Ulcerated Basal Cell Carcinomas Masquerading as Venous Leg Ulcers

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ABSTRACT

BACKGROUND: Nonmelanoma skin cancers rarely arise from venous leg ulcers (VLUs). Although basal cell carcinoma (BCC) is the most common nonmelanoma skin cancer, its association with lower-extremity ulcers is not as frequently reported as other malignancies.

OBJECTIVE: To report a case series of biopsy-proven BCC from lower-extremity ulcers of patients who presented at a multispecialty wound clinic.

METHODS: Four male patients (mean age, 82.75 years) with 4 chronic VLUs (duration ranging from 2 months to 10 years) underwent a biopsy of their ulcerative lesions.

RESULTS: Histologic examination of the specimens revealed 4 cases of BCC. All of the lesions were surgically excised, followed by split-thickness skin graft (n = 2) or healing by secondary intention (n = 2). All of the patients remained healed at follow-up ranging from 15 to 27 months, except for 1 patient who opted for conservative management and had not completely healed at 14 months' follow-up.

CONCLUSIONS: Biopsies are warranted for any VLU with documented stalled healing following 3 months of standard of care. One biopsy is performed at the periphery of the ulcer and another at the base in order to rule out the presence of malignant transformation because of BCC, squamous cell carcinoma, sarcoma, melanoma, lymphoma, or metastases.

KEYWORDS: basal cell carcinoma, biopsy, lower-extremity wound, nonmelanoma skin cancers, venous leg ulcer

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INTRODUCTION

Malignancy in venous leg ulcers (VLUs) is a rare occurrence. Squamous cell carcinoma (SCC) is the most commonly encountered cancer arising from VLUs,[1] and basal cell carcinoma (BCC) is much rarer.[1] However, 2 case series over the past decades have reported increasing incidence of BCC in VLUs.[2,3] Making this diagnosis is important because patients with BCC have a 10-fold risk of developing BCC at distant sites.[4] This article reports on a series of 4 cases of biopsy-proven BCC in lower-extremity ulcers, previously diagnosed as VLUs.

CASE SERIES

A clinical summary of the patients' demographic information, ulcer features, and follow-up intervals is listed in Table 1.

Case 1

An 84-year-old man was referred to the authors' multidisciplinary wound clinic for a nonhealing ulcer on his left lower extremity. The patient denied any knowledge of lower-extremity swelling, venous insufficiency, or radiation exposure. He ascribed the development of the ulcer to minor trauma. The ulcer had been present for over 6 months prior to presentation, and it had been treated as a VLU at another institution. Physical examination revealed tortuous varicose veins and stasis dermatitis on his bilateral lower extremities. The patient had a beefy left lateral ulcer (1.8 × 1.1 cm, Figure 1-1A) with granulation tissue and heaped-up borders. Workup for the ulcer etiology included duplex ultrasonography, which failed to reveal any venous reflux. Punch biopsies (4 mm) including the base and margin of each ulcer were obtained. Biopsies of the ulcer showed a nodular BCC. The ulcer was treated with Mohs micrographic surgery (MMS), healed by secondary intention, and remained healed at 16 months' follow-up (Figure 1-1B).

Case 2

An 83-year-old man was referred by his primary care physician for a 2-month-old ulcer on his right lower shin, thought to be a VLU. The patient could not recall any prior trauma. The patient's caregiver described the original wound as a coin-shaped painless ulcer that was not associated with edema and bled occasionally with increased friction. Physical examination revealed a bright red ulcer (1.3 × 1.3 cm, Figure 1-2A) with hypertrophic granulation

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Table 1.

