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MARJOLINE ULCER: A RECENT CHANGE IN LATENCY PERIOD

Plastic Surgery

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ABSTRACT

Malignant neoplasm arising in chronic, non-healing wounds has been known since ages and it was named Marjolin's ulcer about one hundred years ago.Marjolin's ulcer refers to a rare but highly aggressive ulcerating squamous cell carcinoma that is most often presented in an area of chronic burn wounds. However, it is also associated with chronic inflammatory states, as in non-healing wounds, venous ulcers, lupus vulgaris, vaccination scars, snake bite scars, pressure sores, osteomyelitis zones, pilonidal abscess, and radiotherapy areas. Marjolin's ulcer may be defined by many pathological types of neoplasms. Squamous cell carcinoma is the most commonly identified histological type followed by basal cell carcinoma , malignant melanoma, sarcomas (fibrosarcoma, liposarcoma, dermatofibrosarcoma protuberans, mesenchymal tumor), mixed tumours and others. There is an agreement over the prevention methods with skin grafting of burned areas and excision with simultaneous grafting of ulcerations appearing in non-healing wounds. To date, there has not been a consensus reached over the treatment protocol. Wide surgical excision seems to be the most preferred method. Inoperable cases and recurrences may be treated with radiotherapy alone or combined with chemotherapy. This potentially fatal complication typically occurs after a certain latency period. This article attempts to reveal the importance of the latency period in the prevention and early treatment of the malignancy.

KEYWORDS

Marjolin's ulcer, Squamous cell carcinoma, Latency period, Chronic cutaneous ulcers, Burn scar.

INTRODUCTION

During the course of MarjolineUlcer, the latency period is defined as the time between initial injury and the confirmation of a pathologic diagnosis of malignancy. This malignant change of the wound happens a long time after initial trauma, usually 10–25 years later. Approximately 2% of burn scars undergo malignant transformation. A malignant neoplasm commonly appears in burn scars in the lower and upper extremities, the presternal region, the scalp region or other parts of the body.

Most Marjolin's ulcers arise in full-thickness burns. Sites that remain ungrafted or where grafts have failed are more vulnerable for developing malignancy. These grafts often develop chronic and recurrent ulcerations before undergoing malignant transformation. Slow initial healing and scar instability result in recurrent ulceration and, in the end, neoplastic changes. Theories concerning pathogenesis remain unclear, controversial, and not explained by one. They include Arons theory of transformation of chronic irritation to atypia and carcinoma, radiation/toxin-induced alteration of mitosis, implantation of epidermal cells into the dermis, induction of dormant neoplastic cells. Ultraviolet rays, ischemia, decreased immunity of affected skin/scar tissue, environmental and genetic interaction.

It's usually slow growth, painlessness (as the ulcer is usually not associated with nerve tissue), and absence of lymphatic spread due to local destruction of lymphatic channels. This carcinoma is aggressive in nature, spreads locally and is associated with a poor prognosis. Diagnosis is histologic, most common squamous cell carcinoma (SCC) followed by basal cell carcinoma. Changes such as the appearance of flat,non-healing ulcers enlarging in circumference with elevated and indurated borders, foul-smelling, painful with exudate and bloody drainage suggest a malignant transformation. Quite often, additional X-ray may show bone destruction. Surgical biopsy performed in multiple sites is recommended to confirm the neoplasmatic conversion.

This report discusses the change of latency period of marjoline ulcer and awareness of early diagnosis and treatment to prevent the development of marjoilne ulcer in a chronic ulcer/wound. In the authors' setting, traditional healers enjoy the patronage of the inhabitants because of strong sociocultural beliefs and majority of times, patients seek the physician too late. Physician may also underestimate case with further loss of time. Consequent on the above, majority of patients in the developing world presented with advanced lesions that precluded curative surgery. We present this study to highlight the sequelae of mismanaged chronic cutaneous ulcers and recommend solutions for prevention and improved outcome of management.

Case report 1

A 45 year old man who cured second and third-degree thermal bums in right lower extremities 6 years previously presented with chronic repeated ulceration in the scar area of the right popliteal fossa for 3 years. The physical examination revealed a scar on the on the right popliteal fossa. The ulcer was located in the middle of the burn scar tissue and measured 5 cm x 3 cm with elevated, inflamed edges and a fragile wound bed with some necrosis [Figure 1]. There was no evidence of lymphadenopathy in the ipsilateral groin. The remainder of the physical examination was unremarkable. The ancillary laboratory workup and radiological studies were negative. Biopsy of the ulcer revealed the pathological diagnosis of well differentiated squamous cell carcinoma. Wide local excision with 2 cm normal margin and grafting was done. The patient is regularly attending our follow-up clinics with no recurrence.

