

SQUAMOUS CELL CARCINOMA PRESENTING AS A TWENTY-YEAR-OLD NONHEALING ULCER

Thomas J. Merrill, DPM

Biren Shah, DPM

Alvin Cowans, DPM

Matthew Bernstein, DPM

Maria Zalles, MD

INTRODUCTION

Squamous cell carcinoma represents 30% of all skin cancers. This disease is the second-most common type of skin cancer and affects mostly Caucasian men. Ulcerative squamous cell carcinoma is unresponsive to topical treatments and is characterized by an area of firm, slightly raised tissue and hypertrophic borders. Areas of the body that are most affected are areas exposed to the sun or to ultraviolet radiation (1). Some studies say only 5% of all squamous cell carcinomas or 1.5% of all primary carcinomas occur in the lower extremities, but according to Levene, squamous cell carcinoma comprised 14% of all lesions. Squamous cell carcinoma has a slightly higher incidence in the foot than either melanoma or synovial sarcoma (2). Differential diagnosis for squamous cell carcinoma includes basal cell carcinoma, Bowen's disease (carcinoma in situ), cutaneous granulomas associated with onychocryptosis or periungual verrucae, osteomyelitis, psoriasis, eczema, tinea pedis, and keratoacanthomas (3).

The key is to biopsy and diagnose squamous cell carcinoma in the early stages because advanced metastasis of this disease has a poor prognosis and the mean survival rate is only a few months. Squamous cell carcinoma can be isolated in situ; it can spread to lymph nodes, or can metastasize to distant sites and organs. In 1835 Hawkins was the first to document squamous cell carcinoma in the presence of chronic osteomyelitis, which was named "Marjolin's Ulcer" (2). Marjolin's ulcer is a squamous cell carcinoma that develops in chronic wounds and post-traumatic scars and was found by Nicholas Marjolin in 1828. These ulcerations show a 3:1 male predilection and with an average time of malignant transformation of 20-35 years.

Squamous cell carcinoma has been known to occur in 1.6-23% of all patients diagnosed with chronic osteomyelitis, whereas 85% of all of the squamous cell carcinoma cases occur in the lower extremity (2). Squamous cell carcinoma

in the lower extremity characteristics include painful, draining ulceration for several months or years with osseous destruction seen on radiographs. In dealing with the feet, tarsal bones account for more than 50% of the cases, metatarsals account for more than 23% of the cases, and phalanges account for only 17% of the cases. Of the 505 tarsal bones affected by squamous cell carcinoma, the calcaneus accounts for 45% of these metastatic cases (4).

CASE STUDY

A 76-year-old Cuban woman visited the Mercy Hospital Emergency Room on September 10th, 2012 for a non-healing ulcer on her left anterior leg (Figure 1). The patient had existing hypertension, Type-2 diabetes mellitus, and dyslipidemia. Her diabetes was well controlled. The patient previously lived in Cuba for 72 years and her occupation was a housewife. Her daily activities included taking care of the household, caring for children and running regular errands. She stated, "An ulcer showed up on her left leg twenty years ago without any incident or trauma" while she was residing in Cuba. According to her, the ulcer was approximately the size of a quarter when she noticed it for the first time. She visited a few physicians and received local treatment that involved a topical ointment, of which the patient could not



Figure 1. Nonhealing chronic ulcer.

recall the name. The patient continued to receive the same treatment for multiple years; however this treatment proved unsuccessful in resolving the chronic ulcer. Despite her ongoing treatment, the patient began to notice that the ulcer would vary in size and shape over time. At one point, the patient claims that the ulcer became the size of a tennis ball. However, the patient continued to receive the same wound care therapy from her Cuban physicians. In addition to her topical ointment, the patient was taking showers daily and soaking her left lower extremity. The patient states that she was never limited in activities due to her ulceration.

