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Marjolin's Ulcer: is Radical Surgery Enough? About 34 Cases

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Abstract **Original Research Article**

Marjolin's ulceris a well-known, but rare, process of malignant degeneration of traumatized skin, especially burn scars, The predominant malignancy in MU is squamous cell carcinoma. It is characterized by its aggressiveness and its increased risk of recurrences and metastases compared to non-scarrings quamous cell carcinoma. Effect of wires is much more important in African countries, and under-medicalized countries in general. Our work is a retrospective study of 34 cases of Marjolin's ulcer, collected in the plastic surgery department of the CHU Mohammed VI in Marrakech, with the aim of raising the epidemiological, therapeutic and evolutionary aspects of this pathology. Early diagnosis and treatment are essential, without forgetting the important role of prevention which consists of coverage by early skin grafts and regular care of any burn scar.

Keywords: Marjolin’s ulcer – burn scar – surgery.

INTRODUCTION

Marjolin’s ulcer (MU) is a rare cutaneous malignancy first described by Dr. Jean-Nicolas Marjolin in 1828 [1]. This entity is well described in the literature as a squamous cell carcinoma (SCC) that develops within a pre-existent cutaneous scar or chronic non-healing wound, such as burn scars that represents most cases, less common settings have included stasis, pilonidal sinuses, chronic venous stasis ulcers, vaccination sites, pressure sores, acne conglobata, osteomyelitis, hidradenitis suppurativa, frost bite, chronic fistulas [2-6]. MU may develop at any age but tends to affect older individuals. This is likely due to the typically long latency period from inciting event to malignant transformation, which averages 20 to35 years. A male predilection exists. Lesions occur at any anatomic site, but the lower extremities and the head and neck region are most frequently affected. The predominant malignancy in MU is squamous cell carcinoma followed by cases of basal cell carcinoma and malignant melanoma which explains that recently, Marjolin ulcer definition is used synonymous with squamous cell carcinomas (SCC) detected on scar tissues. The treatment of choice is wide surgical resection. MU is typically an aggressive malignancy with a high recurrence rate and poor 5-year survival. The tumors behave aggressively and have a propensity for local recurrence and lymph node metastases. Marjolin’s ulcers have a high tendency to metastasize [4]. Early recognition and proper staging offers the best chance for cure [7]. There are no confirmed effective protocols for treatment of this disease. This paper reviews our approach for the treatment of 30 patients with Marjolin’s ulcer whom we have treated at our department

MATERIEL AND METHODS

Our work is a retrospective study over a period of4 years (from 2008 to 2022) within the unit restorative plastic surgery and burns in Marrakech, where we collected 34 patients who all presented a Marjolin's ulcer on burn sequels. Epidemiological, clinical, therapeutic and evolutionary data were collected from the HOSIX operating system, patient files and reported on a pre-established operating sheet.

RESULTS

Totally 34 patients were evaluated with the diagnosis of Marjolin ulcers on burn scars. 20 of these patients were male (58%) and 14 were female (42%). Average age was found as 49.7 years with extremes ranging from 20 years to 82 years. All our patients had initially presented deep thermal burns by flames mainly with 69% (butane, candle, petrol, lighter, etc.) or by scalding. The majority of our patients were of low socioeconomic status. 10.5% of our patients received inadequate non-specialized medical care in the acute

phase and only 5.1% received non-medical care in the acute phase without any medical follow-up. The mean latency interval between the occurrence of the burn and the installation of the tumor was 24.6 years, with a minimum period of 4 years and a maximum of 59 years.

Clinically, 20 patients presented with ulcerative-budding tumors (Fig 1), whereas 14 patients presented with ulcerated scarring (Fig 2). We also found clinically palpable lymphadenopathy in the drainage area corresponding to the affected limb in 13 patients. The most frequent localization in our series is the lower limb, essentially in the vicinity of the joints (Table I & II).

