

CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Basal cell carcinoma presented and mistreated as chronic venous ulcers – report of five cases

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Introduction Basal cell carcinoma (BCC) is the most common non-melanoma skin cancer in Caucasians and one of the most frequent malignancies in general, especially in older adults. Squamous cell carcinoma is the most frequent tumor developing on chronic leg ulceration, while BCC rarely occurs and is often misdiagnosed. In addition, since older adults commonly have coexisting chronic vein insufficiency, the ulcerated BCC is frequently mistaken as being of venous origin.

Outlines of cases We present five cases of BCC presenting as chronic venous ulcers.

Conclusion Long-lasting ulcers with no healing tendency must be considered malignant until proven otherwise. Knowing the characteristics of malignant ulceration may help in early detection and treatment.

Keywords: malignancy; skin cancer; ulcers; chronic vein insufficiency

INTRODUCTION

Basal cell carcinoma (BCC) is the most common non-melanoma skin cancer in humans and one of the most frequent malignancies in general [1]. Although BCC is a slow-growing cutaneous cancer with a low rate of metastasis (0.0028% to 0.5%), if left untreated, it can cause extensive and deep tissue destruction [2]. It may be an ulcer or malignant transformation of existing chronic leg ulceration (CLU). Since the most common cause of CLU is chronic vein insufficiency (CVI), malignant CLUs are frequently misdiagnosed [3]. Early diagnosis prevents the development of giant forms of skin cancers and improves prognosis. Therefore, it is crucial to differentiate between malignant (either primary malignant or CLU that underwent malignant transformation) CLU and venous leg ulcers (VLU). In this article, we will describe five cases of BCC that were misdiagnosed as VLU and mistreated for years until finally diagnosed as skin cancers.

CASE REPORTS

We present five patients aged 75–82 years with non-healing ulcers of the lower legs, which were present 1–21 years. All the patients had coexisting CVI. The characteristics of patients are summarized in Table 1.

The first patient had a history of long-lasting CVI and excessive sun exposure without sun protection creams; he denied exposure to chemicals and any trauma of this region. Physical examination revealed an irregular bleeding ulcer on the anterior part of the left lower leg, with

a granulated base filled with fibrin and raised edges (Figure 1A). Histopathology showed micronodular BCC (Figure 1B).

The second patient had no history of sun exposure and denied any trauma to the area. However, clinical examination revealed an ulcer on the anterior part of the right lower leg with a base filled with granulation tissue that formed elevated, translucent structures (Figure 2A). Biopsy showed nodulo-infiltrative BCC. The lesion was excised, and split-thickness skin graft placement was performed. In the follow-up period of 10 months, no recurrence was observed (Figure 2B).

The third patient had a history of type 2 diabetes mellitus and congestive heart failure. No record of sun exposure or previous trauma was reported. Physical examination showed an ulcer with flat edges and a transparent, granulated base (Figure 3A). The histopathological finding revealed nodular BCC. The lesion was excised, and split-thickness skin graft placement was performed. In the follow-up period of 10 months, no recurrence was observed (Figure 3B).

The fourth patient denied exposure to the sun or any trauma. Physical examination revealed an oval ulcer with raised edges on the left lower leg, above the lateral malleolus, filled with granulation tissue. No signs of inflammation were observed. Later, after one month on check-up, the ulcer became hyper granulated, and a biopsy was indicated (Figure 4A). Histopathological findings of edges and base showed infiltrative BCC (Figure 4B).

The fifth patient had a long history of CVI and a history of breast cancer. Physical examination revealed an oval ulcer with a clear, granulated base on the distal anterior part of

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Table 1. Summarized characteristics of the patients

Case	Age (years)	Sex	Duration of ulcers (years)	Diameter (cm)	Localization	Histopathology	Therapy
1	79	M	21	7 × 4	anterior part	Micronodular BCC	Excision
2	75	M	4	4.5 × 3.5	anterior part	Noduloinfiltrative BCC	Excision
3	82	F	5	2 × 2.5	anterior part	Nodular BCC	Excision
4	75	F	1	1 × 1.5	above the lateral malleolus	Infiltrative BCC	Excision
5	79	F	2	2 × 2	anterior part	Carcinoma basosquamousus	Radiotherapy + Excision

