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Marjolin's Ulcer, A Frequent and Preventable Complication

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ABSTRACT

Marjolin's ulcer is a malignant neoplasm originating from long-standing or previously healed skin lesions. Well-differentiated squamous cell carcinoma (SCC) is the most common histologic type. It is an aggressive neoplasm with a poor prognosis and high recurrence rates. It predominates in men and has a higher incidence in the fifth decade of life. The diagnosis is histopathological. Surgical excision is the treatment of choice. Early diagnosis and prevention in wound management reduce complications and guide the correct therapeutic approach.

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GENERALITIES

The term Marjolin's ulcer (UM) was coined in 1903 by DaCosta. In the eighties the French surgeon Nicholas Marjoline first described the transformation of burn scars, however the risk of malignancy was unknown. (1)

Marjolin's ulcer has classically been referred to as squamous cell carcinoma arising from burn scars; however, it is also used to describe aggressive malignant degeneration (basal cell carcinoma, malignant melanoma, or sarcomas) in any chronic wound or lesion (1,2, 9)

Injuries frequently associated with UM are burn injuries [by flame (19%), by contact (12%), by scalds (8%)], pressure ulcers, long-standing venous ulcers, amputation of stumps, frostbite injuries and trauma. (23)
The risk of malignant transformation leading to a Marjolin ulcer is increased in scars resulting from skin burns (76.5), non-healing chronic traumatic wounds (8.1%), and venous leg ulcers (6.3%). (3)

EPIDEMIOLOGY

There is a 2:1 male:female distribution. (3) The factors associated with this distribution are unknown; it is postulated that it could be due to a higher incidence of burns, the most frequent cause of Marjolin's Ulcer, in men than in women. (4) Approximately 1.7% of wounds show malignant transformation. The highest predisposition to malignancy occurs in full-thickness burns that heal by secondary intention, which present an incidence of 0.77 to 2%. (9).

RISK FACTOR'S

Marjolin's ulcer is associated with scar tissue, most commonly from burns, but it has also been described in post-traumatic wounds, from bites, fistulas, cystostomy sites, radiotherapy, in the genitals due to a complication of Fournier's gangrene or pressure ulcers.

CLINICAL PRESENTATION

The median age of diagnosis is 50 years of age. A mean latency period of 31 years is reported. (3)

It can occur in any location, the lower limbs (53.3%) are the most frequent topography followed by the upper limbs (18.7%), scalp and neck.
In the systematic review published by Kowal-Vern and Criswell, 71% of the cases were squamous cell carcinoma, 12% basal cell carcinoma, 6% melanoma, 2% squamous cell carcinoma-basal cell carcinoma, 1% basal cell carcinoma-melanoma, and 5% others. (4)

Clinical findings indicative of degeneration in a chronic wound according to the reviewed literature include: nodule or wart formation, surrounding induration, everted and irregular margins, excessive granulation tissue, contact bleeding due to tumor angiogenesis, lack of tendency to heal in 3 months or

more despite adequate treatment and wound enlargement, spontaneous pain, malodorous exudation, and necrosis. (5,6)

Marjolin's ulcer is classified according to the time of onset. An acute ulcer corresponds to a malignant transformation in the first 12 months after the skin lesion occurred, while the chronic form originates after 12 months.(3)
According to Chang et al (7) people under 40 years of age are more likely to develop acute ulcers, while those over 50 who suffered burns at an earlier age have been shown to develop chronic UM more frequently. In addition, he explains that the acute form is often associated with smaller, partial-thickness burns and that it usually manifests as superficial multicentric basal cell carcinoma, while, conversely, the chronic form presents as squamous cell carcinoma arising on deeper, full-thickness burns. (8,9)

PATHOPHYSIOLOGY

Various mechanisms are involved in malignant transformation. It is postulated that areas of chronic scarring lose immune system cells (natural killer cells) and this triggers some malignant cells to evade immunological detection. Chronic inflammation has been established as a causal factor in the development of cancer since it stimulates tissue proliferation and can cause mutations. (4,5,9)

Virchow's theory explains that with chronic irritation (a non-healing scar) and repeated tissue injury (folded or trauma-prone areas), as well as possible DNA damage in the area of injury, the epithelium becomes it becomes less stable, loses contact inhibition, and undergoes malignant change due to the increased rate of spontaneous mutations. This is explained by the chronic inflammatory microenvironment, which favors angiogenesis, promoting uncontrolled growth and malignant cell transformation. This mechanism of cell proliferation is also developed by constant cures that cause a continuous secretion of cytokines, chemokines, and growth factors.(10,11)

