Marjolin's ulcer at Soba University Hospital, Khrtoum, Sudan: a case series of fifty patients

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Background: Marjolin's ulcer (MU) is a rare aggressive skin malignancy that complicates chronic non-healing wounds and scars. Studies have been conducted worldwide to report the risk factors and clinic-pathological features of this disease. Sudanese literature on the subject is scarce.

Objective: To describe the clinico-pathological features of Marjolin's ulcer (MU) among a sample of Sudanese patients who have been diagnosed with MU at Soba University Hospital (SUH), Khartoum, Sudan.

Patients and Methods: This is a descriptive, analytical, hospital-based study. Data was collected from records of all patients with Marjolin's ulcer who were treated in the Unit of Plastic Surgery between 2008 and 2015.

Results: A total number of fifty patients were studied; male to female ratio was 2.8**:**1. The mean age was 43±12 years and the mean latency period (the mean period between scarring and the diagnosis of Marjolin's) was 10.3±5.7 years. Significant association was found between age and latency period (P<0.001). Forty two percent of patients had duration of illness for 1-5 years before presenting to hospital. Non-healing ulcers and increasing pain were the main presenting complaints (52% and 26% respectively). Burn scars were the most frequently reported risk factor (72%). Lower extremities were the commonest site (74%). The average tumor size was 9±2.5cm and the majority of patients (75.7%) had tumor size of ≥5 cm in diameter. In addition, regional lymph nodes were clinically palpable in 15(30%) patients, while 11 (22%) patients had distant metastasis at the time of presentation. Squamous cell carcinoma (84%) was the most reported histological variant and surgery in the form of wide excision of the ulcer and split-thickness skin graft or flap coverage was performed in 41(82%) patients.

Conclusion: Clinico-pathological features and risk factors of Marjolin's ulcers in our case series are similar to regional reports with characteristic shorter latency period and advanced clinical stages at the time of presentation. Biopsy of chronic non-healing ulcers is needed to exclude Marjolin's ulcer and to allow early diagnosis of the disease.

Introduction

Marjolin's ulcer (MU) is a rare and aggressive malignant condition that arises on chronic skin lesions and represents about 1.2% of all skin cancers.[1-3] The precise mechanism by which chronic skin lesions develop malignancy is not well understood and many theories have been postulated.[4,5] Nevertheless, it is possible that multiple mechanisms may play a role in malignant transformation of chronic skin lesions.[5] Chronic irritation and repeated traumas induce cell mitotic activity of regeneration and repair leading to malignant changes.[6, 7]

Burn scars are the most frequently reported initial skin insult.[1-6] However, other risk factors were also reported including: chronic infections, bed

ulcers, chronically traumatized skin, animal bites and chronic venous ulcers [1-5]. The classic triad of nodule formation, induration, and ulceration at the scar site suggest the malignant transformation.[5, 6]

The lower extremities are most commonly affected anatomical sites.[1-7] Macroscopically, Marjolin's ulcers exist in two forms which are of prognostic importance: the *exophytic form* and the *infiltrative form.*[4] Squamous cell carcinoma is the most common histological variant resulting from malignant transformation, although other rare variants are reported in several studies.[5-7]

The management of Marjolin's ulcers requires multidisciplinary approach.[1] Surgery remains the main stay of treatment for MU. Wide local excision (WLE) with safe margins of 2 to 4 cm has been suggested by several authors and then reconstruction with skin graft or flap as decided by the site of the lesion.[5-8]

The current study aimed to report risk factors, latency period, clinical, histopathological features and management options of Marjolin's in patients who presented to SUH during the period from January 2012 to May 2015. To the best of our knowledge there are no similar reports on Sudanese patients.

Patients and methods

This is a retrospective, descriptive, analytical, hospital-based study. Data were collected by reviewing medical records of patients who presented with Marjolin's ulcer to the plastic and reconstructive surgery unit.

A predesigned questionnaire was used to collect demographic and clinical data which included: patient's age, gender, original cause of skin lesion and its duration, site and size of lesions, regional lymphadenopathy and evidence of metastasis. Pathological diagnosis was established histologically in all patients and methods used in the treatment were also documented.

Data were analyzed using the SPSS software package (version 21 windows). To determine the statistical significance of differences the Pearson test was used and probability test (*P*. value) with $P < 0.05$ was considered as significant at 95% confidence interval.

Results

Fifty patients were studied; males were 37 (74%) and females were 13 (26%) with male to female ratio of 2.8**:**1.

The mean age of the patients at the time of presentation was 43 ±12 years, the range was 19 to 67 years and 20 patients (40 %) were between 40-60 years of age. The duration of the ulcer in 42% of patients was 1-5 years before presentation and nearly one third (33.4%) of the patients presented five years after ulceration. The average latency period was 10.3 **±5.6 years and it ranged from 4 to 24 years , while it was significantly less than 10 years in those who were less than 40 years old(83%)***(P*<0.001).

Non-healing ulcers and increasing pain were the commonest presenting complaints in 52% and 26% of patients respectively.

Burn scars were the most common reported original insult factors (74%) followed by trauma and road traffic accidents in four patients (10.8%) **(Fig.1).** the lower extremities were the most affected location 38(76%) followed by head and scalp in eight (16%) cases.

The average size of the ulcers/ tumors was 9 ± 2.5 cm with a range of 4 to 22cm and in more than 77% of the patients the ulcer was 5 cm in diameter.

Regional lymph nodes were clinically palpable in fifteen patients (30%) and eleven patients (22%) had liver and or lung metastatic disease.

