Melanoma presenting as a Marjolin ulcer on the lower extremity

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To the Editor:

Malignant degeneration of chronic wounds has been long-reported in the literature and are frequently referred to as "Marjolin ulcers." The leading cause of Marjolin ulcers are old burn scars, but they can arise from scars produced from other causes as well [1]. In the majority of Marjolin ulcers, the malignant neoplasm is a squamous cell carcinoma, but very rarely, other types of neoplasms have been described [2,3]. Reports of melanoma arising in chronic ulcers or scars are exceptionally rare [2-6]. In this report, we describe a case of melanoma arising in a chronic, non-healing lower extremity ulcer that had been present for nearly a decade.

A 66-year-old man presented to the dermatology clinic in October 2011 with history of a cicatricial subepidermal blistering dermatosis recalcitrant to multiple therapies including prednisone, doxycycline, and methotrexate. Examination showed multiple erosions with scarring and tense bullae on the trunk and extremities, as well as superficial erosions with scarring on both lower extremities (**Figure 1A**). Biopsy showed a subepidermal blistering dermatosis with eosinophils and linear deposition of IgG and C3 at the dermal-epidermal junction on direct immunofluorescence. The differential diagnosis included inflammatory epidermolysis bullosa acquisita, atypical presentation of bullous pemphigoid, and Brunsting-Perry pemphigoid. He did not have any mucosal findings other than mild gingival erythema. The patient was subsequently followed for many years with multiple treatments for his recalcitrant blistering disease, including prednisone, dapsone, doxycycline, minocycline, nicotinamide, sulfasalazine, methotrexate, rituximab, and mycophenolate mofetil. The ulcerations on his right lower extremity were especially resistant to treatment and would improve for short periods of time and then worsen again.

In December 2020, the patient was admitted to another hospital for an unrelated illness. Examination showed a large, approximately 15cm scar-like plaque on the right lower extremity with focal ulcerations and mottled hyperpigmentation (**Figure 1B**). A 4mm punch biopsy was performed within the scar-like plaque at the edge of an ulcer, which showed atypical melanocytes at the dermal-epidermal junction and a dense proliferation of atypical spindled cells in the underlying dermis, extending to a depth of at least 2.5mm (**Figure 2**). The spindled cells were positive for S100 and SOX-10 immunohistochemical stains and negative for other markers such as pancytokeratin, desmin, CD34, and CD31, consistent with spindle cell melanoma (at least pT3a). The patient passed away shortly after the biopsy due to unrelated causes.

This is a rare case of a melanoma arising within a chronically ulcerated wound. Reports of melanomas

