

Marjolin's Ulcer. A Retrospective Study on the Clinicopathological Features and Management.

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ABSTRACT

Background: Although reported rare by most literature the incidence of Marjolin's ulcer appears to be on the rise and outcome of treatment remains poor. **Methods:** It is a retrospective study on cases of Marjolin's ulcer treated at the Department of Surgery from 1st May 2016 to 31st April 2018. Data's like aetiology, duration of latency, site, surgical managements, histopathological results were studied. **Results:** The mean age was 54.62 years. The etiologies were flame burn (57.14%), electrical burn (2.85%), cellulitis (17.14%), trauma (14.28%), decubitus ulcer (5.71%) and osteomyelitis (2.85%). The most prevalent site was lower extremities (48.57%) followed by upper extremities (37.14%), buttock (5.71%), trunk (2.86%) and axilla (2.86%). The histopathological findings were well differentiated (57.14%), moderately differentiated (20%) and poor differentiated (8.57%) squamous cell carcinomas. Most cases occurred more than 20 years after the initial injury. The most common surgical procedure was wide excision with STSG or flap coverage. **Conclusion:** Lower extremities remains the most common site usually occurring because of neglected old burn injuries. The most common aetiology flame burn still prevalent in rural low socioeconomic population explains its high incidence in developing countries.

Keywords: Marjolin's ulcer, squamous cell carcinoma, burn scar, latency period.

INTRODUCTION

In 1828 Jean Nicholas Marjolin, a French physician, described an ulceration in scar tissue in Dictionaries de Medicine without stating its potential for malignant transformation. Dupuytren in 1839 made a more comprehensive description of these lesions by observing this phenomenon in a Belgian man who was treated for a cancer of a scar sustained from sulphuric acid burn. Aurelius Cornelius Celsus was the first to described cancer in burn scar which dated back to the 1st century A.D.^[1] In 1903 John Chalmers DaCosta, professor of surgery at Jefferson Medical College, reported two cases of carcinomatous change in chronic varicose ulcers of the leg.

The predisposing lesions for Marjolin's ulcer are post burn wound, venous ulcer, cellulitis, osteomyelitis, pressure ulcer, chronic fistula, trauma etc. The classic definition applies to the squamous cell variant,^[2] whereas the term "scar tissue carcinoma" is used for all malignancies arising in scars.^[3]

The latency period is defined as the time between initial injury and the confirmation of a pathologic diagnosis of malignancy. The incidence of Marjolin's ulcer appears to be still high and outcome of treatment remains poor in advanced carcinomatous cases as noted in the present study. We aimed to define the aetiology, topography and histopathology of Marjolin's ulcer and to evaluate the surgical management and outcome.

MATERIALS AND METHODS

It is a retrospective study of records on 35 patients diagnosed as Marjolin's ulcer at the Department of Surgery, from 1st May 2016 to 31st April 2018. Data's like age, sex, socioeconomic status, aetiology, duration of latency, morphology, site, type of surgical managements and histopathological results were studied. Definitive diagnosis was confirmed post-operatively from histopathological examination reports. Results of routine laboratory examination and imaging to detect other organs involvements were analysed using SPSS Software version 20. Reports of clinical lymph node assessments and imaging were also included in the study. Wide excisions of the lesion were performed for each case. The type of coverage used such as split skin grafting, local flap coverage and distant flaps etc., and regional lymph node dissections performed were

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also recorded. The necessary permission for the study was obtained including ethical clearance. The patients with previous history of malignancy, advanced squamous cell carcinoma requiring palliative treatment and previous history of surgery were excluded from the study. 44 patients were considered initially for the study out of which nine were later excluded either due to paucity of data or were lost during the follow up period. The routine follow-up period was done postoperatively on the seventh day, third week, and every three months for two years.

RESULTS

Patient's demography

The mean age of the patients at the time of diagnosis was 54.62 years (Range: 14-80, SD: 14.37). Maximum of the patients studied were between 30-65 years of age.