Fig 1: Ulcerated tumor of the leg on a 45-year-old gasoline flame burn

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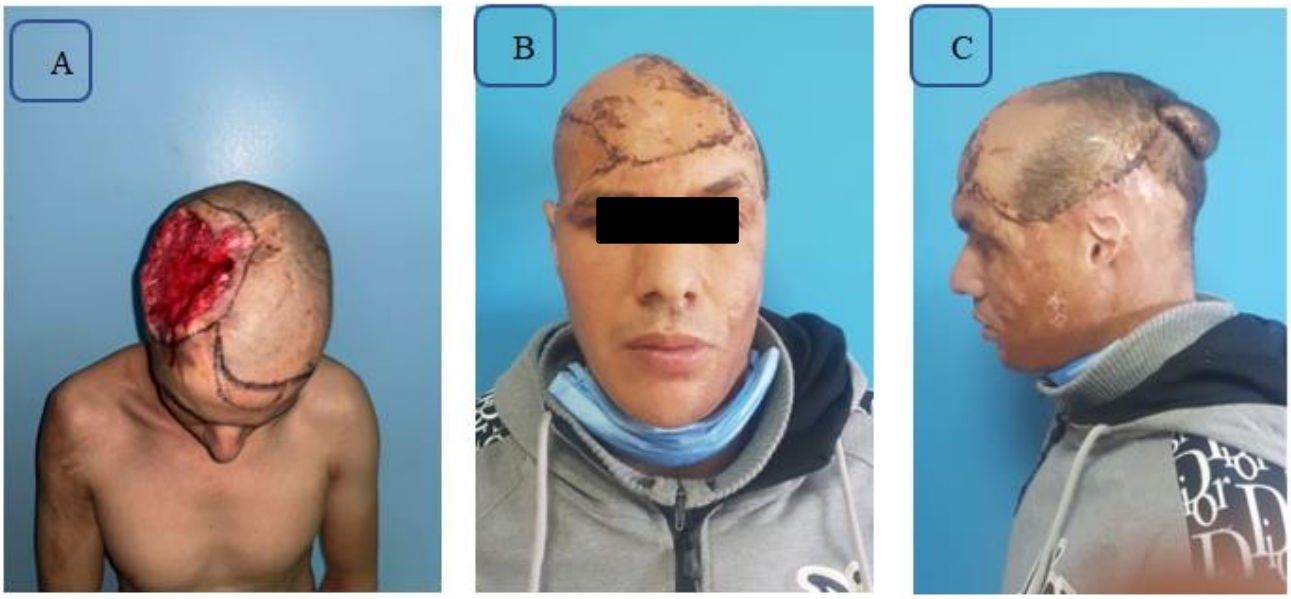

Fig 2: A: CE of the scalp in a 28-year-old patient, 27 years after the burn (candle). B/C: Wide resection of the tumor and coverage with a scalp rotation flap

All our patients benefited from prior biopsies, which were negative in 3 patients. The anatomo-pathological examination of the lesion after its total excision proved positive in all these patients objectifying a squamous cell carcinoma, except for a single case of basal cell carcinoma. The extension assessment made of

thoraco-abdominal CT scan and ultrasound of lymph node drainage areas revealed lymph node metastases in 8 patients, and pulmonary metastases in 6 patients, bone in 2 patients and cerebral in 1 patient.

Table I: Distribution of locations of Marjolin ulcer

Location	Number of cases
Lowerlimb	23
Upperlimb	6
Scalp	2
Back	2
Ischial/Gluteal region	1

Table II: Distribution of locations in the lower limb of Marjolin ulcer

Locationín the lowerlimb	Number of cases
Thigh	3
popliteal fossa	7
Leg	4
Heel and Achilles region	5
Ankle	3

Therapeutic management consisted in all our patients of a first operation for a wide excision of the tumor, with a safety margin of at least 1 cm, follow-up after anatomo-pathological examination of the specimen and histological control of the margins, a second stage of surgery to cover the loss of substance except in the event of exposure of noble structures or the cover was immediate in two patients.

