Marjolins Ulcer: Clinicopathological Profile and Treatment Patterns

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Abstract: Purpose: Marjolins ulcer is a malignant transformation arising from chronic ulcers or previously traumatized scars that occur usually after burns. This article aims to study the clinicopathological profile and treatment patterns of Marjolins ulcer.

Materials and Methods: Retrospective analysis of all Marjolins ulcer patients presented to Vydehi Cancer Centre from 2018 to 2021 was done. A total of 27 patients of all age groups were included in the study. All information regarding detailed history, clinical examination, treatment details were retrospectively collected and analysed.

Results: Most of the patients were in the 5th decade of life with an overall male preponderance. The most common cause for Marjolins ulcer was Burns scars followed by Trauma. Lower extremities were found to be the most predominant site. The mean latency period for the development of Marjolins ulcer was 11 years. Squamous cell carcinoma was the most common histological subtype, Adjuvant Radiotherapy was given to the patients with high-risk features.

Conclusion: Chronic non-healing ulcers that do not respond to treatment should be carefully examined for malignant transformation. Surgery is the mainstay of treatment and Adjuvant Radiotherapy should be considered in high-risk cases to reduce locoregional recurrence.

Keywords: Marjolins, Squamous cell Carcinoma, Burns, Surgery, Trauma, Radiotherapy.

INTRODUCTION

Marjolin’s ulcer, a cutaneous malignancy was first described by a French surgeon Jean Nicholas Marjolin, and he described the ulcer formation over the burns scar, although they were not recognized as malignant at that time [1]. The term Marjolin’s ulcer was defined by DaCosta, for the carcinomas arising from the burns scar [2]. Marjolin’s ulcer is considered as a highly aggressive disease that develops from chronic wounds and skin scars and almost 65% of these ulcers have been diagnosed on underlying burn scars [3]. It can also develop on discoid lupus erythematosus lesions, ulceration and chronic osteomyelitis, amputation stumps, regions of chronic fistulas, chronic wounds etc [4-7]. It can occur in any age group but is less common in children [8]. Marjolin's ulcer are predominantly seen in males, [6,7]. The malignant transformation is often very slow, with an average latency period of around 15-25 years.[9] Squamous cell carcinoma is the most common histologic variant, other variants are basal cell carcinoma (BCC), angiosarcoma, fibrosarcoma, malignant melanoma, liposarcoma osteosarcoma etc, [10].

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The mechanism of malignant transformation is very well understood. A lot of theories have been mentioned in the literature [11]. Few theories state that the mutation by inflammation in the injured tissue causes carcinogenesis [12]. Others describe that foreign body reaction at the damaged tissue leads to malignant transformation [13]. Few other studies also state that repeated damage to the ulcer and long-standing chronic irritation, which leads to continuous mitotic activity to reduce the defect ultimately results in Carcinogenesis [14]. Patients with inherited immune deficiencies are at increased risk for this Carcinoma formation [15]. Marjolin's ulcers are divided into two types, acute and chronic. In acute, malignant transformation happens within one year of the injury [15] and the chronic transformation occurs over years of long latency peiod. Marjolins ulcer is confirmed by histological examination of the tissue from the damaged site. The incidence of Marjolin's ulcer is estimated at 1.3–2.2% of all chronic ulcers and the incidence however shows regional differences due to sociocultural and economic influences. There are limited data that systematically review management and outcome in the era of more advanced forms of treatments like systemic therapy and radiotherapy [16,17]. Hence, the present study is to conducted analyse the Marjolin’s ulcers clinicopathological profile and treatment patterns in patients who were presented to a tertiary care hospital in India.
MATERIALS AND METHODS

Retrospective analysis of all cases of Marjolin’s ulcer from 2018 to 2021 who had presented to our institute was done. The diagnosis had been confirmed by histopathological examination. Demographic features like age at the time of presentation, gender, etiologic factors, latent period between the first damage and development of Marjolin’s ulcer, anatomic location, tumour size, histologic type of the tumour, lymph node involvement, metastasis, treatment modalities and their outcomes were documented for these patients.