Incisional biopsy was performed in ulcers that exceeded 2cm in diameter (77%) and all patients with metastatic disease (22%), while in the rest excision biopsy was performed.

Treatments given before presentation to SUH included: topical antibiotics in 27%, of cases, herbal medicines by traditional healers in 32.3%,

topical antibiotics in 22% and 16% were on regular dressings at health centers, rural or peripheral hospitals. However, biopsy was advised before presentation in seven cases. Sixty percent of the patients were treated by wide excision and split-thickness skin graft.Wide excision and flap coverage was performed in 12%, and amputation in 10% of patients.

Lymphatic nodes dissection was performed in 13 patients (26%) **(Fig.2)** and the histopathology of all of them was positive for metastatic disease and 18% patients were re-treated by radiotherapy due to either small resection margin or incompletely excised tumor.

The histopathology results revealed: squamous cell carcinoma in the majority of cases (84%). Other histological variants were: basal cell carcinoma (8%), dermatofibrosarcoma (2%), leiomayosarcoma (2%). Pathological reports were not available in two (4%) of the patients.

Table 1. Initial skin insult

Initial Skin Insult	Percentage (%)
Burn scar	74
Trauma	11
Chronic wounds	5
Pressure ulcers	4
Venous ulcers	2
Missing data	4
Total	100

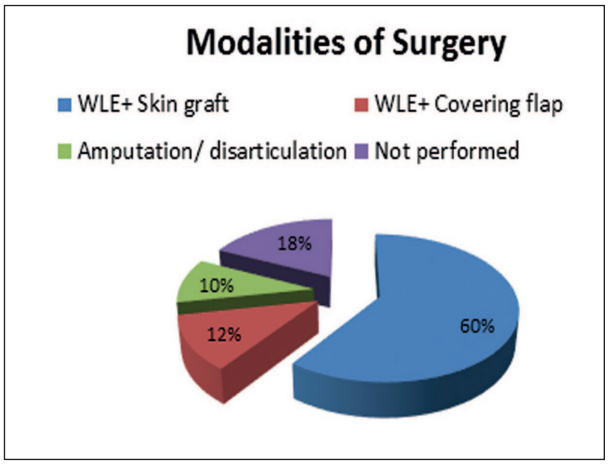

Figure 1.Surgical modalities performed.

Discussion

The mean age of presentation in this series was 39.5 years which is quite similar to that found in regional reports from Tanzania (38 years) [1] and Nigeria (39 years) [9], but lower than that reported in Kenya (48 years) [10]. However, this mean age is far below that reported in USA (59 years) [11] and Iran (50 years) [12]. In fact, a number of confounding variables such as etiologic factors may influence this age of onset [3, 13]. Some regional literature has reported characteristic trends in the epidemiology of Marjolin's ulcers that affect young patients in particular.[14, 15]

In this report, a significant association was found between age at presentation and latency period i.e. younger patients had shorter latency period whereas 83.3% of those who were younger than 40 years had latency period of less than 10 years (P<0.001) , a finding which is in keeping with previous reports .[1, 5]

The average latency period was 10.3 years which is nearly similar to a reports from Tanzania (11 years) [1] , and it is lower than other African figures[10,16] , Nigeria (18 years)[16] and Kenya (19 years).[10] However, Nthumba reported a latency period of 16 years in African Sub-saharan patients [10]. The reasons for this relatively shorter latency period amongst African patients are not fully understood [1].

Sex distribution is fairly comparable to other reports i.e. a remarkably higher prevalence among

males [1-5], Environmental factors might explain this finding as males in general are more exposed to the risk factors. Nevertheless, sex- related genetic differences may also contribute to this observation[3]

In agreement with regional and international literature [1, 3, 4]; the burn scar was the most frequent cause of original skin insults (70%). In Sudan, Marjolin's ulcers were reported in 2.6% of burns patients who had conservative management which is similar to international literature.[17]

In keeping with the literature[1-7], the lower extremities were the most frequent sites of MU. This could be due to their vulnerability to trauma.

The advanced clinical presentation in our series (regional lymph nodes involvement and distant metastasis) is largely consistent with the pattern observed in other African countries [1, 2, 19]. However, late presentation is rare where health facilities are more available. [13, 18]

In Sudan, like other African countries, MU patients often present with advanced stages of the disease as a result of various factors including poor health, low awareness about chronic non-healing ulcers and lack of adequately trained staff and specialized centers. [19]

Similar to regional and international literature, squamaous cell carcinoma is the commonest histological variant (78.4%), followed by basal cell carcinoma (10.8%) and other rare variants have been also reported in this series.[1-6]

Surgery is the main stay of management of Marjolin's ulcers.[1-3] As in other reported series, wide excision and split-skin grafting was performed in 62.1% of patients.[1, 3, 5] Lymphatic node dissection was performed in 29.7% which is consistent with advanced clinical stages in our patients [3]. Prophylactic lymph node dissection was not performed as most authors agree that it is not usually recommended in the absence of clinical or radiological nodal involvement.[5]

Six patients (12%) were not offered surgery as they presented with metastatic disease and they received palliative radiotherapy. However, the literature reported poor response to radiotherapy as a result of poor vascularity of ulcers due to extensive fibrosis[20]

Conclusion

Clinico-pathological features and risk factors of Marjolin's ulcers in the present series are comparable to what has been reported in regional literature. Younger patients presented after shorter latency period with advanced clinical stages. Biopsy of chronic non-healing ulcers is recommended to exclude Marjolin's ulcer and to allow diagnosis at an earlier stages.

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