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Marjolin's ulcer – epidemiology and the pattern of care: Experience from a tertiary cancer care center

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ABSTRACT

Background: Marjolin's ulcer (MU) reflects the malignant transformation of scar tissue or chronic inflammatory skin lesions. Due to the low incidence, only a few case reports and case series were reported in the literature to date. **Aims and Objectives**: In our retrospective analysis, we report our experience regarding MU over the past 16 years with a significant range of latent period, histology, and as well as underlying skin conditions, from Kolkata, India. **Materials and Methods:** This was a single institutional retrospective study carried out in the department of radiotherapy at the tertiary cancer, Kolkata. We focus mainly on data pertaining to the type of injury, the time gap between the initial injury and development of MU, histology, clinical stage, and treatment received, along with demographic details. **Results:** A total of 39 patients with histopathologically proved MUs were included according to the inclusion and exclusion criteria. The median age of patients at the time of development of MU was 52 years and with a range of 32–71 years. Out of 39 patients who participated in this study, 29 were male (74%) and ten were female (26%), 31 patients have localized disease (80%) and eight patients have metastatic disease (20%). The most common histology is squamous cell carcinoma and the least common histology was spindle cell sarcoma. The majority of the patients were treated with curative intention and a small proportion of patients were offered palliative therapy. **Conclusion:** Ulcers refractory to basic wound care, chronic in nature, and recent change of character of long-standing scar or wound, diagnosis of MU should be ruled out by biopsy. The management of MU should be supervised by a multidisciplinary tumor board and in the areas of epidemiology and treatment, more research is needed.

Key words: Burn scar; Non-healing ulcer; Marjolin's ulcer

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INTRODUCTION

Marjolin's ulcer (MU) reflects the malignant transformation of scar tissue or chronic inflammatory skin lesions. Although it can arise from a scar from a burn injury, traumatic wound, venous stasis ulcer, lupus, vaccination site, amputation; osteomyelitic fistulae, or pressure ulcer, the most common association is an old burn scar.[1,2] Approximately 2% of burn scars and 0.2–1.7% of osteomyelitic fistulae can undergo malignant transformation to MU.[3,4] The mechanism of malignant transformation is probably multifactorial and the exact mechanism of how an ulcer or scar would undergo malignant transformation is an unknown process, but genetic predisposition, local damage to the skin's immune mechanism, chronic irritation repeated re-epithelization, and toxins released from local tissue damage are proposed.[5] Chronic irritation and repeated trauma cause continued mitotic activity of regeneration and repair which can lead to a malignant change. Avascularity, obliterated lymphatics of scar tissue, leads to impaired mobility of lymphocytes,

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thereby delaying or preventing delivery of (antigen-presenting cells); thus, immune escape mechanism of malignant cells would prevail.[6] Either due to medication or disease state, patients with suppressed immunity may be prone to develop MU.[7] Due to the low incidence, only a few case reports and case series were reported in the literature. The largest reported clinicopathological features of 83 cases from the Republic of Iran.[8]

Aims and objectives

In our retrospective analysis, we report our experience regarding MU over the past 16 years with a significant range of latent period, histology, and as well as underlying skin conditions, from Kolkata, India.

MATERIALS AND METHODS

Study design

This was a single institutional retrospective study carried out in the department of radiotherapy at NRS Medical College and Hospital, Kolkata. The inclusion criteria were (1) HPE confirmed MU report (2) of age >18 years; the exclusion criteria were (1) patients without HPE reports and (2) patients without proper records.

Data collection

From January 2006 to January 2022, according to inclusion and exclusions criteria, as mentioned earlier, a total of 39 HPE-proven MU patients were selected for this retrospective study. We focus mainly on data about the age at the time of skin injury, type of injury, the time gap between the initial injury and the development of MU, histology, clinical stage, and treatment received, along with demographic details. As per the ethical guideline Helsinki, the confidentiality of patients was assured.

Data analysis

All the collected data were recorded on an Excel sheet and analyzed on SPSSVs24.

