Marjolin’s Ulcer of the Hallux

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We report the case of a 51-year-old woman with malignant degeneration of a right hallux nail bed ulcer of 20 years’ duration. Histologic examination confirmed the diagnostic features of Marjolin’s ulcer, a well-defined but uncommon malignant ulcer that occurs in chronic wounds and cutaneous scars. In this report, we describe the clinical and histopathologic features and the differential diagnosis of this unusual lesion. (J Am Podiatr Med Assoc 103(3): 250-253, 2013)

Marjolin’s ulcer is a rare malignancy that originates in chronic nonhealing wounds and cutaneous scars.1,2 This type of malignant transformation is most commonly associated with burn wounds but may be seen in many other types of nonhealing wounds, such as traumatic wounds,3,4 pressure sores,5 osteomyelitis,6 venous stasis ulcers,7 fistulas,8 lacerations,1 and chronic trophic ulcers in leprosy.9 The development of malignancy tends to be slow, with an average latency time of approximately 25 years.10,11 Well-differentiated squamous cell carcinoma is the most common histologic type of Marjolin’s ulcer.12,13 This entity is frequently overlooked, thus leading to a poor prognosis. A high index of suspicion should be held by health-care providers when evaluating a chronic, nonhealing wound. Biopsy with histopathologic interpretation remains the gold standard for diagnosis, with radical surgical excision being the treatment of choice. Marjolin’s ulcers involving the digits are very rare.14 Herein, we report a case of Marjolin’s ulcer arising in a hallux nail bed of a patient with a long-standing history of a nonhealing wound.

Case Report

The patient is a 51-year-old woman with a medical history of type 1 diabetes mellitus, hypercholesterolemia, and hypothyroidism who presented with a nonhealing wound on the right hallux. The wound was located in the nail bed and was first noted approximately 20 years earlier. At that time, an ingrown toenail was diagnosed and was repeatedly resected without resolution. Six years before presentation, the patient had been given a diagnosis of underlying chronic osteomyelitis of the distal right hallux and underwent complete removal of the entire nail.

Physical examination revealed an irregular area of granulation tissue involving the nail bed region of the right hallux, with erythema and tenderness on palpation (Fig. 1). Pedal pulses were palpable bilaterally. Capillary refill time was immediate to all of the digits, without evidence of telangiectasias or varicosities in either lower extremity. Perception of sharp-dull, vibratory, and proprioception sensations were within normal limits. Radiographs of the right foot revealed no significant changes compared with radiographs performed 4 years earlier. Magnetic resonance imaging (MRI) with and without intravenous contrast showed no significant abnormal signal intensity in the bones of the hindfoot, midfoot, and forefoot. There was no gross evidence of osteomyelitis. Routine laboratory tests were unremarkable. A 5-mm punch biopsy of the proximal portion of the lesion was performed. The histologic examination revealed erosion involving the entire breadth of the epithelial surface with underlying squamous proliferation. There was an associated brisk lichenoid lymphoplasmacytic host inflammatory response with a mixed CD4 and CD8 lymphocytic population. The base of the proliferative squamous epithelium had modest pushing borders with underlying fibrosis (Fig. 2A). Higher-power magnification revealed intraepithelial malig-
nant transformation of the squamous epithelium identified by scattered isolated malignant degenerated keratinocytes and atypical mitotic figures (Fig. 2B). The Mib1 proliferative marker demonstrated increased nuclear uptake in the epithelium. These findings were consistent with well-differentiated squamous cell carcinoma in situ with surface erosion. Taking into account the patient's medical history along with radiologic and histologic features, the diagnosis of Marjolin's ulcer was rendered. The patient was referred to the radiation oncology department for further treatment. She has completed external beam radiotherapy with overall improvement and no evidence of persistent disease. There was slight residual hyperpigmentation and thickened dry skin at the site of the lesion (Fig. 3). However, approximately 6 weeks after radiotherapy, the lesion reappeared and a subsequent biopsy confirmed the diagnosis of squamous cell carcinoma. The patient further underwent Mohs micrographic surgery. The surgical site was repaired with a free full-thickness skin graft.

Discussion

Marjolin’s ulcer is an uncommon lesion and represents malignant transformation arising in chronic wounds and cutaneous scars. Early clinical recognition of this lesion is critical because a delay in diagnosis can convert a potentially curable lesion into an incurable one. Malignant transformation of an ulcer is most commonly associated with burn wounds. However, it has been reported in many other types of nonhealing wounds, such as traumatic wounds, pressure sores, osteomyelitis, venous stasis ulcers, fistulas, lacerations, and chronic trophic ulcers in leprosy. Traumatic wounds constitute the second most common cause of malignant ulcers. The development of malignancy tends to be slow, with an average latency time to malignant transformation of 25 years.