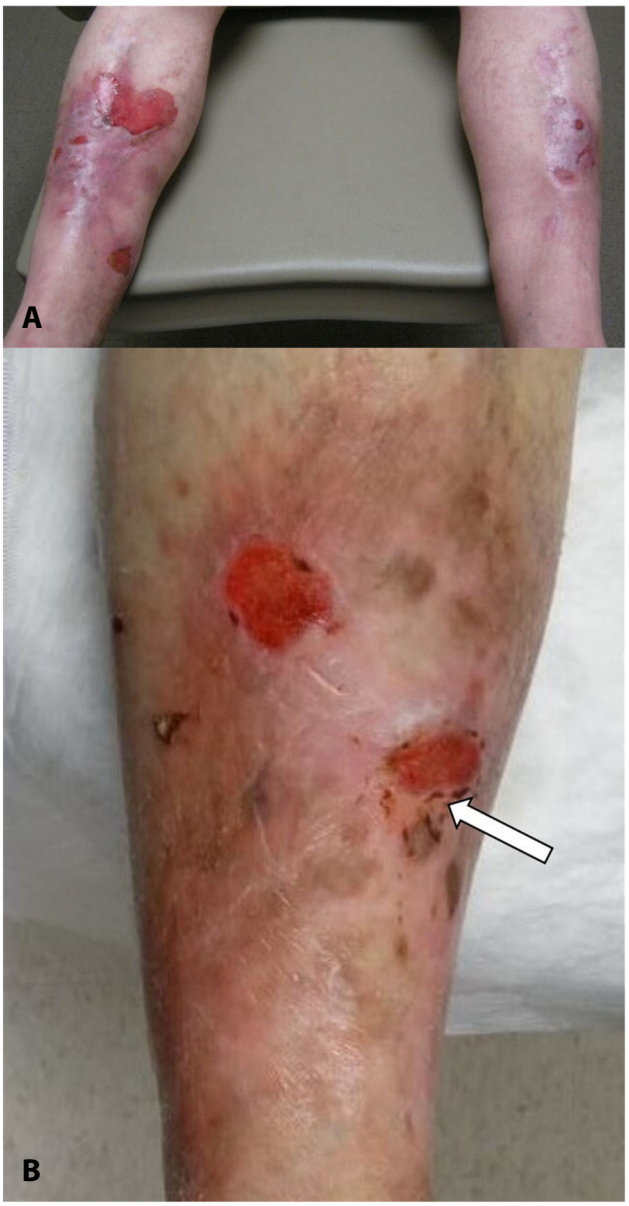

Figure 1. ***A)*** *Initial presentation in 2011: multiple erosions with scarring are seen on bilateral lower extremities.* ***B)*** *At the time of biopsy in 2020: there are still focal ulcers present on the right lower extremity, within a background of ~15cm scar-like plaque that now has areas with darker pigmentation that were not previously present in 2011. Biopsy was obtained from the ulcer edge, within the scar-like plaque (arrow).*

arising in scars or chronic ulcers are extremely rare and have been mostly reported in burn scars [6]. In a review by Kowal-Vern and Criswell of 412 cases of neoplasms arising in burn scars, 6% (23 cases) were melanoma and the average duration of ulceration

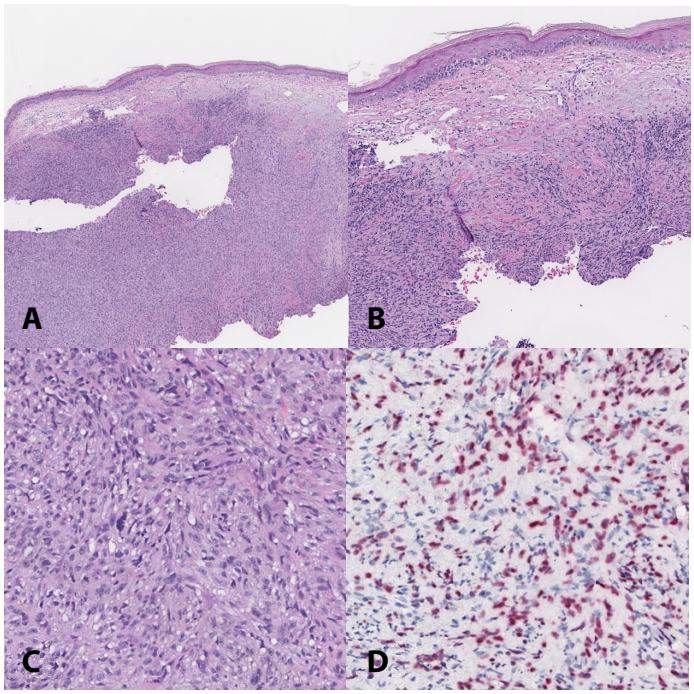

Figure 2. *Histopathology showing a dense proliferation of atypical spindled cells in the dermis with focal melanoma in situ in the overlying epidermis.* ***A)*** *4×;* ***B)*** *10×;* ***C)*** *40×.* ***D)*** *SOX-10 immunohistochemical stain showing positive staining in the spindled cells, consistent with melanoma, 40×.*

was 7 months [6]. In our case, the scar was a result of chronic ulcerations related to a recalcitrant autoimmune blistering disease and the time from ulceration onset to melanoma diagnosis was about 10 years, although the precise timeline of malignant transformation is unclear. Although there was subtle hyperpigmentation overlying the scar-like plaque at the time of biopsy, there was no development of any nodules or tumors to suggest malignant transformation. This case shows that malignant transformation in chronic scars and ulcers can involve cells of any lineage, not just epithelial cells. There should be a low threshold to biopsy chronically non-healing wounds, even in the absence of marked clinical changes such as development of nodules or tumors.

Potential conflicts of interest

The authors declare no conflicts of interest.

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