RESULTS

A total of 39 patients with histopathologically proved MU s from January 2006 to January 2020 were selected according to the inclusion and exclusion criteria mentioned earlier. The median age of patients at the time of development of MU was 52 years and with a range of 32–71 years. Out of 39 patients who participated in this study, 29 were male (74%) and ten were female (26%), 31 patients have localized disease (80%) and 8 patients have metastatic disease (20%). The most common inciting injury was burn injury (87%) followed by post-traumatic scar. All the epidemiological and treatment details are shown in Table 1. The most common histology is squamous cell carcinoma (SCC) and the least common variety is spindle cell sarcoma (Figures 1-4). Out 39 of patients, 28 patients underwent wide local excision (WLE) and three patients received radical radiotherapy, and the rest eight patients received palliative radiotherapy, that is, the majority of the patients were treated with curative intention and a small proportion of patients offered palliative therapy. Eleven patients received adjuvant radiotherapy with doses ranging from 60 to 66Gy/30# over 6 weeks. The indications for adjuvant radiotherapy were a post-operative residual disease, margin positive, and close margins. Ten patients who underwent WLE developed local recurrence on subsequent follow-up and received radical radiotherapy with a dose of 60–66 Gy/30–33 # over 6 weeks. Eight patients received palliative radiotherapy as they were presented with metastatic disease with doses ranging from 33 Gy–40Gy/13 # over 2 and 1/2 weeks. Palliative chemotherapy was given for 6–8 cycles with a regimen of paclitaxel and carboplatin; docetaxel and gemcitabine; and dacarbazine and cisplatin.

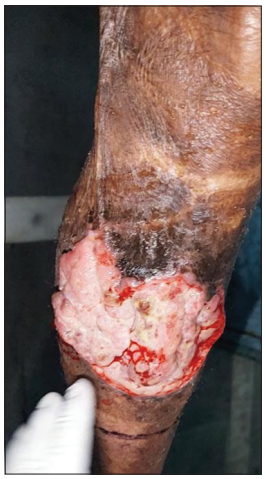

Figure 1: Marjolin's ulcer over the upper end of tibia in a background of post-road traffic accident skin grafting

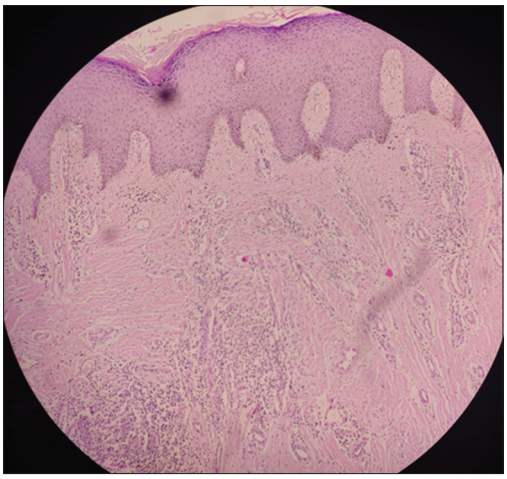

Figure 2: Low-power view of the adjoining skin

Table 1: Showing demographic profiles of patients and treatment details

S. No	Age at the time of diagnosis	Sex	Histology	Time gap (years)	Treatment
1	48	F	SCC	32	WLE
2	62	F	BCC	27	WLE+local RT
3	71	M	SCC	42	Local RT
4	47	M	SCC	29	WLE+RT
5	36	F	MM	37	WLE+RT
6	56	M	Spindle cell tumor	31	Palliative RT+CCT
7	46	M	SCC	29	WLE+RT
8	49	M	BCC	30	Local RT+CCT
9	58	M	SCC	34	Local RT
10	67	M	BCC	38	Palliative CCT+T
11	61	F	SCC	28	Local RT
12	55	M	SCC	32	Local RT
13	54	F	BCC	34	WLE
14	67	M	SCC	41	WLE+RT
15	65	M	SCC	29	Palliative CCT+local RT
15	56	M	SCC	35	WLE+RT
16	46	F	MM	34	Palliative CCT+local RT
17	44	M	SCC	29	CCT+RT
18	51	M	SCC	41	WLE
19	56	F	MM	36	Palliative CCT+RT
20	56	M	SCC	29	RT
21	61	F	SCC	26	WLE+RT
22	63	M	SCC	34	WLE
23	58	M	SCC	32	WLE
24	57	M	SCC	29	Local RT
25	68	M	SCC	36	Palliative RT
26	56	M	SCC	31	WLE+Local RT
27	59	M	SCC	38	WLE+Local RT
28	66	M	SCC	30	WLE
29	59	M	SCC	33	WLE
30	48	M	BCC	30	Local RT
31	55	F	SCC	27	Palliative RT
32	57	M	SCC	37	WLE
33	68	M	SCC	33	Local RT
34	61	M	SCC	36	WLE+RT
35	50	M	SCC	31	WLE
36	56	M	SCC	40	Local RT
37	59	F	Adeno ca	32	WLE+local RT
38	69	M	BCC	29	Palliative RT+CCT
39	57	M	SCC	31	WLE

