Marjolin's Ulcer: Update on Concepts, Diagnosis, and Treatment

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ABSTRACT

Marjolin's ulcer is any aggressive cutaneous neoplasm that arises in scar lesions with chronic inflammation. The most common histopathological finding is squamous cell carcinoma, basal cell carcinoma, or other types of malignant cells. Early diagnosis is essential for correct therapeutic management; the most widely used and sensitive method is a biopsy of the affected tissue. The most common treatment is surgical, involving early excision and skin grafting; however, over time, new techniques and approaches have been introduced to manage lesion progression, providing a better prognosis for the patient.

Keywords: Ulcer, Scar, Squamous cell carcinoma, Biopsy

Úlcera de Marjolin: actualización de conceptos, diagnóstico y tratamiento

RESUMEN

Se entiende como úlcera de Marjolin cualquier tipo de neoplasia cutánea agresiva que surge en lesiones cicatriciales con inflamación crónica. El hallazgo histopatológico más frecuente es el carcinoma escamocelular, seguido del basocelular y otro tipo de células malignas. El diagnóstico debe realizarse de manera temprana para su correcto abordaje terapéutico; el método más implementado y con mayor sensibilidad es la biopsia del tejido comprometido. El tratamiento más utilizado es el quirúrgico por medio de la escisión temprana y el uso de injertos de piel, pero con el paso del tiempo se han presentado nuevas técnicas y enfoques que cuidan la progresión de la lesión y así darle un mejor pronóstico de vida al paciente.

Palabras clave: úlcera, cicatriz, carcinoma de células escamosas, biopsia (DeCS).

INTRODUCTION

There are few reported cases of malignancy in cutaneous scars in clinical practice. "Marjolin's ulcer" (MU) refers to ulcerative lesions that present malignant neoplastic degeneration in cutaneous tissue with chronic inflammatory processes that do not respond to conventional treatment[1]. MUs occur in 0.77-2% of burn scars and account for 2% of all squamous cell carcinomas[2]. Previously, their etiology was mainly associated with burn scars, with a rate of 76.5%, according to the 2009 literature review by Kerr-Valentic et al.[3]. However, the current literature encompasses all neoplasms that develop in scar tissue, chronic ulcers, and inflammatory processes[4]. The most frequently identified tumors are squamous cell

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carcinoma and basal cell carcinoma, with frequencies of 88% and 12%, respectively. Recently, other neoplasms or coexistence with sarcoma (5%), melanoma (6%), or others (6%) have been described[4]. After an extensive literature search, we only found one report by Hobbs et al. on the occurrence of multiple synchronous MUs[2] and no reports related to poorly maintained external fixators[5].

STATE OF THE ART

The first reports of MU were described by Aurelius Cornelius Celsus as malignant lesions in burn scars; however, it was only in 1828 that Jean-Nicolas Marjolin formally described this degeneration in chronic ulcers. Subsequently, Dvork proposed that prolonged wound healing, alongside the generation of tumor stroma and the development of atypical cells during the wound healing process, could lead to malignancy. Other researchers have suggested that scar tissue, which lacks good blood supply, may interfere with the action of lymphocytes, which are crucial for the early identification of cancer cells[3-6].

Today, biological and mechanical factors have been implicated in the development of MU, proving that chronic wounds are not merely localized inflammatory processes but can create conditions conducive to malignant degeneration. For this reason, Marjolin ulcer(MU) is presently defined as the formation of an invasive neoplasm in a wound that has been chronically affected[6].

