotherapy, immunotherapy with anti-PD-1 antibodies (cemiplimab, pembrolizumab) is the first-line systemic treatment. Second-line systemic treatments include EGFR inhibitors (cetuximab, panitumumab) combined with platinum-based chemotherapy or radiotherapy [6, 7]. A multidisciplinary approach is imperative for all patients with advanced disease, given the risks of toxicity, age, and frailty of patients, in addition to the presence of co-morbidities, including immunosuppression.

In advanced cases of cSCC, as in our case, a vegetative appearance with islets and filamentous extensions may be observed, highlighting the importance of dermatologists being alert to atypical presentations. Chronic leg ulcers with exophytic growth, irregular edges, and excessive granulation tissue that resist healing despite treatment warrant suspicion of

malignancy. In such cases, multiple biopsies should be taken persistently to rule out malignancy and prevent complications through early histologic diagnosis [8].

Ethics

Informed Consent: The patient in this manuscript has given written informed consent for the publication of case details.

Authorship Contributions

Surgical and Medical Practices: P.K., Concept: H.M.E.M., İ.K.Y., B.N.A., Design: H.M.E.M., B.N.A., Data Collection or Processing: H.M.E.M., P.K., A.O.H., Analysis or Interpretation: H.M.E.M., İ.K.Y., B.N.A., Literature Search: H.M.E.M., Writing: H.M.E.M., B.N.A.

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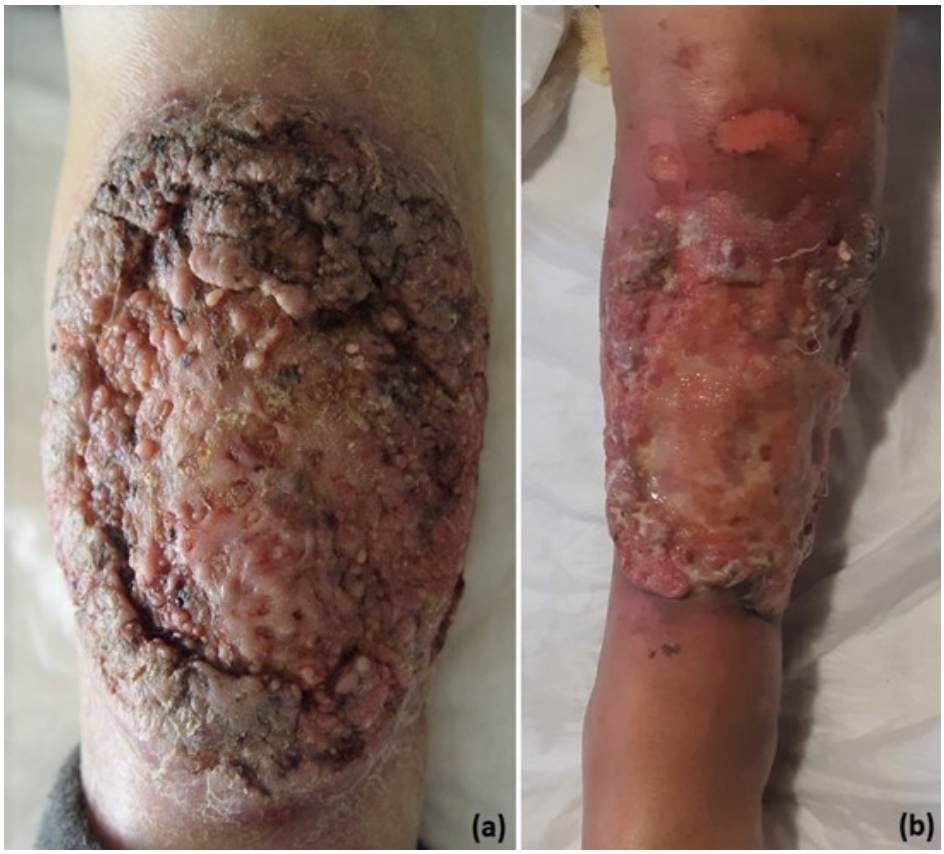

Figure 1. Clinical presentation of the patient before and after the treatment. **(a)** Clinical picture at initial presentation. **(b)** Partial response to cisplatin and radiotherapy after 1 month