CLINICAL SUMMARY OF PATIENT CHARACTERISTICS AND FOLLOW-UP

Case No./ Gender	Age, y	Presumed Initial Etiology of Ulcer	Venous Insufficiency of Affected Limb	Ulcer Location	Ulcer Duration, mo	Ulcer Size, cm	Pathology Findings	Follow-up
1/M	84	Minor trauma	No	Left lateral leg	6	1.8 × 1.1	Nodular BCC	MMS, healed, no recurrence at 16 mo
2/M	83	Venous insufficiency	Yes	Right lower shin	2	1.3 × 1.3	Nodular, focal, and infiltrative BCC	MMS, STSG, healed, no recurrence at 28 mo
3/M	76	Venous insufficiency	Yes	Right posterior midcalf	12	2.2 × 2.5	Nodular and infiltrative BCC	Excision, STSG, healed, no recurrence at 27 mo
4/M	88	Venous insufficiency	Yes	Right proximal supramalleolar	120	5.0 × 5.5	Infiltrative BCC	MMS, healing slowly at 14 mo with no recurrence

Abbreviations: BCC, basal cell carcinoma; M, male; MMS, Mohs micrographic surgery; STSG, split-thickness skin graft.

tissue and violaceous margins amid a background of stasis dermatitis. Vascular studies showed right proximal popliteal vein reflux. A 4-mm punch biopsy of the ulcer base and edge revealed a nodular, focal, and infiltrative BCC. The patient underwent MMS with split-thickness skin graft (STSG) placement, and he remained healed at 28 months (Figure 1-2B).

Case 3

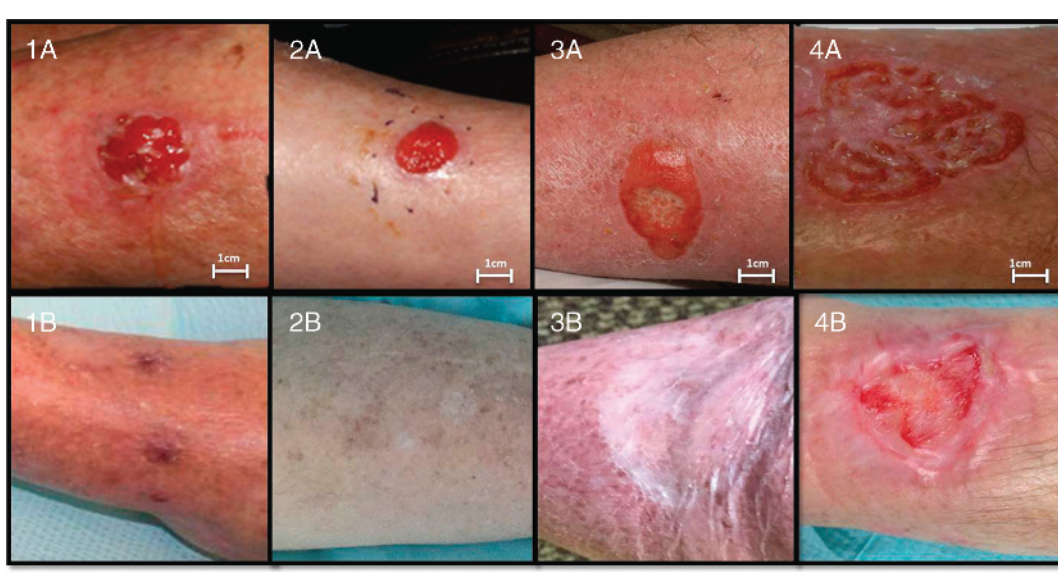
A 76-year-old man with bilateral chronic venous insufficiency (diagnosed by duplex ultrasound) with edema and poor compliance with compression dressings presented with a 1-year history of VLU, which he ascribed to trauma. Physical examination revealed a right posterior midcalf shallow, pearly, ovoid ulcer (2.2 × 2.5 cm, Figure 1-3A), with red granulation tissue, an outer rim of erythema, and dermatitis. A 3-mm punch biopsy was done. Ulcer histopathology revealed a nodular and infiltrative BCC, along with a dense dermal scar. The patient remained healed at 27 months after surgical excision and STSG (Figure 1-3B).