BCC – basal cell carcinoma; M – male; F – female; + – positive; - – negative

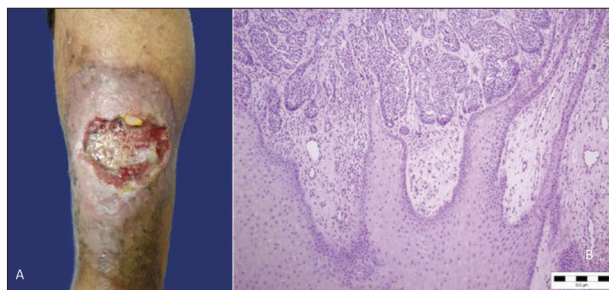


Figure 1. A: An irregular, bleeding ulcer located on the anterior part of the left lower leg; B: histopathology of the ulcer; H&E, 100 ×

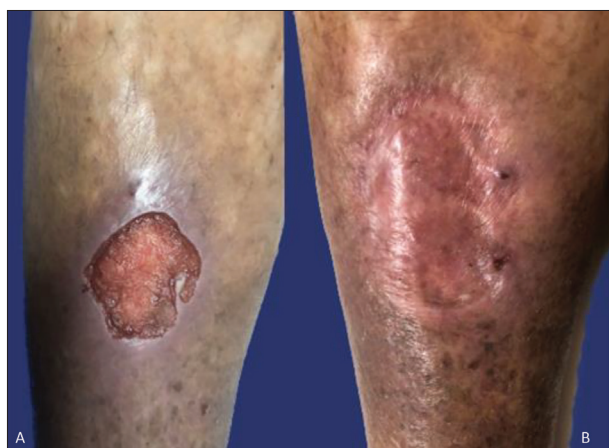


Figure 2. A: An ulcer with the base filled with granulation tissue that formed elevated, translucent structures; B: the ulcer eight months after reconstruction

Table 2. Differences between malignant and venous ulcer

Characteristics	Malignant ulcer	Venous ulcer
localization	atypical	medial malleolus
size	small (< 3 cm ²)	varying size
margins	elevated	sharp, irregular
depth	deep	shallow
base	soft pink granular tissue	fibrinous material

the right lower leg. The histopathological finding showed basosquamous carcinoma (Figure 5A). The patient was referred to the Oncology department and treated with radiotherapy. The ulcer showed central epithelization during radiotherapy, but small shallow ulcers covered with crusts on elevated livid edges have occurred (Figure 5B). This was highly suspected to be a cancer recurrence, so the patient was referred to the Department of Oncology for total excision of the lesion.



Figure 3. A: An ulcer with flat edges and a clear, granulated base; B: the ulcer eight months after reconstruction

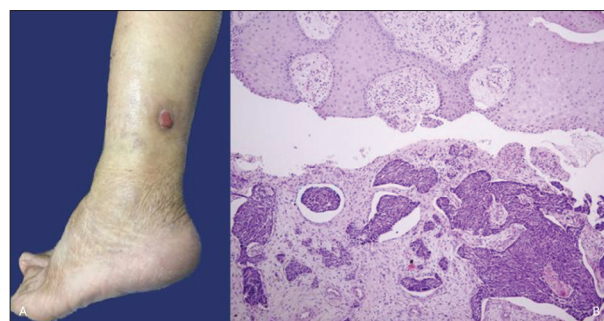


Figure 4. A: An oval ulcer on the left lower leg above the lateral malleolus filled with granulation tissue and with elevated livid edges; B: histopathological finding; H&E, 100 ×

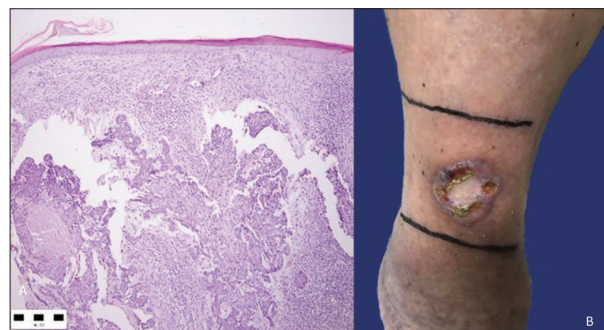


Figure 5. A: Histopathological finding before treatment; H&E, 100 ×; B: ulcer with central epithelization and small shallow ulcers covered with crusts on elevated livid edges

The patients have given written consent for the publication of this article. This study was done in accordance with the institutional committee on ethics.