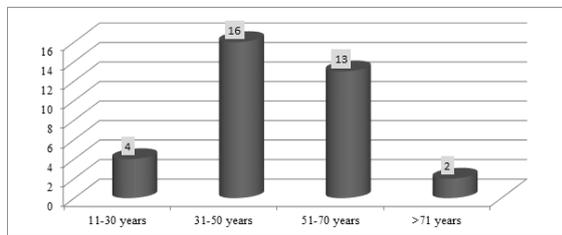


Figure 1: Number of patients in age ranges.

Table 1: Gender Distribution.

Gender	Number patients	Percentage
Female	14	35.1
Male	21	64.9

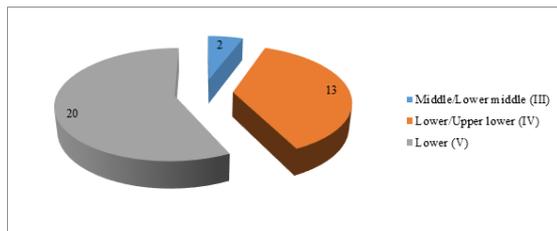


Figure 2: Distribution of socioeconomic classes.

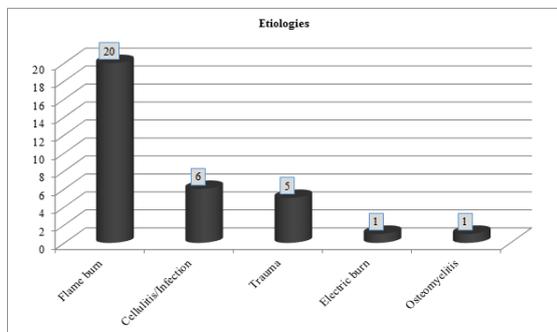


Figure 3: Different etiologies of underlying skin lesions.

Most of the patients in the study were from low socio-economic rural agricultural population. Based

on Kuppaswamy's socio-economic status scale,^[4] 33 patients (94.28%) were from low socio-economic background.

Aetiology (Previous aetiology)

The main aetiology was flame burn. Other sources were cellulitis/infection, trauma, previous decubitus ulcer and Osteomyelitis.

Morphological characteristics of Ulcer/tumour^[1]

Majority of the lesion were flat, indurated or ulcerative. Most of the clinical features of SCC such as bleeding to touch, everted margins and necrotic tissues/debris were observed in the patients studied.

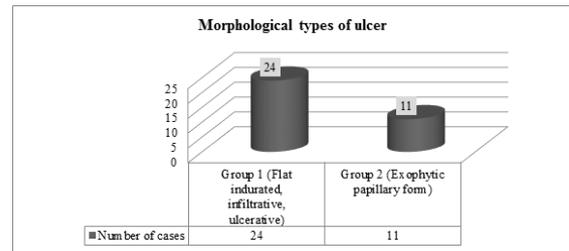


Figure 4: Morphological types of ulcer/tumour

Latency period (duration of previous lesions)

The average latency period was 24.39 years (SD: 12.93). Interestingly there were two acute Marjolin's ulcer cases that developed within one year.

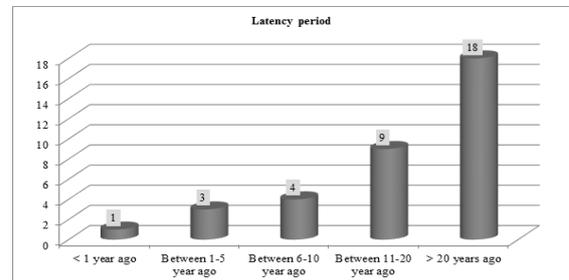


Figure 5: Different time intervals between primary lesion and Marjolin's ulcer

Site

The most frequent site of the primary lesion was lower extremities. The ankle joint areas, flexor and lateral aspect of the lower limb were the most common site. The next most frequent site was the forearm.

Table 2: Frequency of primary site of skin lesions

Site	Number of patients
Lower Limb	16
Upper limb	13
Buttock	2
Axilla	1
Back	1
Scalp	1

Treatment

Wide excisions with a free margin of two centimetres from the tumour border were performed

in each case. Reconstruction of the resultant defect was then performed; the most common being STSG and local flap coverage. There were three amputation cases.

