

Chronic ringworm infestation and Marjolin's ulcer, an association unknown in the literature

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Abstract

We report here a case of Marjolin's ulcer developing in a long-standing, inadequately treated, chronic ringworm infestation of the lower limb. A 35-year-old female patient with a ten-year history of a chronic ringworm infestation had developed a non-healing ulcer in an area of infestation on the right leg. A biopsy revealed well-differentiated squamous cell carcinoma associated with the ringworm infection. A below-knee amputation by an inguinal block dissection was performed. We conclude that proper and timely treatment of fungal infections of the skin is needed to allow for healing of dermal infections and thus the prevention of the disastrous consequences that recurrent mechanical trauma from scratching of the affected area, leading to occult malignancy, which may occur in a small number of patients.

Introduction

Marjolin's ulcer is a rare but aggressive squamous cell cancer most often associated with chronic burn wounds.¹ However, it can arise in any chronic wound. Most commonly occurring in the presence of osteomyelitis or burn scars, Marjolin's ulcers have also been reported with radiotherapy, hidradenitis suppurativa, and diabetic ulcers.² In addition, they have been described in previously traumatized and scarred tissue of various etiologies, such as frostbite, venous stasis ulcers, skin graft donor sites, chronic pressure ulcers, poorly fabricated prostheses, gunshot wounds, puncture wounds, dog bites, and blunt trauma.³ As far as we can ascertain, no reports are available in the literature documenting Marjolin's ulcer associated with a chronic ringworm infestation of the skin. We report a case of malignant transformation in chronic ringworm infection of the skin of the lower extremity in a young female patient.

Case Report

A 35-year-old female from the Midnapur district of West Bengal, India, presented with a one and a half-year history of a foul-smelling, non-healing ulcer over the right ankle region to the outpatient department of surgical oncology of the Chittaranjan National Cancer Institute, Kolkata, India. The patient had been suffering from a cutaneous ringworm infection of the upper extremities, anterior abdomen, and lower extremities for more than ten years; however, she had not sought a proper dermatological opinion receiving only irregular over-the-counter treatments for six years. The records of the treatments received and the medications used were not available. The rash and the associated itching would abate for some period only to reappear again after discontinuation of the local treatment. Approximately one and a half years before presentation to our hospital, the patient developed a small ulcer at the site of infestation superior to the anterior right ankle. The ulcer would develop encrustations, which often would be dislodged because of scratching. This lesion increased indolently in size and did not show any signs of healing despite the alleged local wound care. Fourteen months after the appearance of the ulcer, the patient had sought the opinion of a general practitioner and a biopsy was undertaken, which reported invasive squamous cell carcinoma. The patient was advised to attend our center, but delayed consultation for six months. The family history did not reveal any cancer predisposition. The patient did not have any other previous or concomitant medical conditions.

On examination, the patient suffered from poor personal hygiene. An ulcer approximately 6x4 cm in diameter was present over the anterior (dorsal) aspect of the right lower leg just above the ankle. The ulcer had irregular, everted margins with necrotic sloughing in the center (Figure 1). The inguinal lymph nodes were enlarged, firm in consistency, but not matted. There were areas of ringworm infestation over other parts of the body including the contralateral lower limb, left inguinal area, lower abdomen, and right upper limb (Figure 2). An X-ray examination of the right ankle and foot showed involvement of tarsal bones by the tumor. A review of the pathological slides of the patient was carried out, in accordance with the established protocol of our institution, which confirmed the diagnosis of squamous cell carcinoma. In addition, a dermatological review and microscopic examination of the scrapings from the associated cutaneous lesions were performed, which confirmed ringworm infestation. A fine-needle aspirate of the inguinal nodes revealed reactive changes.

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Histopathological results revealed a well-differentiated squamous cell carcinoma with periosteal infiltration of two tarsal bones and direct bony involvement of another.

In view of the advanced nature of the lesion, involvement of the ankle joint, the overall inefficient compartmentalization in peripheral extremity lesions and increased chances of recurrence, increased costs of reconstructive surgery, the dismal financial condition of the patient who was a single woman living in a remote area, and thus the practical difficulties on the part of the patient for a close follow-up, the institutional tumor board reluctantly decided in favor of a below-knee amputation. The patient received a prolonged course of antibiotics after surgery. However, there was no clear response of the inguinal pathology to the antibiotics over the following three months. The patient then received an inguinal block dissection. Postoperative recovery was uneventful. The histopathological examination revealed microscopic deposits of tumor, in three of the dissected lymph nodes. A follow-up tumor board review decided in favor of only close follow-up with physical examination every two months, an ultrasound examination of the inguinal area, pelvis, and abdomen every four months, and a chest X-ray on a four-monthly basis for the first two years. The patient is attending a follow-up clinic diligently every two months, and she has remained free of recurrence for 21 months.