We performed coverage with expanded thin skin grafts, after preparation of the recipient area, in 21 patients. 3 patients benefited from a neurosural flap for the reconstruction of defects of substance located at the level of the ankle and the heel (Fig 3) and 2 others of a flap of the scalp for reconstruction of the defects of substance directly after excision tumor due to bone and cerebral invasion. Amputation was necessary in 8 patients, including 5 at the level of the lower limb and 3 at the level of the upper limb, 1 for bone invasion and the 2 others after failure of a first attempt at conservative treatment to ensure margins oncological.

We carried out lymph node dissection in 22 patients, 17 at the inguinal level and 5 axillary, including 14 patients who immediately presented with clinically palpable lymphadenopathy and 8 patients in whom an ultrasound of the lymph node areas objectified the presence of suspicious lymphadenopathy. Dissection was positive in 9 patients. Additional external radiotherapy was performed on the tumor site and lymph node drainage areas in 7 patients in whom the deep margins were economical (less than 5 mm). While it was performed on the lymph node areas in the 9 patients whose dissection proved positive. Chemotherapy was prescribed in 6 patients with lung metastases at diagnosis.

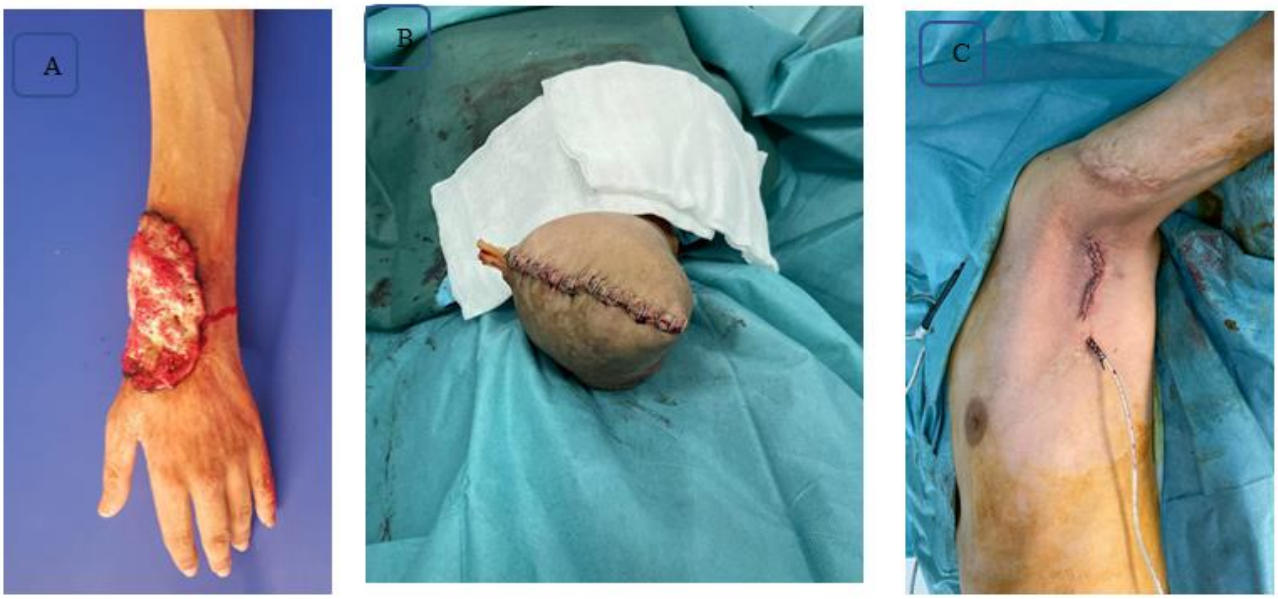

Fig 3: A: EC in a 47-year-old patient with a gasoline flame burn involving the face and upper extremity 52 years ago with a locally infiltrating tumor without palpable PDA. B/C: a mid left forearm amputation with homolateral axillary curage was indicated

