

Development of Bilateral Lower Extremity Marjolin Ulcers After Childhood Burns

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A Marjolin ulcer is a carcinoma, usually squamous cell, that originates in a chronically irritated or traumatized area, most commonly secondary to a deep tissue burn. The cancer is commonly aggressive and carries with it a poorer prognosis than a traditional squamous cell carcinoma does.¹ The lesion commonly presents unilaterally with localized pain, foul-smelling discharge, and hemorrhage usually on the extremities or trunk, often with a time lag of decades from initial injury to malignancy.² In a literature search, we identified only 2 instances of bilateral presentation.

In this report, we describe a rare clinical case of bilateral lower extremity Marjolin ulcers and detail the common clinical presentation, treatment options, and prognosis of this aggressive carcinoma.

CASE REPORT

Our patient gave informed consent to our publishing photographs and case studies in order to advance medical science and education with the understanding that his identity would not be revealed. In addition, he was given the opportunity to read the manuscript but declined.

A man in his late 50s presented with a very large growth on the right lower leg. History revealed that he had suffered third-degree burns over both lower extremities about 45 years earlier, when he was a child. At that time, his burns were treated conservatively and were allowed to heal by secondary intention.

The patient denied fever, chills, nausea, and vomiting. Physical examination revealed a fungating, foul-smelling, purulent mass that completely involved the right lower extremity extending from the tibial tubercle distally into the foot (Figure 1). The patient's ankle range

of motion was limited, and examination revealed that the tumor had invaded the anterior compartment of the lower leg. The differential diagnosis included skin carcinoma (squamous cell, basal cell, other), pseudo-epitheliomatous hyperplasia, massive abscess with hemorrhage, chronic osteomyelitis, chronic cellulitis, and chronic tissue inflammation. Incisional biopsy results revealed a moderately differentiated grade II squamous cell carcinoma with a clinical appearance consistent with that of an ulcerated lesion (Figure 2). Metastatic workup was negative.

The patient decided on external radiation for palliation, but it failed because of persistence of the tumor and development of an infection that ultimately resulted in an above-knee amputation. The amputation was uneventful, and the patient recovered at a rehabilitation center.

Three years later, the patient presented with a nearly identical lesion on the contralateral left leg (Figure 3). Biopsy results again revealed squamous cell carcinoma, and the patient underwent another above-knee amputation. The patient's postoperative course was uneventful, and he was again transferred to a rehabilitation center.

DISCUSSION AND LITERATURE REVIEW

Marjolin ulcer is a carcinoma, commonly squamous cell, that develops in a chronically inflamed, traumatized, or scarred area of the skin. Early in the first century, Celsus was the first to describe a neoplasia that developed in a chronic ulcer.³ The term *Marjolin ulcer* is associated with this finding because of Marjolin's 1828 description of malignant lesions that developed in scar areas.⁴ There is controversy about who first described the condition, but Marjolin has continued to receive the credit.

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Figure 1. Right lower extremity purulent fungating lesion originating from a scar from a burn injury sustained 45 years earlier.

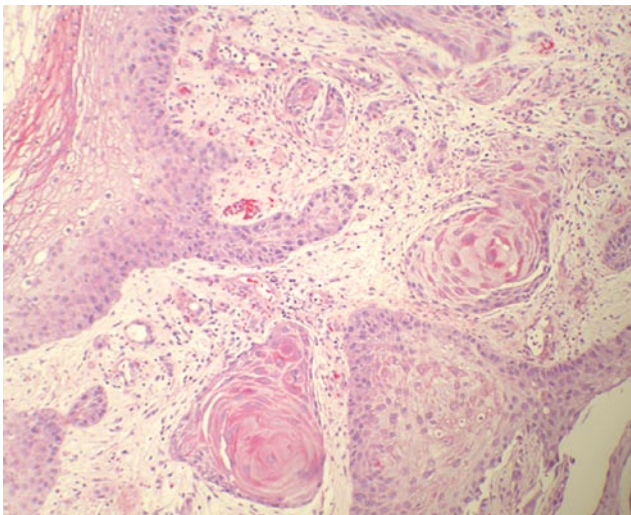


Figure 2. Microscopic histology of the right lower leg incisional biopsy shows invasive islands of moderately differentiated squamous cell carcinoma with keratin pearl formation (hematoxylin-eosin, original magnification $\times 10$).