Case 4

An 88-year-old man presented with a 10-year history of venous insufficiency and vascular ablation of the right saphenous vein.

Figure 1.

PHOTOGRAPHS ILLUSTRATING EACH PATIENT CASE BEFORE TREATMENT (UPPER PANEL 1A TO 4A) AND AFTER TREATMENT (LOWER PANEL 1B TO 4B)



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The patient had 2 recurrent right VLUs that had been treated with standard of care (wound debridement, dressings, and compression therapy), as well as advanced treatment (including bioengineered grafts). Examination revealed a right supramalleolar proximal ulcer (5.0 × 5.5 cm, Figure 1-4A) with a cribriform pattern and few skin islands. The distal ulcer (4.1 × 1.9 cm) had a fibrinous base. A deep shave biopsy of the proximal ulcer revealed an infiltrating BCC, granulation tissue with skin ulceration, and no evidence of carcinoma for the distal ulcer. Repeat duplex ultrasound confirmed reflux in the right distal calf. The patient underwent MMS, which resulted in a 6.5 × 7.5-cm defect. The patient was offered STSG placement; however, he opted for conservative management of the excised ulcer. At 14 months after MMS, his ulcer measured 2.0 × 3.5 cm (Figure 1-4B).

DISCUSSION

Although BCC is the most common nonmelanoma skin cancer (NMSC), its association with VLU is not as frequently reported compared with SCC.[1] This may be because BCC is most common on the head and neck region, followed by the trunk, and last on the lower extremities.[5] The incidence of NMSC is difficult to determine because NMSCs are excluded from the cancer registry.[6,7] The annual incidence of BCC ranges from 0.1% to 0.5%,[8–10] with approximately 3.5 million patients diagnosed in 2006.[8] In the United States, the age-adjusted BCC incidence was 1488 cases per 100,000 in a male cohort and 1019 cases per 100,000 in a female cohort.[11] This correlates with previous studies that have reported a higher incidence of BCC in males than in females.[5,12–14] Interestingly, recent series have identified higher numbers of BCC in leg ulcers.[2,3]

The differential diagnosis of chronic leg ulceration includes venous insufficiency from varicose veins; post-thrombotic and/or post-phlebetic syndrome; arterial disease; microcirculatory disorders (Raynaud disease); chemical or physical trauma; infection; neuropathic diseases such as diabetes; vasculitis; hematologic disorders; and, less commonly, malignancies such as SCC, BCC, Kaposi sarcoma, angiosarcoma, melanoma, lymphoma, and metastases.[1,15–19] In some instances, the etiologies may overlap.[16,18] Venous leg ulcers are typically shallow, with irregularly defined margins and with viable granulation in the wound bed underlying yellow fibrinous exudate (Table 2). The classic characteristics of a VLU usually do not raise concern for malignancy.

On the other hand, BCCs are described as pearly lesions with a smooth surface and telangiectasias that can ulcerate over time, with raised and rolled borders (Table 2).[19] Some of the typical features of BCC are not seen when they occur within venous ulcers. However, the appearance of granulation tissue with translucent and shiny margins of the ulcer should prompt suspicion.[20]

The literature is unclear whether NMSC within VLUs is of primary or secondary origin. Some have suggested that chronic ulceration and inflammation may lead to NMSC.[1,3] A 5-year review of lower-extremity BCC reported stasis changes in 24.8% of cases and concluded that there was no correlation between lower-limb BCC and venous insufficiency. Study authors suggested that whereas SCC may originate from precursor lesions, BCC is unlikely to follow the same path; rather, BCC arises de novo.[21]

In addition, a retrospective analysis of 705 patients with leg ulcers found 20 patients (3%) with malignant skin lesions.[2] Among those lesions, 3 were SCCs and 12 were BCCs. The authors stated that malignant transformation or Marjolin ulcer takes 20 to 30 years, or at least 2 to 3 years. Because the ulcer duration prior to diagnosis in some cases was as little as 2 months, and there was no previous history of radiation or known risk factors, the authors concluded that the NMSCs were not secondary to the ulcer chronicity.[2]