Discussion

The Ancient Roman physician Aurelius Celsus first described abnormal tissue growth in burn scars, in the first century AD.⁴ Although the French surgeon, Jean Nicolas Marjolin, was credited with the first description of the phenomenon of malignant ulcers in the early 19th century, Hawkins and Dupuytren were the first to describe this malignancy in a chronic wound.⁵ Marjolin's ulcer is a malignant transformation of chronic wounds⁶ and a rare but aggressive squamous cell carcinoma that is most often associated with chronic burn wounds.¹ Other less common histologies like basal cell carcinoma and melanoma have also been reported.⁷ There are several dermatological conditions known to be associated with malignant transformation. These



Figure 1. Anterior aspect of the right lower leg just above the ankle showing the irregular, everted margins of the ulcer with necrotic sloughing in its center.



Figure 2. An area of ringworm infestation on the calf of the left lower leg.

include genital *lichen sclerosus et atrophicus*, oral *lichen planus*, *erythema ab igne*, and burn scars.⁸ A case of squamous cell carcinoma at the site of the extravasation of doxorubicin (a chemotherapeutic agent) has also been reported.⁹ Overall, the incidence of Marjolin's ulcer is low and represents 2-5% of all squamous cell cancers, and is found three times more frequently in men than women.¹⁰

Although Marjolin's ulcers are most commonly found on lower limbs,¹¹ they can occur at any dermal site and can be more aggressive at other sites, as has been reported by Emsen in a case report of a scalp ulcer.¹² Despite the wide prevalence of wounds in which this malignancy may develop, Marjolin's ulcer remains a relatively rare entity.¹³ An estimated 1.7% of chronic wounds undergo malignant transformation.² However, according to Smith *et al.* chronic ulcers that undergo malignant transformation are more prevalent in developing countries, where patients consult physicians only after they experience complications.¹⁴ The latent period for malignant transformation ranges between 25 and 40 years (average 32.5 years).^{15,16} However, Thio *et al.*¹⁷ have reported malignant transformation within 4-18 months in lower limb wounds. Soto-Davalos *et al.*¹⁰ have reported malignant transformation as early as three months. Our patient belonged to a remote village in the West Bengal state of India and did not have access to a proper dermatological facility. The general practitioner was consulted only after the dermal lesion had developed a malignant wound that refused to heal.

The pathogenetic factors of malignant transformation may be multiple. In the past few years, a different paradigm for the understanding and treatment of chronic wounds has evolved. The emerging view is that chronic wounds are characterized by resident cells that have undergone phenotypic changes that need to be corrected for optimal healing to occur.¹⁸ The impaired healing observed in chronic wounds is because the intricate balance of cytokines, growth factors, proteases, and cellular and extracellular elements that play important roles in different stages of the healing process become defective.¹⁹ Cellular responses to inflammatory mediators, growth factors, cytokines, and mechanical forces must be appropriate and precise. However, this orderly progression of the healing process is impaired in chronic wounds, including those associated with diabetes. Several pathogenic abnormalities, ranging from disease-specific intrinsic flaws in blood supply, angiogenesis, and matrix turnover to extrinsic factors because of infection and continued trauma, contribute to failure to heal and may contribute to malignant transformation.²⁰

We report this case because, to the best of our knowledge, there is no such case described

in the literature. Neither has any report been published, whereby malignant transformation of a chronic wound or an ulcer associated with ringworm infection has been established. Our case highlights that negligence on the part of the patient and consequent scratching of the affected area causing recurrent mechanical trauma can lead to malignant transformation associated with the chronic ringworm infection. Although a fungal infection of the skin may not lead to malignant transformation in every case (especially in developed countries), it can pose a problem in the developing world, as has been pointed out by Smith *et al.*,¹⁴ where not all patients have access to a proper medical facility. In India alone, an estimated 37.2% of the population live below the poverty level and cannot afford proper treatment. This leads to delay by these patients, owing to economic constraints, in seeking qualified advice. Proper and timely treatment of fungal infections of the skin is needed to alleviate symptoms and promote healing of dermal infections. Negligence on the part of the patient and scratching of the affected area causes recurrent mechanical trauma with consequent ulceration. Scratching and thus recurrent trauma inhibit progression of the healing process, in some cases may contribute to malignant transformation.²⁰

Conclusions

The formation of a non-healing ulcer should alert the physician about the sinister behavior of this condition and prompt a histopathological evaluation and early excision of the malignant lesion to prevent such disastrous consequences. Early excision of the suspicious lesion may be warranted even when the biopsy results are equivocal but the clinical features favor a malignant phenotype. Although neoplastic transformation in ringworm infection is the exception rather than the rule, the present study shows that such an association can exist. The exact mechanism of this transformation is difficult to ascertain but recurrent trauma over a long period with consequent interference with the healing process possibly explains the underlying mechanism of this process.

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