In 2008, the patient and her husband moved to the US. The patient says that the ulceration remained the size of a tennis ball on her left anterior distal leg. The patient continued doing dressing changes and local wound care on her own. Over the past month or so, the patient noted worsening of the ulceration, periwound erythema, and edema on the left leg associated with increased pain. She then presented to a local hospital on August 15, 2012. She was admitted to the hospital for approximately two weeks and was given local wound care. Radiographs and magnetic resonance imaging (MRI) were ordered with routine laboratory work. She also received intravenous (IV) antibiotic treatment as well as hyperbaric therapy. She was eventually discharged home on IV antibiotics that she completed for an additional 2 weeks while receiving home health care for wound management. The patient obtained no relief from the antibiotic therapy and the ulceration continued to increase in size. She then presented to a second local hospital on August 31, 2012 where she stayed for

nearly a week for proper treatment. Her pain, swelling and erythema on the left leg persisted. MRI, radiographs, and laboratory results were repeated there also. Osteomyelitis of the left lateral malleolus was discovered and she was advised to have a below the knee amputation for the left leg as a form of treatment. The patient, unhappy with the surgical option that was presented to her, decided to continue wound care for about a week. She was eventually discharged home.

On September 9th, 2012, the patient decided to get a third opinion for her left leg wound, and she presented to the emergency room at Mercy Hospital with the chronic wound. She was afebrile with temperature of 96.9. Radiographs of the tibia and fibula on the left leg showed ill-defined periosteal reactive changes in the distal fibula that was concerning for osteomyelitis. Arterial doppler of the left lower extremity showed complete occlusion of the tibioperoneal trunk on the posterior tibial artery. The patient was admitted for evaluation and treatment of her nonhealing left leg ulcer (Figure 2) with evidence of arterial occlusion and possibly osteomyelitis. A vascular surgeon performed an atherectomy on September 12th, 2012 and infectious disease was consulted. The patient's wound culture was positive for *pseudomonas aeruginosa* infection. The patient received Zosyn and Vancomycin for osteomyelitis.

The wound measured 12.5 cm x 9.5 cm and was 0.3 cm in depth. The wound was ~70% granular, ~28% fibrotic, and ~2% necrotic. Periwound erythema and edema were present. Wound edges were tunneling and no malodor was noted. Moderate purulence was noted from the ulceration site and the skin did not appear to be of normal color or



Figure 2. Clinical appearance of ulcer.



Figure 3. Punch biopsy.

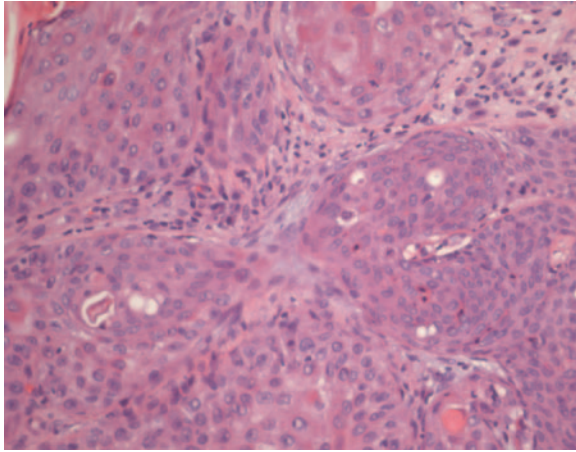


Figure 4. Rapid division of cells in squamous cell carcinoma.

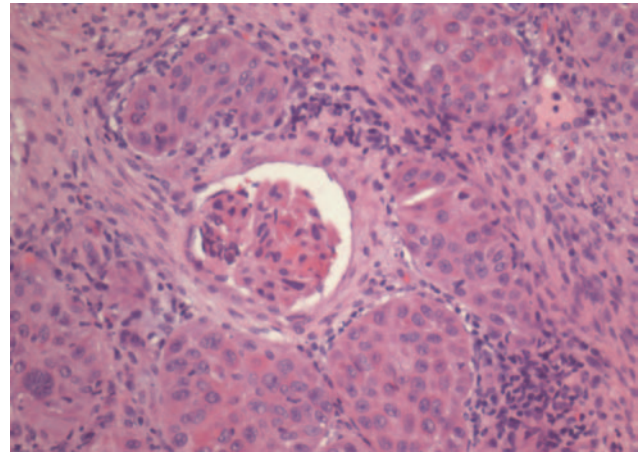


Figure 5. Squamous cell carcinoma invading a vessel.