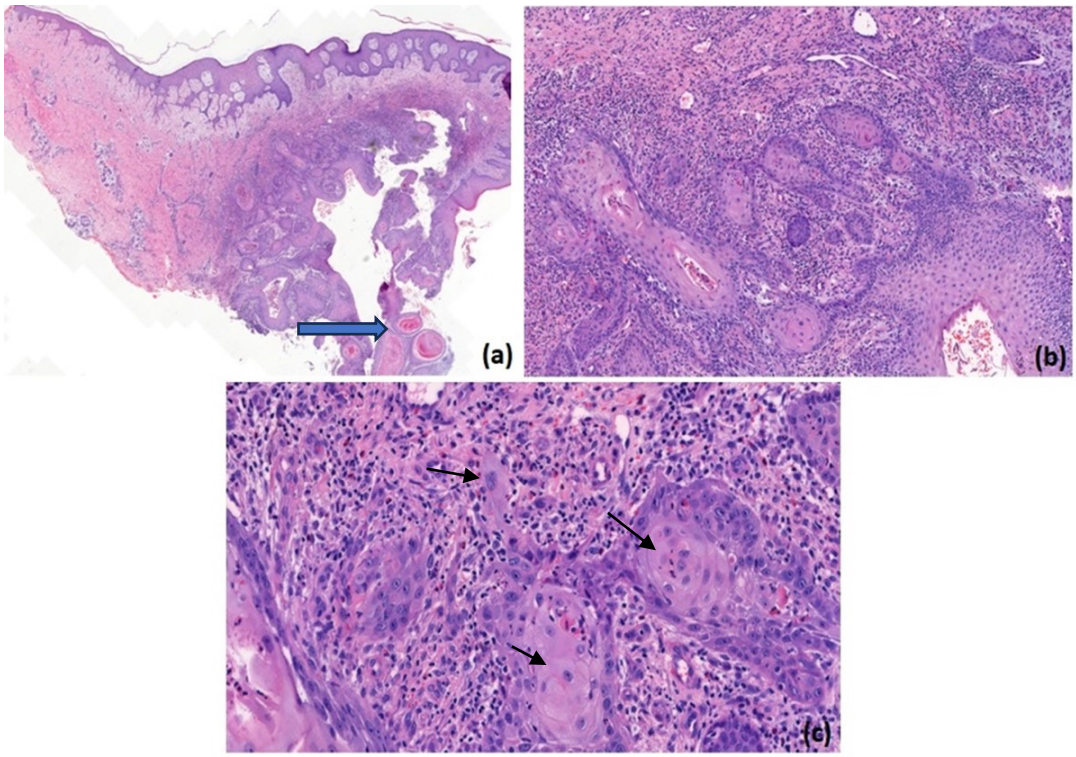

Figure 2. Histopathological features of the lesion**. (a)** Infiltrative tumoral growth and keratin pearls (blue arrow) in the reticular dermis (H&Ex10). **(b)** Invasive cell nests and cords (H&Ex40). **(c)** Atypical squamous cells with large oval vesicular nuclei and abundant eosinophilic cytoplasm (black arrows) (H&Ex100)

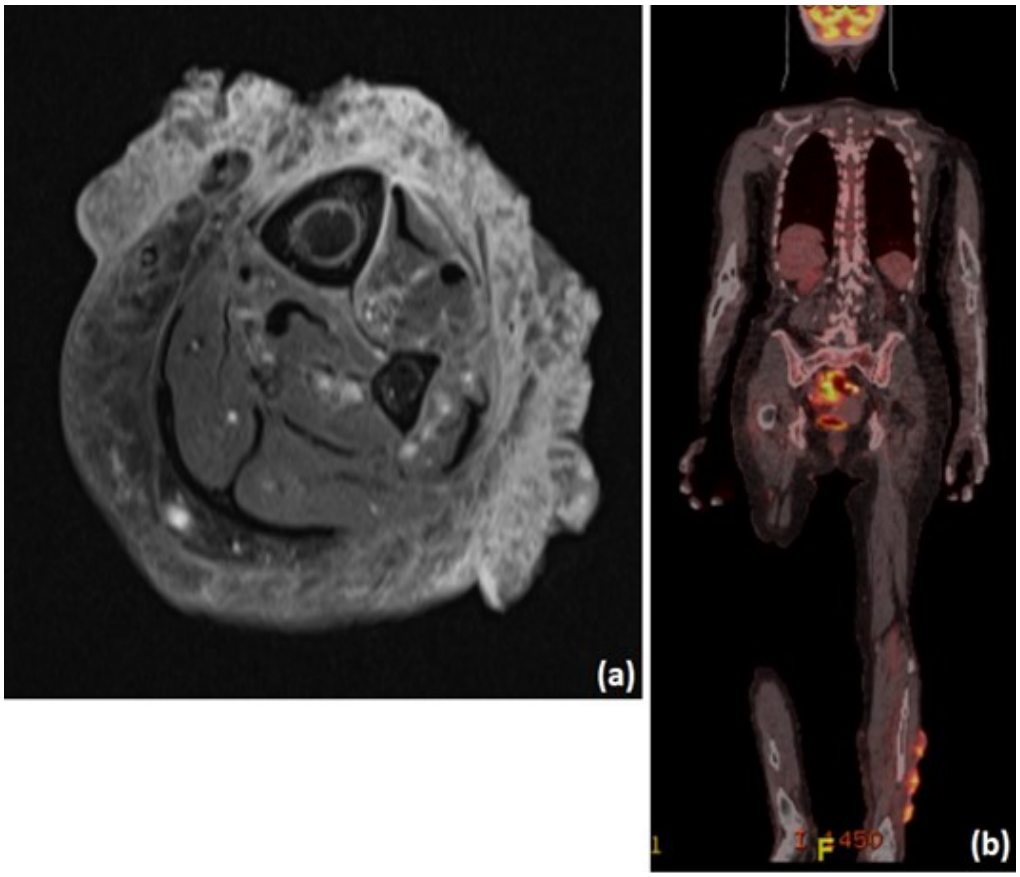

Figure 3. MRI and PET-CT imaging results of the patient**. (a)** MRI of the left cruris showed periosteal infiltration in an 8 cm bone segment and infiltration in the superficial fibers of the tibialis anterior muscle and crural fascia. **(b)** PET-CT showed dense enhancement of pathologic activity in the skin at the distal anterolateral aspect of the left tibia (SUV_{max}: 9.6)