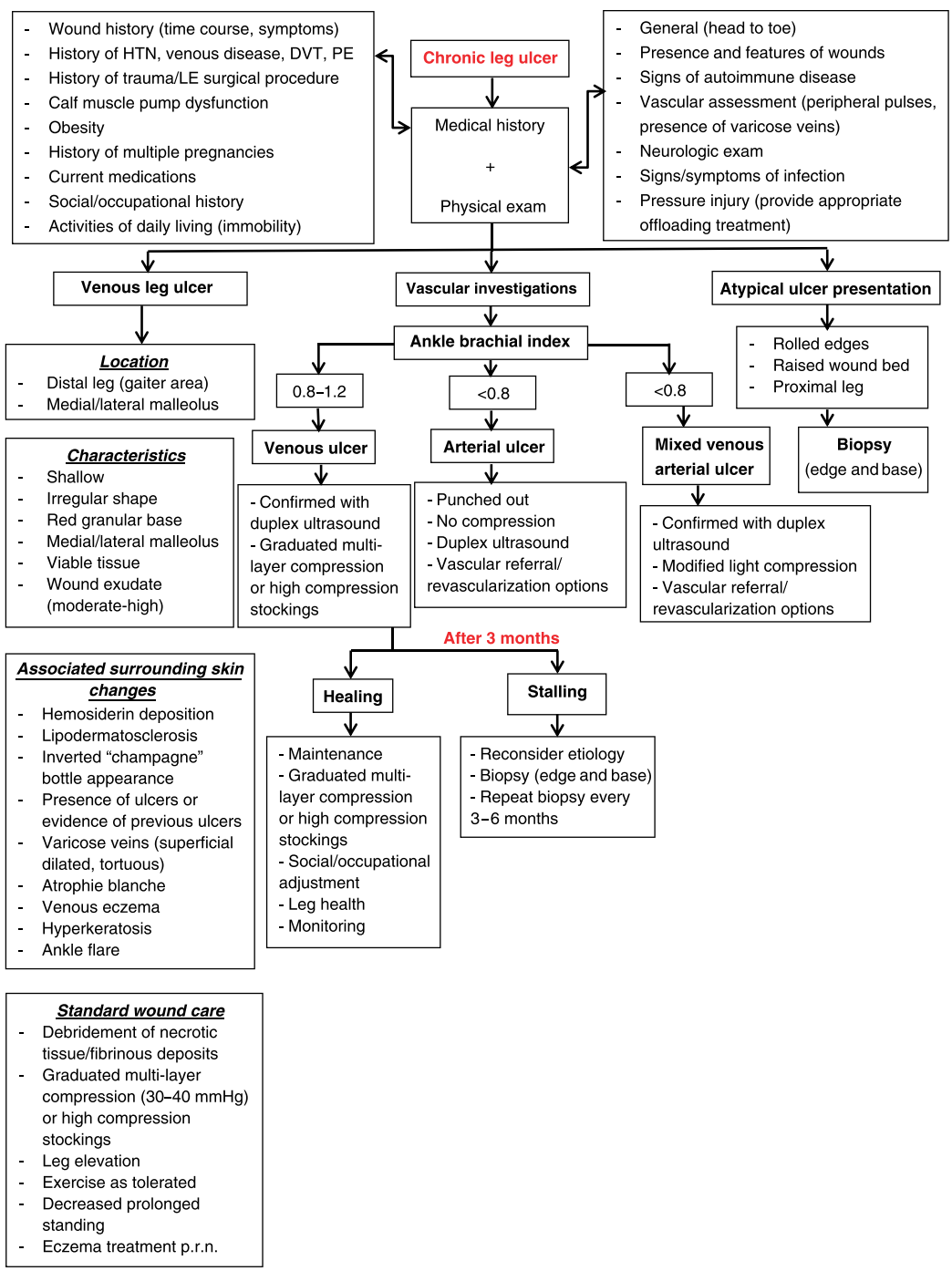
Another prospective cross-sectional study of 144 patients with nonhealing VLUs following 3 months of standard treatment found a 10.4% frequency of skin cancer, including 9 SCCs, 5 BCCs, 1 melanoma, and 1 leiomyosarcoma.[22] The authors did not find a significant

Table 2.