All patients had been treated by surgery as the main modality of treatment. Adjuvant Radiation was given to the patients who met high risk criteria. After completion of the treatment all patients were followed up every 3 months with clinical and radiological examination. All details were documented and analyzed. Statistical analysis was done by using the software SPSS 22.0 and R environment version 3.2.2 and Microsoft word and Excel was used to create tables etc. Descriptive analysis and inferential analysis have been done in the study.

RESULTS

Total Twenty-Seven cases of Marjolin’s ulcers were identified and included in the study. They were stratified according to the age, gender and the anatomic location. The age of the patients studied ranged from 35 to 70 years, with majority of the patients in age range of 40 to 56 years (81.7%). The median age of the study population was 52 years. Males were more commonly affected than females. Lower extremity was involved in 59% (16) of the patients followed by Upper Extremity. The most common etiologic factor was the burns scar followed by trauma. The time between the etiological factor and occurrence of disease was 7 to 15 years (Mean 11years). Patient and tumour characteristics are given in Table 1.

All patients had undergone imaging of the locoregional site to rule out locoregional nodal spread. Surgery was the main modality of treatment. Wide Local Excision with 2 cm margin was conducted as the standard of management followed by reconstructions with Split Skin Graft (SSG) or locoregional flaps.

Out of the 16 lower extremity patients inguinal nodal dissection was done in 6 patients due to involvement of lymph nodes either clinically or radiologically. Four patients were presented with extensive bony involvement in which amputation followed by reconstructions with split skin graft (SSG) was conducted. Example of Lower Extremity Marjolins ulcer shown in Figure 1.

In upper extremity tumours, one patient presented with axillary nodal metastasis for which Axillary Nodal dissection was done. All patients with Marjolins ulcer in head and neck region underwent WLE with adequate margins (Figure 2). One patient developed Marjolins ulcer due to Discoid Lupus Erythematosus and he underwent wide local excision with parascapular flap reconstruction (Figure 3).

On Histopathological examination, the size of the tumour ranged from 2x3 cm to 10x10 cm. Squamous cell Carcinoma (SCC) (23) was the most common histology followed by, Basal Cell Carcinoma (BCC) (3) and Dermatofibrosarcoma (1). Five patients were found to have positive lymph nodes.

Table 1: Patient and Tumour Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number</th>
<th>Percentage</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean)</td>
<td>52 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
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<td></td>
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</tr>
<tr>
<td>Male</td>
<td>17</td>
<td>62%</td>
<td>0.203</td>
</tr>
<tr>
<td>Female</td>
<td>10</td>
<td>38%</td>
<td></td>
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<td>Site</td>
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<td>0.065</td>
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<tr>
<td>Lower Extremity</td>
<td>16</td>
<td>59%</td>
<td></td>
</tr>
<tr>
<td>Upper Extremity</td>
<td>5</td>
<td>18%</td>
<td></td>
</tr>
<tr>
<td>Head and Neck</td>
<td>5</td>
<td>18%</td>
<td></td>
</tr>
<tr>
<td>Trunk</td>
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<td>4%</td>
<td></td>
</tr>
<tr>
<td>Etiologic factors</td>
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<td></td>
<td>0.012</td>
</tr>
<tr>
<td>Burns</td>
<td>17</td>
<td>62%</td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>9</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>DLE</td>
<td>1</td>
<td>5%</td>
<td></td>
</tr>
</tbody>
</table>
Figure 1: A 37-year-old male presented with a Marjolins Ulcer of the right foot (a). He underwent Surgical Excision and Reconstruction (b).

Figure 2: A 63-year-old male presented with a Marjolins Ulcer in the right Parotid region (a). He underwent Surgical Excision and Reconstruction (b).

Figure 3: A 42-year-old female diagnosed case of DLE presented with a Marjolins Ulcer in the right upper back (a) and she underwent Surgical Excision and Reconstruction (b).
Adjuvant Radiotherapy was given in the patients with high-risk criteria such as positive lymph nodes and larger tumour size of more than 10 cm. On these basis five patients received adjuvant Radiotherapy. All patients were followed up every 3 months with clinical and radiological examination of primary site and nodal areas. At the median follow-up of 14 months, all patients showed complete response except one. This patient with SCC of the foot came back with inguinal lymph nodal recurrence after 1 year of surgery.