Intra-operative findings

No underlying bony or organs involvements were found intra-operatively for majority of the patients except for one patient who had an underlying bony metastasis. Recurrence was detected within one month after the initial wide excision. The patient had subsequently refused to give consent for below knee amputation. Lymph node dissection was done for two patients with palpable nodes.

Table 3: Types of surgical procedures.

Operative procedures	Number of patients	Percentage
Wide excision + STSG	21	60
Wide excision + Local flap coverage	6	22.86
Amputation	3	8.57
Wide excision + Cross leg flap coverage	2	5.71
Wide excision + ALT flap coverage	1	2.85
Wide excision + Adipofascial flap coverage	1	2.85
Wide excision + Local advancement flap	1	2.85

Histopathological examinations

Well differentiated squamous cell carcinoma constituted half of the histopathological findings in the study.

Table 4: Frequency of Histopathological types of SCC

Histo-pathological types	Numbers
Well differentiated SCC	20
Moderately differentiated SCC	7
Poorly differentiated SCC	3
Differentiation not reported	5

Table 5: Mean age and different histopathological types of SCC.

Histopathological types of SCC	Mean age	SD
Well differentiated SCC	54.30	14.49
Moderately differentiated SCC	43.62	4.75
Poorly differentiated SCC	73.86	6.12

The mean age of poorly differentiated squamous cell carcinoma patients were much higher compared with the moderate and well differentiated types. The dissected lymph nodes for two patients did not show any signs of invasion.

The aetiologies for the two patients who had a poorly differentiated histopathology were flame burn and cellulitis. The time period from initial injury to the diagnosis (Latency period) were more than 20 years for both the patients. Osteomyelitis as the original aetiology was found to have the shortest period of latency.

Follow-up

The patients were followed up for a minimum of two years' period. There were two recurrent cases within two years among the poorly differentiated type. Both were then referred to the oncology department in anticipation of further treatment necessary.

DISCUSSION

Malignancy arising from scar was officially named Marjolin's ulcer in 1903 by Da Costa.^[5] The incidence of Marjolin's ulcer after long term inflammatory or traumatic insult to the skin is reported to be 0.1 to 2.5%.^[6,7]

There are several skin pathologies known to be the aetiology of Marjolin's ulcer, among them are osteomyelitis,^[8] decubitus ulcers,^[9] chronically traumatized skin,^[10] chronic fistulas,^[11] frost bite,^[12] chronic venous failure,^[13,14] vaccination sites and skin graft donor sites.^[15,16]

Several theories have been proposed on the evolution of Marjolin's ulcer.

Virchows theory of chronic irritation: The less stable epithelium after chronic irritation loses contact inhibition.^[17]

The co-carcinogenic theory:^[18] By this theory a burn may be an "initiator," while actinic radiation or some other carcinogenic stimulus may act as the "promoter."

The toxin theory:^[1] Some suggested that toxins liberated by the damaged cell results in a nutritional deficiency at the cellular level with resultant accumulation of mutated DNA and subsequent malignant change.

Theory of epithelial element implantation: Epithelial elements implanted into the dermis, undergo a disordered regeneration leading to carcinomatous change.

The immunologically privileged site theory: Some author suggested that the poor lymphatic flow in scar tissue impairs immunosurveillance.

The hereditary theories: It is based on the discovery of p53 and Fas gene mutations in patients with Marjolin's ulcers.^[19,20]

The environmental and genetic interaction theory: This theory suggested that genetic differences make the individual more susceptible to the environmental insult, resulting malignant changes with a short latent period.

None of the theories could independently explain the evolution of Marjolin's ulcer individually. Therefore, most of the authors are on the view that a combination of theories best explains the process of malignant transformation of chronic scar or ulcer and the eventual evolution of Marjolin's ulcer.