DISCUSSION

Although BCC most commonly occurs on the head and neck, BCC occurs on limbs in approximately 3.3% of cases [4]. On extremities, BCC may present as a chronic leg ulcer [3]. Since older adults commonly have coexisting CVI, the ulcerated BCC may be mistaken for the venous origin. Besides cases of primary BCC of lower extremities, some articles also show the malignant transformation of existing VLU [5–10]. The most common malignancy arising from non-healing chronic ulcers is squamous cell carcinoma (SCC), but a few cases of BCC are also described. In a retrospective study of 85 malignantly transformed ulcers, 98% were SCC, whereas just 2% represented BCC [5].

On the other hand, Yang et al. [9] recorded that 2.2% of reported leg ulcers were skin cancers – 75% BCC and 25% SCC. Their results also indicated that 2.4% of venous ulcers would undergo malignant transformation. Factors that promote this transformation are chronic inflammation and tissue proliferation due to long-lasting nature of the ulcer. Kirsner et al. [6] estimated that 1–7% of all chronic wounds would develop malignant properties; this number may be lower than real, primarily due to frequent misdiagnosis. Gil et al. [7] described some of the clinical features when CLU should be investigated in the direction of malignancy. Tchanque-Fossuo et al. [8] recommended taking biopsy samples of the edges and the base to rule out malignancy. Serial biopsies every 3–6 months of ulcers that do not tend to heal have been proposed by various authors [11, 12].

We have to point out that typical characteristics of chronic venous ulcers were absent in our patients. On the contrary, all patients had a history of long-lasting CVI. Furthermore,

the study, which included 125 cases of BCC, found that 25% of patients had concomitant chronic venous stasis, suggesting a relationship between venous disease and BCC [13]. Since patients were initially treated in other institutions and no biopsies were performed in the early stages of lesions, we can only speculate if BCC in our patients resulted from malignant transformation of pre-existing ulcers or *de novo* lesions. However, a biopsy was performed at our institution, and histopathological findings were similar in all the patients, showing histopathological features of BCC.

Mohs micrographic surgery is the best management option for these cancers since it provides maximal margin control and minimal defect in the already compromised areas of stasis dermatitis and poor wound healing on the shins. Also, the procedure is performed under local anesthesia, with minimal impact on general health in older individuals, and is well tolerated in ambulatory settings. On the other hand, radiation therapy should be avoided in treating ulcerated BCCs, not just to avoid further compromise of already damaged vascularization in the area but also due to the risk of future cancerization and the appearance of new tumors in the treated skin, years post radiation therapy.

Long-lasting ulcers with no healing tendency must be considered malignant until proven otherwise. This article aims to point out the possible malignancy in chronic venous insufficiency. Carcinomas may mimic granulation tissue which can mislead the correct diagnosis. Atypical wound morphology, localization, and refractoriness to conventional treatments may suggest malignant transformation. Most of these ulcers are managed in primary care clinics, and only a minimal number of such ulcers are referred to the specialized tertiary clinic. The education of practitioners about the possibility of malignant transformation of chronic venous ulcers is essential. Further investigations are necessary to clarify the exact algorithm for diagnosing malignant ulceration.

Conflict of interest: None declared.

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Базоцелуларни карцином погрешно дијагностикован и лечен као хронична венска улцерација – приказ пет болесника

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САЖЕТАК

Увод Базоцелуларни карцином најчешћи је немеланомски карцином код припадника беле расе и један од најчешћих малигнитета генерално, нарочито код старије популације. Сквамозелуларни карцином је тумор који се најчешће развија на терену хроничних улцерација, док се базоцелуларни карцином ретко јавља и често се погрешно дијагностикује. С обзиром на то да се код старије популације на доњим екстремитетима често јавља и хронична венска инсуфицијенција, егзулцерисани базоцелуларни карцином се често погрешно дијагностикује и третира као венска улцерација.

Приказ болесника Приказујемо пет болесника са базоцелуларним карциномом доњих екстремитета, са клиничком презентацијом хроничних венских улцерација.

Закључак Улцерације које дуго трају без тенденције зарастања морају се схватити као малигнитет, док се не докаже супротно. Познавање карактеристика малигне улцерације може помоћи у раној детекцији и лечењу.

Кључне речи: малигнитет; карцином коже; улцерације; хронична венска инсуфицијенција