DISCUSSION

Non-healing ulcers developing on the chronic scars are highly risky because of their malignant transformation potential. Hence, these ulcers should be examined carefully to exclude the presence of malignancy. Clinical profile of both benign and malignant ulcers is same, although some variations are noted [18, 19]. Hence, any non-healing ulcer on burns or traumatic scar should be treated like a cancerous one unless proved otherwise by histological examination [20]. This retrospective analysis was done to study the clinicopathological profile and treatment outcomes of Marjolins ulcers.

Marjolins ulcers may occur at any age with no strong racial predisposition [21]. It is most commonly seen in men, and male to female ratio in our study was 1.9:1. Men are at major risk for developing Marjolins ulcer, possible explanations of this occurrence may be due to the genetic mutations [15] and more physical activities by the males. The mean age of our study cases was 52 years with an age range from 35 to 70 years which is identical to other studies [22, 23]. Most frequently observed site was lower extremity in our study. However, Marjolin's ulcer may occur on any site, but, commonly observed at lower limbs followed by upper limbs, head and neck, and trunk [24].

Our objective was to analyse the clinicopathological profile and treatment outcomes in the biopsy-proven Marjolins ulcer. In our study, squamous cell carcinoma (SCC) was the most common histological subtype. These findings are in an agreement with literature [25]. We recorded the cutaneous ulcers within the scars in majority of cases included in our study (23 out of 27), fungating ulcers in 4 patients, while clinical or radiologically significant lymphadenopathy was found in six patients. The extensive bony involvement was found in four cases. The mean dimension of the ulcers in our study was 6-8 cm (ranging from 2 to 12 cm). According to literature, ulcers with more than 6 cm are more likely to undergo malignant transformation [26].

Marjolin's ulcer rarely metastasize. It is generally considered that prophylactic nodal dissection has no influence on recurrence and should not be encouraged [27]. However, few studies reported that, lymph nodes spread in the lower limbs cases is relatively higher and such patients without lymph node spread should be considered for prophylactic nodal dissection [28]. Few studies also report that Lymph node metastasis in Marjolins ulcer is 22% [29]. Lymph nodal involvement observed in our study was 22%.

Surgery is the standard treatment method for Marjolin's ulcer. Post-excision, repair and reconstruction of the surgical site using skin grafts is done to improve the quality of life. Skin grafting should be considered as much as possible while skin flap repair should be considered if underlying bones are exposed. Local skin flap repair should be done if possible, otherwise skin flap graft repair may be considered as an alternative option.

The histological subtype SCC has a worst prognosis compared to other types, hence aggressive treatment in this subtype is encouraged-excision and radiotherapy are recommended for managing the recurrence [30]. A study done by Ozek and Cankayal found that the radiation should be given in patients with positive lymph nodes after nodal dissection, tumours with more than 10 cm in diameter. In our study adjuvant radiation was given to the patients with positive nodes. Overall, literature reviews support the use of adjuvant radiation in poor surgical candidates, positive nodes and large-sized tumours to reduce the recurrence [31].

Marjolin's ulcer has a very short recurrence time [32,33]. However, recurrence rates in our study did not show any statistical significance. The main reason for this is the smaller number of patient population and the shorter duration of follow-up. However, one patient in our study of lower extremity Marjolins ulcer had presented with inguinal nodal recurrence.

CONCLUSION

Chronic non-healing ulcers that do not respond to treatment should be carefully examined for their malignant transformation. This retrospective review showed that the most common etiological factor for Marjolins ulcer was burns scar. Squamous cell carcinoma is the most common histological variant. Based on our study we suggest that all the Chronic non-healing ulcers should be carefully evaluated by Multidisciplinary team. Surgery is the standard of
treatment for Marjolin’s Ulcer and Adjuvant Radiation should be considered in high-risk patients to prevent recurrence or relapse.

REFERENCE


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