Previously, UM events appeared to occur chronically with an average latency of 28.7 years; however, they have been reported to develop chronically and acutely. MUs are classified as chronic when they appear 12 months after the injury and as acute when they occur within the first 12 months, with the latter being considered extremely rare. There are no clinical, histological, or prognostic differences between the two.[2]

So far, no specific pathophysiology has been established for the development of MUs, whether caused by burns or other types of wounds, but their origin is considered multifactorial. The possible mechanisms relevant to the appearance of this pathology are associated with the inflammatory environment of ulcers, the release of cytotoxic products derived from macrophage activity in the wound, high mitotic capacity, poor vascularization, inadequate lymphatic drainage, and the co-carcinogen theory. This theory suggests that chemical and/or physical injury stimulates the proliferation of an already existing but latent malignant cell in an immunologically unfavorable context for the patient, creating ideal conditions for carcinogenesis and the formation of neoplasms such as MU.[2,7] The involvement of the Fas gene in scars has also been proposed.[4] Cells undergo a process of basal hyperplasia, pseudoepithelial hyperplasia, and, ultimately, atypical changes.[6]

DIAGNOSTIC METHODS AND TREATMENT

The diagnosis depends on the combination of clinical signs and symptoms. The clinical triad of MUs consists of nodular lesions, induration, and lesion ulceration for more than 3 months. Other signs and symptoms include everted wound margins, excessive granulation tissue, purulent and fetid discharge, enlargement, bleeding upon contact, crusts, epithelial pearls, and pain.[4,5] The anatomical locations where this pathology most frequently occurs are the extremities in 60% of cases, the head in 30%, and the trunk in 10%.[6]

The reference procedure (gold standard) for diagnosis is a histopathological study through biopsy, indicated in chronic ulcers that do not heal, to determine the presence of malignant cells. It is necessary to perform biopsies in a mapping manner to avoid false negatives, taking samples from both the edge and the base of the lesion to ensure a representative sample that facilitates an accurate diagnosis.[4,5] Unfortunately, the appropriate timing for performing the biopsy is unclear; some authors suggest doing it at 3 weeks with conservative management, while others prefer waiting 3 to 4 months, as many of the ulcers where these lesions are situated take several weeks to heal completely.[6] However, it is worth noting that when signs like those mentioned earlier appear, it is preferable to perform the biopsy earlier to achieve the earliest possible diagnosis.

Although there is no established treatment protocol, surgical management is the cornerstone, consisting of surgical excision with safety margins of at least 1 centimeter, accompanied by using partial-thickness grafts to cover the defect.[5,6] Regarding the extremities, in patients with tumor invasion, large size, hemorrhages, or involvement of adjacent structures, amputation of the affected area is necessary.[6] Another alternative for patients with inoperable tumors or those who refuse surgery is the use of adjuvant treatments such as chemotherapy or radiotherapy.[8] There is controversy regarding lymphadenectomy; most authors suggest performing this procedure only if palpable lymphadenopathy or confirmed tumor is evident, not prophylactically.[6] Modified variants of the above procedures include the use of free flaps, Mohs micrographic surgery, and cryosurgery, in which the surgeon, assisted by the Dermatology and/or Pathology Service, performs a comprehensive evaluation of the superficial and deep margins using frozen section histology. If the margins are positive, resection or amputation is warranted; however, these are high-cost options that require a properly trained team.[5] Other alternatives to surgical management include intralesional interferon, photodynamic therapy, and CO2 laser therapy, the latter appearing effective for early lesions, small in size, and without deep tissue invasion.[6,7]

PROGNOSIS, FOLLOW-UP, AND CONTROL

The survival of these patients depends on factors such as the site of the lesions, as those originating on scar tissue are more aggressive and have a worse prognosis than those originating on healthy skin; the clinical presentation, with ulcerative forms being more aggressive than exophytic ones; the location, with lesions on the trunk and lower limbs having a worse prognosis; size; longer latency periods; histology; and the presence

of lymph node and distant metastases. Overall survival rates are reported to be between 66% and 80% at 2 years, 65% to 75% at 3 years, and 34% at 10 years. The recurrence rate after surgery ranges from 16% to 37%, with a latency period between excision and tumor recurrence of 4.6 months.[2,5-8] Metastases may occur in 22% to 35% of cases, with the most frequent sites being the lymph nodes, lungs, liver, and brain.[4,6]

CONCLUSION

This article aims to present MU as an infrequent and aggressive tumor pathology that must be identified early, with follow-up and monitoring of scar lesions found on the skin, taking into account its clinicopathological evolution to facilitate timely intervention. Otherwise, it could progress and develop complications such as lymphatic nodal metastases, worsening the patient's prognosis.

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