

Malignant transformation of a chronic leg ulcer: a case report

Kristina KOSTIĆ*, Tomislav MLADENOVIĆ, Radoš ZEČEVIĆ

Department of Dermatology and Venereology, Military Medical Academy, Belgrade

*Correspondence: Kristina KOSTIĆ, E-mail: zokikost@eunet.rs

UDC 616.5-006.6:611.98



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. After further investigations, amputation of the right lower leg was suggested. Therefore, in cases with extended CVUs without no adequate therapeutical response during a long period of time, malignant transformation should be considered, and multiple biopsies at various sites should be performed.

Long-lasting chronic leg ulcers (CLUs) of vascular origin are at increased risk for transformation into carcinomas. Malignant transformations are rare, and often misdiagnosed complications of CLU. However, the most common among them are well-differentiated squamous cell carcinomas (2). Clinical sings of malignant CLU include abnormal granulation tissue, the edges of the ulcer well differentiated from the surrounding skin, failure of progress despite accurate diagnosis and treatment, unusual pain and abnormal bleedding. Malignancy in CLU is confirmed by histopathology, taking multiple biopsies from different sites of the ulcer (3). It is necessary to determine the clinical stage of lesions, whereas histopathological differentiation reveals the extention of lesions, important for proper treatment.

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



Figure 1. The ulceration on the front side of the right lower leg

were effective. Since the ulcer was refractory to treatment, a malignant alteration was suspected. In short period of time, two biopsies were taken and both histopathological findings revealed granulation tissue without dysplasia. During the following month, conservative therapy (antibiotic, antiseptic and compressive therapy) was continued, but it resulted with increased granulation tissue formation at the bottom and borders of the ulceration.

On the next admission, a sample was taken again for cytological examination, and malignant cells were found. The third biopsy was taken from the border of the ulceration, and histopathological analysis revealed a squamous cell carcinoma, grade III (Figure 2). Radiography of the right lower leg showed incipient osteolysis, but neither lymph node involvement, nor visceral metastases were established by ultrasound. There was no evidence of malignancy dissemination, and the disease regressed to stage Ib. After consulting plastic, vascular and orthopedic surgeons, amputation of the right lower leg was recommended, and rejected by the patient. She was dismissed with symptomatic therapy.

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

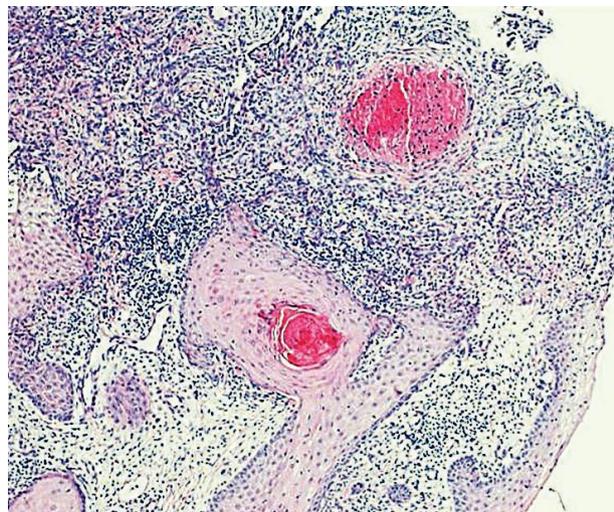


Figure 2. Skin biopsy, exulcerated and infiltrative keratinized squamous cell carcinoma (HE x 100)

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, podriivenih i eleviranih ivica, dna prekrivenog obilnim fibrinskim naslagama i granulacionim tkivom. 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 viđeno je granulaciono tkivo. Bolesnica je lečena ambulantno i u više navrata hospitalno različitom lokalnom

i antibiotskom terapijom, hidrokoloidnim pločama, kompresivnim zavojima, oksigenom terapijom u hiperbaričnoj komori bez zadovoljavajućeg efekta. Zbog dalje sumnje na malignu alteraciju uzet je otisak rane za citološku analizu i viđene su ćelije koje mogu da odgovaraju planocelularnom karcinomu, što je tek trećom biopsijom i dokazano, isptivanjima 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.