This study found foot to be the most prevalent site for Marjolin's ulcer, a finding which is similar to other study.^[21] Flame burn (61.53%) was also found to be the most common aetiology in the present study comparable to a study which reported as

87.9%.^[21] We found the average latency period of Marjolin's ulceration to be 24.39 years while one study reported an average of 31.5 years.^[22] Similar to the findings in our report N Yu et al,^[23] observed the mean age at diagnosis of Marjolin's ulcer as 62 years. In 82% of cases, more than 10 years had elapsed during the latency period, with an average time of 29 years.

Lawrence EA et al,^[24] hypothesized that a patient's age at the time of the burn is inversely proportional to the interval to formation of cancer. Malignant transformation is delayed in younger injury victims. The older the patient is at the time of injury the shorter the lag period for a scar to become malignant. Two distinct type of Marjolin's ulcer are therefore described. Acute Marjolin's ulcer with a lag phase of less than one year, and chronic Marjolin's ulcer with a lag phase longer than a year. The former which is quite rare is seen more often following burn injuries in the older age groups. Nancarrow suggested that the skin is less able to withstand trauma and indeed carcinogenic insults,^[25] as it ages. Overall survival rates have been reported to be 52% and 34% at 5 and 10 years respectively.^[26] Determinants of poor prognosis include short latency period, lower limb involvement, tumour size and lymph node involvement. Although earlier study by Epstein reported Marjolin's ulcer to be less aggressive,^[27] other authors like Kowal-Vern A et al and Gamatsi E et al,^[15,20] confirmed its aggressive nature. Alamoodi MS,^[28] also emphasises its aggressive nature resulting in poor survival in his paper on abdominal metastasis from Marjolin's ulcer. All cases in the present study were squamous cell carcinoma with mostly low malignant character similar to other findings.^[22] However, it's a known fact that delay in diagnosis results in metastasis to lymph nodes and surrounding organs and the importance of early diagnosis of Marjolin's ulcer cannot be overemphasized. It has been suggested that lymph-node dissection should be carried out only if they are palpable during an examination.^[3]

Marjolin's ulcer is commonly mistaken for an infected ulceration occurring at the scar tissue sites. Marjolin's ulcer should be ruled out if a patient describes the development of an ulcer within the boundaries of a burn scar that increases in size, persists, crusts, bleeds, or is painful. In this study few patients were excluded as their histopathological exam came out to be benign lesions.

The treatment of Marjolin's ulcers requires a multidisciplinary approach. Wide local excision with a margin of up to two to four centimetres have been suggested by various authors, Nancarrow advocated excision of the entire scar tissue where possible and not just the area of malignant degeneration.^[25] Excision defect should be skin grafted except where the bed may not be suitable for a skin graft, in which a flap may be used. According to Novick et al,^[16] there should be a minimum of 12-month interval

between tumour extirpation, and definitive reconstruction to avoid obscuring local recurrences. Block dissection of regional lymph nodes should be done in presence of clinically palpable lymph nodes.^[3] Some authors however suggest prophylactic node dissection, based on the low salvage rate for regional node metastases.^[28]

Amputation is indicated in advanced lesions of limbs, where there are bony and joint involvements and where local excision is not possible. The response to radiotherapy is poor due to their relative poor vascularity due to local fibrosis.^[29] This factor may also explain the same poor response to chemotherapy which is indicated when surgical extirpation is not possible or as neo or adjuvant therapy.^[16]

CONCLUSION

The most common aetiology in this study was flame burn which explains the high incidence of Marjolin's ulcer in developing countries. Lower extremities remain the most common site. The average latency period in this study was 24.39 years. Well differentiated squamous cell carcinoma was the most common histopathological findings.

Advance Marjolin's ulcer has a poor prognosis and requires aggressive treatment. However, early diagnosis and treatment showed good outcome. The low socio-economic patients belonging to rural population are the most vulnerable group highlighting the need for provision of proper burn wound care and ulcer management in such groups. Those patients with long standing scar/ulcer should be advised the importance of monitoring their skin for changes which may indicate malignancy. Finally, this study further proves the importance of prevention through awareness regarding the potential changes of chronic scar or ulcer to malignancy.

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