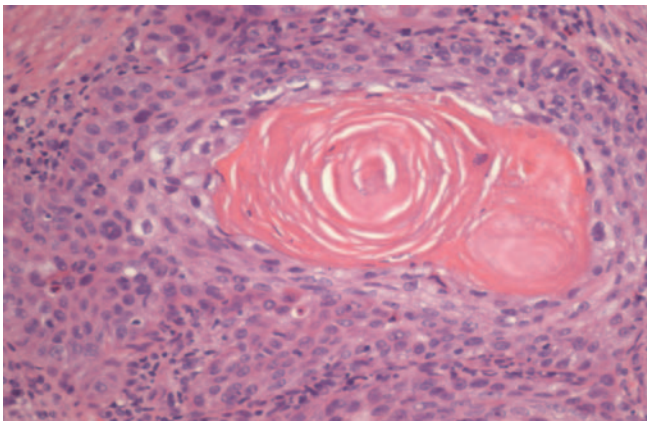


Figure 6. Carcinoma in lymphatic channel.

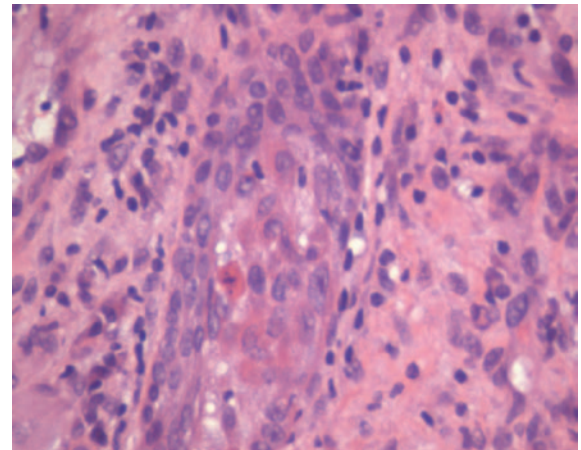


Figure 7. Cell migration and division.

texture. No periwound maceration was noted. At this point, the patient was receiving antibiotics and wound care. Even after visiting multiple hospitals during the last twenty years, no biopsy had ever been performed. On September 14, 2012, a punch biopsy was done on the left anterior distal leg to rule out squamous cell carcinoma (Figure 3).

On September 15, 2012, pathology confirmed that the patient had moderately invasive to vascular level squamous cell carcinoma (Figures 4-8). Upon receiving the results of the punch biopsy, oncology was consulted due to the invasive nature of the cancer. Oncology recommended a lymph node biopsy to further evaluate the depth and nature to which the cancer had metastasized. The patient was also placed on chemotherapy and ordered to continue with wound care and antibiotics. On September 18, 2012, the primary care physician discharged the patient from the hospital. The patient was instructed to follow-up with the oncologist for chemotherapy and a wound care specialist for routine wound care.

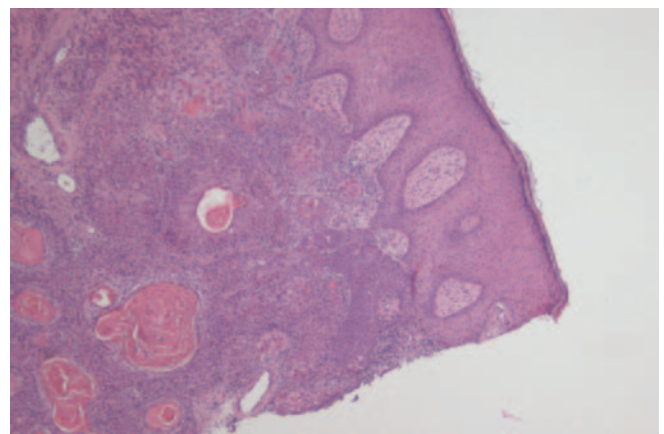


Figure 8. Overview of deeply invasive squamous cell carcinoma.