The major histopathologic type of Marjolin’s ulcer is well-differentiated squamous cell carcinoma. Less than 2% of all squamous cell carcinomas arise in chronic wounds without actinic damage. Basal cell carcinoma is the next in frequency, but other malignancies have also been reported to occur in Marjolin’s ulcer. The data on possible exacerbating factors are scant and include trauma and

Figure 1. Physical examination revealed the right hallux nail bed lesion with irregular margins and base and erythema that was tender to palpation.

Figure 2. A, Skin biopsy showing atypical squamous epithelial proliferation with pushing borders, surface erosion, and lichenoid lymphoplasmacytic infiltrate (H&E, ×40). B, Higher-power magnification shows scattered isolated malignant degenerated keratinocytes and atypical mitotic figures (H&E, ×400).
ultraviolet irradiation. In a review of all cases of Marjolin-type squamous cell carcinoma involving the lower extremity, only 2.3% involve the foot. Marjolin’s ulcers involving the digits are very rare.

Several theories have been postulated regarding the pathogenesis of Marjolin’s ulcer. It has been proposed that long-term irritation with repeated damage and attempted repair of the damaged cutaneous tissue leads to malignancy. Some authors have suggested that toxins released from damaged tissue lead to cellular mutagenesis and eventually a tumor. Others postulate elevated expression of proto-oncogenes, which could be favored by chronic inflammation, as a mechanism for malignant degeneration in Marjolin’s ulcers.

The gold standard for the diagnosis of Marjolin’s ulcer is biopsy of suspicious nonhealing lesions along with histopathologic interpretation and clinical correlation. Some of the clinical features suggestive of malignant transformation that occur in an ulcer include exophytic growth, everted edges, irregular base or margin, and excess granulation tissue extending beyond the margins. In the case of the present patient, the ulcer had irregular margins and granulation tissue involving the nail bed region of the right hallux. There was erythema without overt tumor growth. However, the lesion was persistent for more than 20 years. Therefore, it has been suggested that any chronic, “ugly-looking” ulcer that is failing to heal despite appropriate treatment should be considered Marjolin’s ulcer unless proved otherwise. Dysplastic changes and subsequent malignant transformation in chronic nonhealing ulcers occur mainly at the edges, where there is rapid turnover of cells. Furthermore, only one edge may undergo dysplastic change, and the rest of the ulcer may lack cytologic atypia. Therefore, it is of utmost importance to extensively sample the lesions at multiple sites and depths to avoid overlooking the presence of squamous cell carcinoma.

Computed tomography and MRI can be very useful tools in the evaluation of Marjolin’s ulcer; MRI is a safe and rapid method, especially in tumors that invade surrounding tissue. In addition, it is an effective means of excluding a metastatic process. Marjolin’s ulcers are aggressive cancers with a higher fatality rate than other types of skin cancer. The metastatic potential of squamous cell carcinomas arising from chronic, nonhealing ulcers and scars is significantly greater than that of squamous cell carcinomas arising in normal skin (30% versus 3%). Metastases to lymph nodes are most common. Hence, lymph nodes should be carefully examined in all patients. Patients with Marjolin-type squamous cell carcinomas without lymph node metastasis have 5-year survival of approximately 90% compared with 39% in patients with squamous cell carcinomas with lymph node metastasis. Metastases have been reported in the brain, lung, liver, bone, and kidney. Moreover, the local recurrence rate is higher in patients with Marjolin-type squamous cell carcinoma than in those with other skin malignancies.

The treatment of choice for Marjolin’s ulcer is wide local excision with a margin of at least 2 cm of normal-appearing tissue and subsequent skin grafting. Regional node dissection is recommended when a clinically palpable lymphadenopathy is present. Wide local excision is usually followed by radiotherapy. Mohs reported that cutaneous squamous cell carcinoma of the foot and toe has a 71.4% cure rate. Any delay in diagnosis may cause deep bone involvement necessitating amputation or may lead to metastases and even death. Therefore, health-care providers should be aware of this rare entity and should not exclude Marjolin’s ulcer when confronted with a long-standing ulcer that is failing to heal despite appropriate treatment.

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References