Abstract

Squamous cell carcinoma (SCC) is a malignant tumor of epidermal keratinocytes which may arise de novo, or at already affected skin areas of different etiology, including chronic vascular ulcers (CVUs). We present a 74-year-old female patient, hospitalized in the Department of Dermatology, with venous ulceration of the lower right leg, 10x5 cm in size, with well-demarcated edges, and the base covered with fibrin and granulation tissue. The ulceration appeared 7 years ago, while 3 years ago it spread rapidly with pain in the right lower leg. In the beginning, the patient was treated with local and systemic antibiotic therapy. Later, hydrocolloid dressings and compressive bandages were applied, and after that hyperoxygenation was performed in the hyperbaric chamber. Although the above-mentioned therapy was applied correctly, it was not efficient. Since malignant alteration was suspected, two biopsies were taken and in both, histopathologic analysis showed granulation tissue without dysplasia. The third biopsy, however, performed a month after the second one, revealed a squamous cell carcinoma. Therefore, in cases with extended CVUs without an adequate therapeutical response during a long period of time, malignant transformation should be considered, and multiple biopsies at various sites should be performed.

Case report

We present a female patient, 74 years of age, admitted to the Department of Dermatology and Venereology of the Military Medical Academy with a lower leg ulceration which appeared 7 years ago. The ulceration increased in depth and width with years until it reached 10x5 cm in size, with intense pain, regardless of time or activity. The patient had no history of diabetes, or other chronic diseases, except for hypertension. It started 3 years ago, and was under good control with antihypertensive therapy. The ulceration was located on the front side of the right lower leg, irregular shaped, with hard edges, while the bottom was filled with granulations and even a slight touch could cause bleeding. The surrounding skin was unchanged, and lymph nodes were not enlarged (Figure 1). Laboratory findings showed a mild anemia, while the other findings were within normal limits. Ultrasonography of the lower extremities revealed insufficiency of perforating venules in the distal third of the right lower leg, without signs of deep venous thrombosis, but degenerative changes were diagnosed on the arteries. Chest radiography and abdominal ultrasound findings were normal in the beginning, and the patient was treated with local and systemic antibiotic therapy. After that, hydrocolloid dressings and compressive bandages were used, without success, so hyperoxygenation in hyperbaric chamber was performed. None of these therapeutic modalities...
Discussion:

SCC is the most common type of tumor arising from a chronic leg ulcer (CLU). Malignant transformations of chronic leg ulcers are mainly encountered in elderly patients over 70 years of age, and more often in females (female to male ratio: 2.5:1) (1).

In our patient, the ulceration appeared seven years before the diagnosis of SCC was made. According to the literature, SCC associated with chronic ulcerations, the above-mentioned period is not a long one. The study of Combemale et al. performed in 2007 in France, included 85 patients with malignant transformation of CLU. In these patients the transformation lasted 27 years, on average (1). In our case report, the patient presented with all clinical characteristics of malignant transformation: abnormal granulation tissue, well defined peripheral margins, protracted course and spreading of the ulcer despite appropriate treatment, unusual pain and abnormal bleeding. However, the diagnosis could not be established after two biopsies. Hanson et al. pointed to the difficulty of obtaining histological confirmation, even in granulating forms, and recommended (5), similar to Bardursson et al., multiple (up to five) biopsies at several sites of the ulcer, estimating a 25% risk of false-negative results upon a single biopsy (4).

Radiography revealed incipient osteolysis in our patient, while there was neither lymph node involvement, nor visceral metastases. In their study Combemale et al. found that 41% of tumors invaded...
the underlying bone, whereas lymph node involvement
and visceral metastases occurred rarely (9%) (1).

Histological differentiation is a major prognostic
factor. Tumors may be well, moderately or poorly
differentiated (6). Treatment depends on the clinical
stage of the disease. Amputation should be considered
for all tumors that are not well differentiated (6).
According to Baldursson et al. radiotherapy is
only palliative. In our patient, amputation was
recommended as the best therapeutic option,
taking into consideration the size and depth of the
tumor invasion and grade III SCC, confirmed by
histopathological analysis, but it was rejected by the
patient.

Conclusion:
In cases of long term CVU and absence of adequate
therapeutic response, malignant transformation
should be considered and multiple biopsies at various
sites of the lesion should be performed.

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Maligna alteracija hronične venske ulceracije na podkolenici: 
prikaz slučaja

Sažetak

Uvod: Planocelularni karcinom kože je maligni
tumor keratinocita koji može da se javi de novo ili na
već izmenjenoj koži različite etiologije, uključujući i
hroničnu vensku ulceraciju.

Prikaz slučaja: Bolesnica starosti 74 godine,
hospitalizovana u Klinici za kožne i polne bolesti, VMA
sa venskom ulceracijom desne potkolenice promera
10x5 cm, podrivenih i eleviranih ivica, dna prekrivenog
obilnim fibrinskim naslagama i granulacionim
tkvom. Ulceracija se pojavila pre 7 godina, a od pre
3 godine se izrazitije širila i produbljivala sa bolovima
u desnoj potkolenici. Uzet je isečak ivice ulceracije za
patohistološku analizu u dva navrata i oba puta videno
je granulaciono tkivo. Bolesnica je lečena ambulan-
tno i u više navrata hospitalno različitom lokalnom
i antibiotskom terapijom, hidrokoloidnim pločama,
kompresivnim zavorijima, oksigenom terapijom u
hiberbaričnoj komori bez zadovoljavajućeg efekta. Zbog
dalje sumnje na malignu alteraciju uzet je otisak rane
za citološku analizu i videne su ćelije koje mogu da
odgovaraju planocelularnom karcinomu, što je tek trećom
biopsijom i dokazano, istivanjima radi određivanja
stadijuma, utvrđeno je da je bolest u IB stadijumu. Uz
konsultaciju hirurga-plastičara, vaskularnog hirurga
i ortopeda, indikovana je amputacija desne potkolenice.

Zaključak: Ukoliko hronična ulceracija nema adekvatan
terapijski odgovor i ne zarasta uprkos terapiji,
neophodno je misliti na malignu alteraciju i učiniti
nekoliko sukcesivnih biopsija sa više različitih mesta
ulceracije radi PH analize.