Fig 4: A: Recurrence in the anterointernal aspect of the arm 1 year later in the same patient (Fig 3) with an axillary ultrasound showing two adenopathies, and a pulmonary metastasis made of nodules. B: a Clean-up disarticulation performed followed by adjuvant treatment with chemotherapy was indicated in this patient

During follow-up, we noted 4 cases of local recurrence, including 2 after initial excision with histologically healthy margins. The first two cases of two patients with EC of the upper limb indicating an upper arm amputation, which presented a recurrence after 8 months for one and 11 months for the other, requiring shoulder disarticulation for both (Fig 4). The two other cases are recurrences, one twice about 3 months after each surgical procedure and the revision consisted each time of wide excision and coverage by thin skin graft (Fig 5), and the other is a recurrence at 5 months after the first gesture and the recovery consisted of a mid-leg amputation (Fig 6). We noted the death of two patients, in a table of generalized dissemination.

Fig 4: A: EC in a 22 year old patient at scalp level following a burn at the age of 1 year, having been operated on twice then presented to us for a third local recurrence without ADP, on brain scan we found a bone lysis with a meningeal infiltration arriving at the contact of the superior longitudinal sinus and the brain parenchyma. B/C: Intraoperative image showing an exeresis with wide margins followed by a covering time by two rotation flaps of right and left scalp with curettage of the bone and meninges. D: Complete healing of the patient, image taken three months after the operation.

DISCUSSION

Most burn scar carcinomas are of the squamous cell type (75–96%); however basal cell carcinoma, adenocarcinoma, melanoma, malignant fibrous histiocytoma, adenoacanthoma, liposarcoma and osteogenic sarcoma have been reported [1, 2]. It is estimated that 2% of burn scars undergo malignant transformation [10]. Its incidence is very differently estimated from one study from one study to another, but it seems to be correlated with the level of medicalization and access to care [8]. This explains its high incidence rate in This explains its high incidence rate in African countries.

There are two variants of Marjolin's ulcer. In acute Marjolin's ulcer, the average latency is 4 months (range 4 weeks to 1 year) while in the chronic type

malignant changes are seen 1 year after arising, with an average latency period of 36 years. The mean latency period in patients at our clinic was 24 years, a period consistent with other reports in the literature. Metastases occur primarily through regional lymph nodes, at around 35–36% [2].

Two clinical types of Marjolin's ulcer present: (1) the flat, indurated, infiltrative, ulcerative carcinoma, and (2) the exophytic papillary form which is infrequent and generally less severe [9]. As commonly reported, burn scar cancers seldom arise when burn wounds are grafted in the primary treatment. The well-differentiated exophytic lesions have a better prognosis than poorly differentiated, ulcerated and infiltrating forms. The majority of burn scar carcinomas occur after a lag period in full-thickness burns, which were not grafted following injury [1, 8]. Therefore, large fullthickness burns should be managed surgically and not allowed to heal by second intention [1]. The average age of onset is in the fifth decade of life with a range of 20–82 years. However, men have a greater tendency toward burn scar carcinoma (M/F: 3/1).

Burn scar cancer is typically seen on the lower extremities (43.7%), upper extremities (22.4%), trunk (11.5%) and head (22.4%). The lesions of our patients varied according to their anatomic location and involved the upper extremities (13.3%), lower extremities (33.3%), scalp (33.3%) and trunk (20.0%). In general, patients with tumors located on the head, neck and upper extremities have a far better prognosis than those on the trunk and lower extremities [1]. Marjolin's ulcer tends to become aggressive and has a poor overall survival rate. The 2-year survival rate varies from 66 to 80% [10, 11]. Aggressive excision and reconstruction is warranted in these highly malignant squamous carcinomas. Predominant patterns of recurrence were present in the local skin and regional lymph nodes (93% of recurrences). Survival rates for this tumor are reported as 52, 34 and 23%, respectively, at 5,10 and 20 years [12].