DISCUSSION

Marjolin's ulcer is a squamous cell carcinoma that develops in chronic wounds and in posttraumatic scars (5). It has been noted that Marjolin's ulcers represent a small proportion of malignant skin lesions, with the exact prevalence ranging from 2-5% of all squamous cell carcinomas (5). Most of these lesions, nearly 60%, are seen on the extremities (6). A majority of these chronic wounds arise from poorly managed acute traumatic wounds, but may also arise from wounds stemming from vascular insufficiency, neuropathy, pressure, diabetes, or hemoglobinopathies (7). While it is clear that chronic wounds are susceptible to malignant transformation, the exact mechanism of this malignant transformation is unknown. Some believe that traumatized skin may be more susceptible to mutation due to fibrotic and avascular scar tissue interfering with immune surveillance (5). It has also been theorized that the malignant transformation of chronic wounds may be due to the induction of neoplastic cells, radiation, or toxin-induced alteration of mitosis and implantation of epidermal cells into the dermis (7). Since most, if not all, of the patients that may have been diagnosed with this malignant skin lesion deal with wounds of a chronic nature; it may be difficult to distinguish the characteristics of these chronic nonhealing wounds from that of a wound that has undergone malignant transformation. Generally speaking, ulceration features that may be indicative of malignant transformation include a chronic ulceration of longer than 3 months duration, excessive granulation tissue beyond the margins, everted wound edges, recurrent breakdown of ulcers after healing, static nonhealing ulcers after appropriate treatment, and ulcers that increase in size and/or pain after appropriate therapy (6).

There have been numerous case reports published in the literature that attempt to determine how many years a chronic wound must be present before malignant transformation takes place with data suggesting that it may take as little 11 years to as many as 21 years or longer (6, 7). The best option for treatment includes a wide local incision with a margin of at least 1 centimeter of healthy tissue (6). However, amputation should be considered when deep bone or joints are involved (8) along with chemotherapy and/or radiation if metastasis has been confirmed.

In the case of the patient presented in this article, one can see how crucial it was for our podiatry department to perform a punch biopsy of this patient's lesion. The patient presented not only with a wound that had been present for

more than 20 years; but also a wound that the patient herself admitted had grown in size and changed in appearance over the years. In addition to this fact, the patient had undergone a wide variety of conservative methods of treatment ranging from wound care, antibiotics, to invasive vascular studies with no resolution to the wound. Although below-knee amputation was presented to this patient as a treatment option, this treatment was recommended based on the chronicity of the wound in combination with the patient's vascular status as opposed to the severe malignant transformation that had occurred in the wound. Without performing the punch biopsy of this lesion, the invasiveness of this malignant lesion would not have been documented, and a below-knee amputation may not have been enough.

CONCLUSION

The ability to recognize those individuals whose chronic wounds may be at risk for malignant transformation is paramount to an appropriate treatment plan. In those wounds that have failed to respond to conservative treatment as well as exhibiting alterations in size, shape, and appearance, biopsy must be considered as a key diagnostic tool to aid in treatment plans. Once malignant transformation is diagnosed, the correct treatment may then be instituted.

REFERENCES

1. Potter BK, Pitcher JD, Adams SC, Temple HT. Squamous cell carcinoma of the foot. *Foot Ankle Int* 2009;30:6.
2. Kersch S, Lakhani S, Ramanujam C, et al. Concomitant acute osteomyelitis and squamous cell carcinoma of the foot: a case report. *Clin Podiatry Med Surg* 2010;27:635-41.
3. Nasca MR, Innocenzi D, Micalli G. Subungual squamous cell carcinoma of the toe: report on three cases. *Dermatol Surg* 2004;30:2.
4. Kaplansky DB, Kademian ME, VanCourt RB. Metastatic squamous cell carcinoma resembling cellulitis and osteomyelitis of the fifth toe. *J Foot Ankle Surg* 2006;45:182-4.
5. Stanford R, Lowell D, Raju R, Shylaja A. Marjolin's ulcer of the leg secondary to nonhealing chronic venous stasis ulcer. *J Foot Ankle Surg* 2012;51:475-8.
6. Shahla A. An overview of heel Marjolin's ulcers in the orthopedic department of Urmia University of Medical Sciences. *Arch Iranian Med* 2009;12:405-8.
7. Asuquo M, Ikpeme I, Ebughe G, Bassey E. Marjolin's ulcer: sequelae of mismanaged chronic cutaneous ulcers. *Adv Skin Wound Care* 2010;23:414-6.
8. Asuquo M, Ugare G, Ebughe G, Jibril P. Marjolin's ulcer: the importance of surgical management of chronic cutaneous ulcers. *Int J Derm* 2007;46:29-32.