The incidence of Marjolin ulcers has not been clearly defined, but it is estimated that up to 2% of burn scars undergo malignant transformation and become carcinomas.^{3,5,6}

The typical clinical presentation is that of a chronic scar or nonhealing ulcer that becomes painful and is acutely associated with change in size, appearance, and odor.^{2,7} The changes include foul-smelling discharge in 68% of cases and hemorrhage in 58% of cases.² Marjolin ulcers present on the extremities in most cases (50%-89%) but also on the trunk and head.^{2,8} These lesions usually present in the fifth or sixth decade of life; the interval from initial injury to malignant transformation is reported to be 31 to 42 years.^{2,8-10} Incidence is higher in males.^{3,9,11} Histologic analysis has determined that invasive squamous cell carcinoma is the most common neoplasm identified.^{6,9} Less often, the malignancy presents as basal cell carcinoma, melanoma, sarcoma, or another rare entity.⁹

Several hypotheses have been proposed, but the exact pathogenesis of this lesion has not been determined.^{8,9} The postulates of Ewing¹¹ provide a set of diagnostic criteria that include evidence of a burn scar; a tumor within the margins of the scar; no previous tumor in the location; tumor histology consistent with cell types found in the skin of the scar; and adequate interval between burn injury and cancer development.

An aggressive surgical approach has become the most appropriate management for Marjolin ulcers.^{8,12} Many of these ulcers appear subsequent to full-thickness burns that were not grafted during initial treatment and were allowed to heal spontaneously.¹ The etiology is again unclear, but most reports detail chronic irritation and the burn mechanism, thermal being the most common, as contributing to the pathophysiology.⁵ More recent theories have included genetic postulations involving human leucocyte antigen (HLA) DR4 and mutations in the p53 and/or Fas genes.^{10,13-15}



Figure 3. Left lower extremity purulent lesion presenting 3 years after right lower extremity amputation. This neoplasm also originated in a burn scar.

To try to decrease the incidence of Marjolin ulcers, one should manage full-thickness burns initially with grafts (vs allowing spontaneous healing) and keep burns protected from repetitive trauma.^{3,6} Aydo du and colleagues⁸ noted that, once a carcinoma has formed, aggressive excision and reconstruction are warranted. Hahn and colleagues² reported a higher recurrence rate with excision and graft than with amputation. Their data were not statistically significant, but they recommended amputation as standard treatment for Marjolin ulcers whenever possible. When the lesion is grade II or III or involves underlying muscle/bone, amputation is recommended.⁷ When amputation is not possible or the lesion does not involve underlying muscle/bone, the recommended treatment is wide excision with 3- to 4-cm margins.^{5,7}

Controversies Surrounding Radiation and Chemotherapy

The role of radiation and chemotherapy is controversial and, frankly, unknown. Coburn⁵ questioned the rationale for using radiation in poorly vascularized scar tissue and indicated that surgery is a better therapeutic option. Dupree and colleagues¹⁶ found that radiation and 5-fluorouracil therapy were ineffective in the treatment of Marjolin ulcer. Novick and colleagues³ wrote that, because of the nature of this carcinoma, radiation treatment is not recommended. In contrast, Ryan and colleagues¹⁷ concluded that 5-fluorouracil induced round-cell infiltrate, creating immunologic benefit and actually eliminating cancer in 3 cases. Overall, a literature review supports adjuvant radiation and/or chemotherapy when resection is not logical or when a patient refuses surgery.⁸

There is no consensus as to indications for lymph node dissection. Although prophylactic lymph node dissection has not been recommended, palpable lymph nodes should be removed and analyzed pathologically.^{5,6,12}

The prognosis with Marjolin ulcers seems to be worse than that with other squamous cell carcinomas because of the propensity of the Marjolin lesion to be more aggressive.^{2,8} Lifeso and Bull⁷ determined that the overall prognosis is poor and that histologic tumor grade is the most useful prognostic factor. In their study, grade I (well-differentiated) tumors were less likely to metastasize, whereas grade II (moderately differentiated) and grade III (poorly differentiated) tumors seemed to spread rapidly to lymph nodes, thus worsening the prognosis.

CONCLUSIONS

Marjolin ulcer has been recognized as a carcinoma developing from a previous injury to the skin. Surgical intervention has become standard treatment, with amputation the procedure associated with the lowest chance for recurrence. A reasonable treatment approach is wide excision with radiation therapy considered and with amputation reserved for unresectable or recurrent lesions. These lesions have a propensity to become aggressive, and therefore a high degree of clinical suspicion and careful monitoring are essential for successful outcomes. Our patient's case of bilateral lower extremity Marjolin ulcers originating in a chronic burn injury and leading to bilateral above-knee amputations is a rarity.

AUTHORS' DISCLOSURE STATEMENT

The authors report no actual or potential conflict of interest in relation to this article.

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