The precise pathogenesis of burn scar carcinomas is not known. However, it is likely to be related to chronic irritation of the affected area. It has been postulated that release of toxins by autolysis and heterolysis of the burn scar, prolonged healing phase, presence of rapidly dividing cells susceptible to mutations, poor lymphatic regeneration in scars, misplaced epithelial cell groups, induced preneoplastic cells by a cocarcinogen could be contributory [1, 4, 5].

The relatively avascular scar tissue may then act as an immunologically privileged site that allows the tumor to resist the body's usual defenses against foreign cells [7]. Recent reports suggest this is a possibly a unique tumor occurring in such an immunologically privileged site. Bostwick reported that lymphatics in scar tissue environment were obliterated; therefore tumor cells must penetrate the thick barrier of scar fibrosis before patent, functional lymphatic vessels were accessible to them. When tumor cells do reach them, metastatic growth within the regional nodes usually can be quite rapid [13]. Scar tissues may limit tumor expansion at the beginning of the tumor occurrence.

Thus, the tumor grows slowly despite its aggressive and malignant behavior [14]. Marjolin's ulcer tends to slowly develop and metastasize, but patients may frequently have systemic metastases after surgery [15]. We propose that when released from their scar tissue, these tumors may become exceedingly invasive.

Castillo and Goldsmith showed that immune system deficiency may have a role on development of Marjolin's ulcer [4, 8]. They noticed that ''a possible depressed immunologic state surrounding a burn may be instrumental in the initiation and speed of development of burn scar tumors'' [8]. Bostwick emphasized that ''once the neoplastic cells are free of this scar barrier, they grow rapidly in the previously unchallenged regional nodes'' [13]. Many different procedures are presented in the treatment of Marjolin's ulcers. Surgery, radiotherapy, chemotherapy, lymphoid nodular dissection and combined procedures are frequently applied.

The treatment of choice is a wide local excision (WLE) was performed in most cases, reserving amputation for more severe cases. The present study reveals a consensus for indications for amputation: significant depth of invasion of the tumor, bone or joint infiltration, or when resection alone would cause worse postoperative function than amputation. These correspond to indications outlined by several hemorrhagedue to erosion of a large vessel, unresectable disease, articular involvement, toxemia secondary to infection of the lesion, when function after local resection would be unsatisfactory, and involvement of major nerves [16, 17]. While variation exists in horizontal margins for WLE, most authors use 2 cm margins and frozen section to confirm full resection. There is no consensus on the depth of resection needed, with two authors specifically resecting the underlying muscle fascia during the excision [18, 19].

The role and efficacy of sentinel node biopsy remains ambiguous, though it is increasingly reported in papers. Eastman *et al*., described successful preoperative lymphoscintigraphy and intraoperative lymphatic mapping in 5 out of their 6 reported patients [20] None of these patients had palpable lymphadenopathy. Of the 5 patients who underwent successful SLNB, microscopic metastases were identified in 4 of them (80%). The authors note that the prognostic significance remains unclear still, though earlier identification of nodal disease allows for accurate staging and earlier management. In contrast, Motamedolshariati *et al*., reported only a 2% success rate of sentinel node mapping in their cohort of 10 patients [21]. They attribute this

failure to scant lymphatic vessels in the traumatized skin surrounding the Marjolin's Ulcer. Further studies are required to elucidate the indications and rate of success for SLNB. Shen *et al*., (2014) used preoperative PET-CT to identify sentinel node metastases, but found on ultrasound-guided biopsy that many nodes were reactive hyperplasia and without metastatic disease [22]. They concluded that PET-CT is insufficient to diagnose regional metastases. Patients with advanced tumors should undergo workup for distant metastases with chest radiography, head CT, and abdominal ultrasound [23].

Enlarged, palpable nodes were the primary indications in nine papers, high-grade tumors in two papers [18, 26], and pathologic diagnosis of melanoma in one paper [22].