Case report 2

42 year old female presented with an exophphytic mass on the posteromedial aspect of the right elbow of 1 year duration. She had suffered a burn 6 years ago by accidental contact with a burning log of wood. Since then, despite the application of dressings using various different types of material, the burn area progressed through periods of partial healing followed by periods of deterioration. Local examination showed a tender, on mobile swelling with dimensions of 20 cm×10 cm progressively growing in size, with abundant, fetid suppuration, increasing pain and expansion of the friable, exophytic area [Figures 2]. Peripheral adenopathies were not found in the axilla.Histology performed on the tissue fragment removed from the mass permitted definitive diagnosis to be made of a well-differentiated squamous-cell carcinoma with deep invasion of the dermis. The patient underwent wide local excision and split-thickness skin graft. The wound healed and the patient was discharged.

Case report 3

A 35 year old female presented with an ulcer over medial aspect of right elbow of 6 month duration .It was associated with mild pain. Elbow movement is normal. she had suffered accidental burn 10 year back . During the ensuing 10 years, there had been no change in the burn scar except in the 6 months before presentation, when he noted an ulcerative wound on his right elbow that had progressively increased in size. General and systemic examination was normal. Local examination show a tender swelling of size 6 cm x4 cm [Figure 3]. The ulcer had a raised border, purulent exudates, and a foul odour. No regional or distal lymphadenopathy was palpable. He underwent an biopsy and the pathologic report showed squamous cell carcinoma. Wide local excision and split-thickness skin graft was done.

Case report 4

A 55 year old man who suffered trauma over left knee 12 years previously presented with chronic repeated ulceration in the scar area over left knee for 5 years. Ulcer is not healing due to continues movement over knee joint which lead to repeated breakdown of scar eventually it is converted to malignancy. Physical examination revealed the presence of a 12 cm x 8 cm exophytic ulcerated lesion with verrucose margins and uneven surface over the left knee (Fig. 1).Biopsy of the ulcer revealed the pathological diagnosis of well differentiated squamous cell carcinoma. The patient underwent wide local excision of the ulcer of the left knee and split-thickness skin grafting.

Case report 5

A 40 year old male presented with multiple ulcer over left leg of 6 years duration .It was associated with mild pain. He had suffered accidental burn 20 year back . During the ensuing 10 years, there had been no change in the burn scar except in the 6 years before presentation, when he noted an ulcer on his left leg that had progressively increased in size. General and systemic examination was normal. Local examination shows multiple ulcers of varying size. No regional or distal lymphadenopathy was palpable. He underwent an biopsy and the pathologic report showed squamous cell carcinoma. Wide local excision and split-thickness skin graft was done.

DISCUSSION

Marjolin's ulcer is an often overlooked pathology arising in burned, constantly injured or chronically inflamed skin. Cancers developing in scar tissues were officially named Marjolin's ulcer in 1903 by Da Costa [1]. In 1828 Jean Louis Marjolin, French physician, described an ulceration in scar tissue, however without stating if it is capable of malignant transformation [2]. Literature contains even earlier reports on scar neoplasms. Earliest from about 100 A.C. by Celsus on cancers developing in burn scars [3]. Marjolin's ulcer is a rare and aggressive cutaneous malignant transformation with an incidence of 0.1% to 2.5% after a long-term inflammatory or traumatic insult to the skin [4,5]. The main etiology tends to be post-burn scars and traumatic wounds [6]. Even though several theories have been postulated to elucidate the mechanisms generating this process, none can fully explain it [7]. Nevertheless, there is a consensus on the importance of chronic irritation. Repeated ulceration to the scar and subsequent initiation of re-epithelialization provides a prolonged stimulus for cellular proliferation and may increase the rate of spontaneous mutations [5,8,9].

Blood vessels and lymphatics regenerate poorly. Scar tissue than becomes an immunologically crippled site where tumor cells can escape the immunological elimination processes [10]. Malignant transformation of chronic ulcers is closely related to the duration of ulceration. This means that the longer the ulcer duration, the higher the risk of dysplasia [11]. Moreover, young patients tend to have a course of cycling between skin breakdown and repair before developing malignancy [12].

In our study, five patients reported that a small portion of their initial injury never completely healed, which means they experienced repeated ulceration shortly after the initial injury. Therefore, the length of the post-ulceration period was almost as long as that of the latency period. While SCC can arise from these kinds of unhealed chronic ulcers, it is not an uncommon source for Marjolin's ulcer [13,14].