MORPHOLOGIC CHARACTERISTICS OF BASAL CELL CARCINOMA IN COMPARISON WITH VENOUS LEG ULCER

Characteristics	Basal Cell Carcinoma	Venous Leg Ulcer
Lesion	Shiny, smooth, pearly papule or nodule with telangiectasias May become ulcerated over time	Granulation may be fibrinous
Margins	Rolled, elevated	Sharp, irregular
Depth	Depressed when ulcerated	Shallow
Exudate	–	Clear, yellow, pink, red, brown, green
Varicosities		+
Hyperpigmentation	+/–	+
Lipodermatosclerosis	–	+/–
Edema	–	+
Duplex sonography with evidence of venous insufficiency (ie, reflux, obstruction, or both)	–	+

Figure 2.
FLOWCHART FOR THE MANAGEMENT OF VENOUS LEG ULCERS



Abbreviations: DVT, deep vein thrombosis; HTN, hypertension; LE, lower extremity; PE, pulmonary embolism. Adapted from Shelling ML, Federman DG, Kirsner RS. Clinical approach to atypical wounds with a new model for understanding hypertensive ulcers. Arch Dermatol 2010;146(9):1026-9.

association of malignancy with either wound size or duration, but could not definitively determine whether malignancies arose within the ulcer as a result of malignant transformation or whether the ulcerated cancer was misdiagnosed as a VLU, because none of ulcers with malignancies were biopsied before inclusion in the study.[22]

The aforementioned studies suggest that ulcers with a short duration and without history of radiation warrant suspicion for a primary malignancy, whereas ulcers of a longer duration are likely to have been misdiagnosed or may have undergone malignant transformation.

A number of authors have suggested that ulcers in the gaiter area that fail to respond to treatment within 3 months should be biopsied, along with atypical ulcers and ulcers occurring in a more proximal location above the gaiter area.[1,2,22,23] A high level of suspicion for malignancy is expected, given the difficulty in distinguishing morphologic differences between benign leg ulcers and malignant ulcerations. As a result, repeat biopsies every 3 to 6 months may be warranted in cases of delayed wound healing with standard-of-care treatment including multilayer compression.[24] Because BCC and SCC originate from the epidermal layer, a deep dermal biopsy is not needed, and a deep shave (or deep scallop) is adequate. A study of 86 specimens obtained from shave or punch biopsies followed by tumor excision showed comparable diagnostic accuracy rates for BCC, with 75.9% and 80.7% accuracy, respectively.[25]

Limitations of this retrospective clinical case series include the lack of a standardized diagnostic algorithm that led to the (mis)diagnosis of VLU. Therefore, the authors propose a flowchart for the management of ulcers (Figure 2).

CONCLUSIONS

These 4 cases underscore that lower-extremity BCC can be misdiagnosed as a VLU in the presence of preexisting stasis disease, and the authors encourage providers to perform a biopsy on any atypical or poorly healing ulcer in these patients. The sampling of the ulcer should include tissue at the periphery to rule out the presence of epithelial-derived malignancy including BCC or SCC. Another biopsy at the base of the ulcer is recommended to probe for tumors of mesenchymal origin, such as sarcoma, along with other tumors, including melanoma, lymphoma, and metastases. Serial biopsies are recommended every 3 to 6 months on wounds that are stalling or increasing in size despite adherence to standard of care. ●

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