Radiation therapy (RT) is an important adjunctive therapy in the treatment of MU when surgery is impossible or inadequate, but it is not without controversy [23]. Tiftikcioglu *et al*., identified guidelines for RT: inoperable regional lymph node metastasis, grade 3 lesions with positive lymph nodes after nodal dissection, tumors greater than 10 cm in diameter with positive lymph nodes after regional lymph node dissection, and head and neck lesions with positive lymph nodes after lymphadenectomy [23]. Conversely, Shen *et al*., notes the lack of evidence to support RT as a successful first line treatment and notes its ability to induce further carcinomatous changes [22]. The role of chemotherapy is even less clearly defined in the current literature. All papers reported working closely with Oncology to identify appropriate candidates for RT and chemotherapy. Most papers discussed the management of patients with MU from an oncologic perspective, with little insight into the reconstructive methods employed after resection [18, 22]. The majority of studies show a trend towards reconstruction with skin grafts after tumor resection. Some report superior ease of monitoring for recurrence with skin grafts, though there is presently little evidence to support this reasoning. Local flaps or free flaps are used when exposure of vital structures necessitates more robust coverage. Furthermore, most studies also failed to delineate if reconstruction was performed concurrently with resection or if a delayed reconstruction was performed; no papers mentioned the time period between surgical resection and reconstruction if performed in a delayed fashion.

Unfortunately, recurrence was reported in 20-50% of patients30. Metwally *et al*., (2017) identified younger age, positive lymph nodes, and reconstruction after wide local excision as predictors of recurrence [25]. Edwards *et al*., reported that, while two thirds of the recurrences they found occurred within the first 36 months after treatment, one quarter occurred after 5 or more years [26].

Lengthy follow up is indicated to monitor for recurrent disease. Bozkurt *et al*., opts to resect recurrent MU with 3-5cm margins and place skin grafts to monitor patients for recurrence [27]. Because of the heterogeneity of the data reported at this time, no conclusions could be drawn with regard to efficacy of treatment modalities and rate of recurrence and survival in Marjolin's Ulcer.

The present study elucidates the lack of consensus in the treatment of MU, particularly with regard to SLNB, chemotherapy, and radiation. Trends were identified with regard to margins, indications for amputation over excision, reconstruction, and adjunctive treatments. Questions still remain about when to perform lymph node biopsy versus formal dissection. Based on the review and pooled analysis, the literature does not yield sufficient outcomes-based data to support a treatment algorithm at this time.

For all these reasons, the only really effective therapeutic weapon effective therapeutic weapon in the case of Marjolin's ulcer is preventive treatment treatment, because it is the only one that allows to avoid the passage from a benign scar to a malignant and virulent tumor. This preventive treatment, which is based on the coverage of acute burns of deep acute burns, rehabilitation and the management of scars, and management of scars by compression. In order to avoid the development of hypertrophic and retractile sequelae that can lead to chronic ulceration, excision-grafting must be performed within two weeks of the deep burn following the deep burn in the "functional" areas, such as the joints, and functional" areas, such as joints, and within three weeks in other areas. As soon as healing is achieved, rehabilitation and compression are started. In the limbs, physical therapy performs active and passive mobilization in order to maintain joint amplitudes and prevent tissue retraction of the tissues.

Compression involves the use of compression garments and the application of silicone plates, during the entire period of scar remodeling, 18 months to two years.

Massages performed by the physiotherapist, allow the scars to become more supple and to limit adhesions. Skin hydration with neutral emollients, prevents the skin from drying out, the appearance of cracks and the reopening of wounds.

CONCLUSION

Marjolin ulcer describes the aggressive malignant degeneration in any chronic wound. It has a very poor prognosis, with a mortality of 21%. Multiple studies have shown that MU is preventable with early wound surveillance, and the timely assessment of any wound changes is necessary via biopsies. It is imperative that wound care providers are aware of the signs and symptoms of malignant degeneration in chronic wounds. This in turn will allow for swifter diagnosis and intervention prior to metastasis, improving patient outcomes.

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