There is a lag period between the development of Marjolin's ulcer in a scar tissue and the time of injury. It has been observed that the latency is inversely proportional to the patients' age. Malignant transformation is delayed in younger injury victims. The older the patient at the time of injury the shorter the lag period. The average latency period is 36 years and the average patients' age at the time of diagnosis is 52.Male/female ratio is 2:1. Incidence in women is greater only in cases of malignant melanoma[15-20].Lower extremities are the most commonly affected sites 60% of the cases in our study. Next is the head region (with face, scalp and neck), followed by the upper extremities and the trunk. Most researchers agree that the best prevention of these scar malignancies is primary skin grafting of the burn sites. Chronic ulcerations appearing in non- healing wounds should be excised and also skin grafted [20-23]. Unfortunately diagnosis is often delayed. As a result approximately 30% of the cases have enlarged lymph nodes with possible metastasis [15,21,23]

Since biopsy remains the gold standard for the diagnosis of Marjolin's ulcer [24,25], it should be applied for suspicious lesions that have not healed in 3 months.As recurrence of Marjolin's ulcer is higher than normal SCC (11–37%), 2–4 cm of free margins should be resected [26,27- 29]. Frozen biopsy during the operation is helpful, for Marjolin's ulcer always occurs in varying depth . Moreover, since the majority of Marjolin's ulcer s occur in long-duration unstable scars of ungrafted full-thickness burns [29], the joint regions, especially flexion creases, are more commonly involved due to predisposition to activity-related repeated ulceration [28]. Early surgical management could also achieve a possible prevention strategy.

Treatment of Marjolin's ulcer should be multidisciplinary.Although there has not yet been a consensus reached over the management protocol,we agree with most of the researchers that surgery is the primary treatment. First of all, excision should be performed with cautery (which is believed to be safer as it may prevent metastasis by preventing tumor cells from being washed into the blood and lymph systems) with the addition of a small margin, for the skin, performed with a surgical scalpel for better healing [21,23].Excision of ulcers should include a 3–4cm margin of normal skin with muscle and fascia due to the high metastatic potential and recurrence tendency [15,21,23]. Defects are usually skin grafted either with free fl aps or split- thickness skin grafts (STSG) [21,23]. If there is a clinically palpable lymphadenopathy, lymph node dissection is recommended [15,10,21,23] with an exception for malignant melanoma, where the sentinel lymph node biopsy should be performed regardless of the presence of enlarged lymph nodes. In cases where surgery is impossible or inadequate, radiotherapy alone or combined with chemotherapy should be performed .

Chemotherapy is usually based on 5-Fluorouracil with a combination of Cisplatin and Methotrexate [20]. In the medical literature, prognosis in cases of Marjolin's ulcer estimates a three-year survival rate of 65-75%, which increases in cases of well-differentiated carcinomas. The presence of distant metastases is obviously indicative of poorer prognosis with a 3-year survival rate of 35-50% [30]

CONCLUSION

Marjolin's ulcer is a rare but highly aggressive ulcerating Squamous cell carcinoma. The formation of an ulcer in the latency period plays an important role in the course of Marjolin's ulcer. Based on the different length of the ulceration periods during the latency period, skin breakdown on chronic scars and chronic unhealed ulcers are two main sources of Marjolin's ulcer. Any suspicious lesions that arise within affected areas should call for multiple biopsies as a gold standard. Patients suffering from burns or other skin pathologies leading to the formation of scar tissue or fistulas must have greater vigilance and receive medical help immediately when their fragile scars ulcerate This potentially fatal complication may be preventable and treatable by surgical management of initial injuries and early diagnosis and treatment of unhealed ulcers. The most logical treatment is to ensure rapid and stable healing of chronic ulcer with skin graft or flap as indicated. Patients should be followed-up for the rest of their life, as Marjolin's ulcer is more aggressive than initial skin carcinomas.

To conclude, Marjolin's ulcer is a rare, but important entity, which may be preventable by the early treatment of non-healing ulcers. These ulcers should be followed up with frequent biopsies and imaging evaluation to detect or exclude infiltration of adjacent tissues by an undetected deeper focus of malignancy. Marjolin's ulcer is preventable and areas of intervention have been highlighted. Educations concerning prevention, risk of chronic ulceration, early presentation, prompt and proper treatment is advocated for improved outcome.

Figure - 1 Showing ulcer in the right popliteal fossa

Figure - 2 Showing exophphytic mass on the posteromedial aspect of the right elbow

Figure - 3 Showing an ulcer over medial aspect of right elbow

Figure - 4 Showing exophytic ulcerated lesion over left knee

Figure - 5 Showing ulcer over left leg

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