Diagnostic Dilemmas
Squamous Cell Carcinoma

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Presentation

A 73-year-old white woman presented to the wound clinic with a chronic wound on the dorsum of her left second toe. The patient reported that the wound developed 3 years after cryotherapy to the toe. She had tried many different dressings and ointments on the wound, including bacitracin, Acticoat (Smith & Nephew, Largo, Fla), and wet-to-dry dressings, without improvement. She had received 2 unsuccessful allogenic grafts. An autologous skin graft resulted in significant but incomplete healing. She noted that the wound had grown in size over the several months preceding presentation.

The patient's medical history was significant for squamous cell carcinomas of the right leg, left ankle, and right forearm, diabetes mellitus, and rheumatoid arthritis. Her medications included methotrexate, leucovorin, risedronate, metformin, glyburide, and prednisone.

Physical Examination

Physical examination revealed a healthy looking woman with photodamage. A sharply demarcated ulcer measuring 1.5 cm x 1 cm with a granulating base and a border of erythematous skin was present on the dorsal aspect of the second left toe (Figure 1). She had peripheral neuropathy with diminished light touch sensation of the foot. Peripheral pulses were palpable, and the ankle brachial pressure index was normal. There was no lymphadenopathy.
Figure 1.
Ulcer on the dorsum of the left second toe.

The differential diagnosis included a neuropathic ulcer secondary to trauma, vasculopathy, vasculitis, or a malignancy. Due to the long duration of the ulcer, a biopsy was performed.

Diagnosis

The biopsy revealed moderately to well differentiated squamous cell carcinoma (SCC) (Figure 2 and 3). In this patient with a known history of cutaneous malignancy, the lesion could have been a SCC that ulcerated or a SCC arising from a chronic ulcer.

Figure 2.
Low power magnification reveals an ulceration aggregates of atypical epithelium filling the dermis (H & E), 4X.
Figure 3.

High power magnification reveals aggregate of moderately to well differentiated squamous cell carcinoma (H & E) 4x.

Discussion

It has been well known and long observed that malignancies, such as SCCs, can arise from chronic ulcers. This phenomenon is known as a Marjolin ulcer. Although Jean Nicholas Marjolin described the concept of the transformation of burn scars to malignancies in 1828, the term "Marjolin ulcer" has been used to describe the malignant transformation of not only burn scars but chronic ulcers, pressure ulcers, amputation stumps, chronic lymphedema, chronic pilonidal sinuses, chronic sinuses, hidradenitis suppurativa, chronic ulcers of leprosy or necrobiosis lipoidica, and discoid and chronic osteomyelitis.

Typically, the longer the duration of chronic leg ulcers, the more likely it is for a malignant transformation to occur. In a tertiary hospital's specialized leg ulcer clinic, the incidence of malignancy was 2.2 per 100 leg ulcers. In venous leg ulcers, SCC is more frequent than basal cell carcinoma. The mechanism by which chronic ulcers transform into malignancies is not well known. However, several theories have been postulated. One theory suggests that toxins released from the damaged ulcer tissue can act as carcinogens and subsequently lead to tumor development. It has also been postulated that with chronic irritation and repeated damage of the ulcer there is repeated attempt at repair. This cycle of damage, irritation, and repair can lead to malignant transformation. Implantation of epidermal cells into the dermis from trauma, which can result in foreign body reaction and subsequent alteration of the normal regenerative process, has also been hypothesized to be a mechanism for malignant transformation. Another proposed theory of malignant transformation is the initiation and promotion phase theory. In the initiation phase, normal cells are converted to dormant malignant cells. In the subsequent promotion phase, the dormant cells are then stimulated to change into a tumor by infection, which can act as a cocarcinogen.

Ulcer features that are suggestive of malignant transformation include a chronic ulcer of greater than 3 months duration, excessive granulation tissue beyond margins, everted wound edges, and translucent or shiny granulation tissue affecting ulcer margins. Other features that may raise suspicion that the ulcer is malignant include recurrent breakdown of ulcers after healing, static nonhealing ulcers after appropriate treatment, and ulcers that increase in size or pain despite appropriate therapy.

Treatment
Several treatment modalities are used in the management of SCC ulcer lesions. These include surgical excision, Mohs micrographic surgery, and radiation therapy. Surgical excision of SCC ulcers is the preferred method of management.[3] In determining the margins of excision, the clinician should take into account various factors, such as the patient's age and general health, tumor size and location, and whether the tumor is primary or recurrent. As a rule of thumb, margins of 4 mm are suggested for noninvasive SCC, while margins of 10 mm are recommended for invasive SCC.[7]

Mohs micrographic surgery is the gold standard for management of SCC ulcers in terms of cure rate, tissue conservation, and margin control. It is far better in management of recurrent lesions[8] with 5-year cure rates up to 90% versus excisional surgery at 76.7%. The role of radiation therapy in SCC ulcers is limited. However, this therapeutic modality can be useful in treating elderly patients who are poor surgical candidates. Radiation therapy can also be used to debulk massive tumors-especially in delicate anatomical sites, such as the face. It is especially useful when used in conjunction with other therapeutic modalities, such as surgery.[3,9]

Squamous cell carcinoma lesions that have not metastasized have good prognosis with a 5-year survival rate of 90% under conventional treatment.[11] With lymph node metastasis, the 5-year survival rate decreases to 39%.[3,10] Chronic ulcers that transform into SCC can be easily treated with simple excision with primary closure or skin graft if they are detected early. Late diagnosis or delay in diagnosis can result in loss of the affected limb or eventual metastasis of the tumor. A high suspicion of malignant transformation should be ascribed to chronic nonhealing ulcers. These ulcers should be biopsied as early as possible to rule out malignancy. The authors' patient was referred for surgical evaluation and will be treated with Mohs micrographic surgery. Surgical amputation of the affected toe may be necessary if the tumor extends to the bone.

References


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