Other authors refer that UM arises from the skin with previously pre-malignant changes or that there is a promoter stimulus called "co-carcinogenic", which accelerates or promotes cancer in a tissue in which the neoplasia had already started. The formation of scar tissue after an injury, such as a burn, can affect lymphatic flow, altering immune surveillance, making it difficult for the organism to respond antigen-antibody to face proto-oncogenes or tumors within the scars.(12,13)

The most frequent type of tumor found is squamous cell carcinoma and generally associated with burn scars, where there is a greater risk of malignant transformation than in other types of lesions. In a study it was reported that this tumor is associated with the mutation of the "FasR (CD95)" gene, a cell surface receptor involved in signaling cell death, whose defects such as the "Fas mutation" interrupt apoptosis and homeostasis and therefore play an important role in the development and progression of tumors in humans.(14,15)

DIAGNOSIS

The standard diagnostic test is histological analysis by biopsy, it must be collected from several areas of the lesion, from within and from the margins, since a single sample may not reveal the presence of squamous cell carcinoma and could lead to false negatives. Once the diagnosis is confirmed, the regional and distant extension of the lesion should be evaluated by means of complementary tests such as an X-ray or an ultrasound examination of the anatomical region of lymphatic drainage to rule out metastasis, due to the negative impact on treatment and survival prognosis. (16,17)

MRI is considered the best method to assess bone level and extent, as well as soft tissue inflammation. Some studies also refer to PET-CT, which has high sensitivity for the detection of metastases in lymph nodes and distant metastases, but they need to be combined with biopsy findings. (18,19,20)

PROGNOSIS

The most important prognostic factor is histological classification; evidence of lymph node metastases is associated with the poorest prognosis. In general, in Marjolin's ulcer, a metastasis rate of 27.5 to 40% is reported. (9)
Some characteristics associated with a better prognosis are latency of less than 5 years from the lesion to the development of malignancy, location in the head, neck and upper limbs, exophytic pattern and absence of metastasis. On the other hand, lymphadenopathy, location in the torso and lower limbs, infiltration pattern, and presence of metastases are factors associated with a poor prognosis. (3, 9)

TREATMENT

Marjolin ulcers are considered very aggressive tumors, with a rapid rate of regional metastases, which is why radical excision is the main treatment option, although there is no consensus on a definitive treatment in the reviewed literature.(21)

Dörr et al (21), refer to the existence of multiple treatment options that can be used in combination giving high cure rates of up to 90%. The most common methods of treatment to treat them are wide local excision and en bloc excision of the lymph nodes. Sentinel lymph node dissection is necessary in patients with sentinel lymph node metastases, but there is no consensus regarding preventative nodal dissection or radiation due to the aggressive nature of UM carcinoma.(22,23)

In case of sentinel node metastasis from squamous cell carcinoma, they may undergo amputation and sentinel lymph node dissection. Amputation is indicated when wide local excision is inadequate due to bone or joint involvement or when unresectable tumor is present. The resection margin

should extend 2 to 4 cm beyond the edges of the lesion in order to perform a curative resection and vertical clearance of the next uninvolved barrier structure to ensure a clean wound. In addition, other types of treatments such as neoadjuvant or adjuvant therapy such as radiotherapy and chemotherapy are recommended in patients with a poor prognosis, distant metastases, or those who are not candidates for surgery.
Chemotherapy may consist of topical or systemic 5-fluorouracil in combination with cisplatin, methotrexate, and bleomycin (9,24,25).

CONCLUSIONS

Marjolin's ulcer is a malignant entity that arises from a wound that has gone through a period of chronic inflammation, although the mechanism by which the transformation occurs is not well known, it is important to monitor those wounds that despite multiple treatments and a long time of evolution do not finish healing completely.

Marjolin's ulcer has different forms of presentation, because not only can the malignancy present as squamous cell carcinoma, but other types of cancer can occur in an ulcer or wound that does not heal. It is important never to delay the diagnosis if there is suspicion, performing the biopsy promptly.

Currently, the first line of treatment is surgical management. In most cases, extensive excision of the lesion is performed, but less conservative management, such as amputation, may be necessary. In cases of very extensive resections, reconstructive surgery is used, mainly skin flaps. Evidence is lacking regarding the usefulness of techniques such as sentinel node mapping on prognosis.
It is an entity that, if an early diagnosis is made, patients can enjoy a high survival rate, since its etiopathogenesis is mainly due to thermal lesions in the dermis, close monitoring of patients with risk factors is important. important risks to avoid their presentation. And in case of already presenting it, delimit the damage that it could present in a systemic way.

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