CCT: Combination chemotherapy, CRT: Concurrent chemoradiotherapy, RT: Radiotherapy, SCC: Squamous cell carcinoma, BCC: Basal cell carcinoma, MM: Malignant melanoma, WLE: Wide local excision

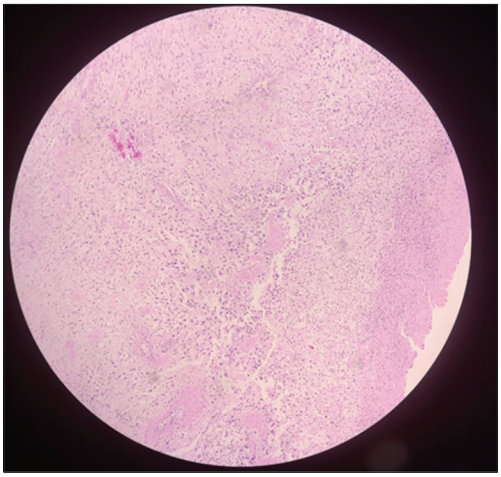

Figure 3: Low-power view from tumor proper showing malignant spindle cells

DISCUSSION

The MU term was coined after French surgeon Jean Nicolas Marjolin who first described this type of lesion in the year 1828.[9] All sex, race, and age are prone to develop MUs with the average age at diagnosis being 59 years.[10,11] Men are 3 times more commonly affected than females.[2] In the reported literature, the average latency period from the time of the initial inciting wound to the development of MUs is between 30 and 35 years. In our study, the average latency period is 34 years with a range from 26 to 42 years and the most common inciting injury was burn injury (87%) followed by post-traumatic scar. For the development of MUs, the burn scar is the most common inciting injury [2] and usually, 0.7–2% of burn scars may undergo malignant degeneration.[3,4] Any chronic scar that changed to a non-

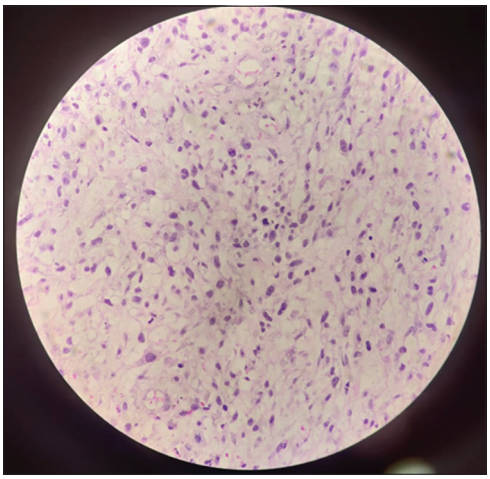

Figure 4: High-power view from tumor proper – malignant spindle cells better appreciated, with sparse mitosis

healing ulcer should be biopsied to rule out MU. Exophytic granulation tissue, bleeding, and regional lymphadenopathy may also suggest a malignant transformation of the scar. The most frequently affected site is the lower extremity followed scalp and upper extremity.[3,8] In our study, the most common site is the lower extremity followed upper extremity and consistence with reported literature. SCC is the most common histology accounting for 80–90% of the cases, followed by basal cell carcinoma (BCC) accounting for around 9.6% of cases.[2] In our study, the most common histology is SCC (77 %), followed by BCC (15%) and spindle cell sarcoma, which is least common histology. The above findings are consistent with reported literature by Elkins-Williams ST and Marston et al.[2] Due to the high risk of nodal metastasis, some authors suggest that, along with physical examinations, an USG of regional node, lymphatic mapping, and sentinel node biopsy could be done.[2,12]

Patients with MU pose a therapeutic dilemma; the treatment is very challenging and therapeutic decisions should be taken by a multidisciplinary team.[13,14] The localized disease may be managed by surgery, RT, and/or chemotherapy.[1] In suitable cases, WLE with 1–2 cm clear margin, or Mohs microscopic surgery is indicated,[15-17] and if WLE or MMS is not possible; then, amputation proximal to the lesion may be the only viable option, especially in presence underlying bone and joint involvement.[12,14] However, in such a scenario, local radiotherapy is a good alternative to amputation. Hence, indications for RT are diseases not suitable for surgery, very large lesions, high-grade lesions, and the presence of regional nodal metastasis post-operative residual disease.[18] However, in cases of advanced disease at presentation, usually managed by treatment modality with palliative RT and/or combination chemotherapy, to which cancers are most likely to respond.

Out of 39 patients, total of 28 patients underwent WLE and three patients received radical radiotherapy, and the rest eight patients received palliative radiotherapy, that is, the majority of the patients were treated with curative intention and a small proportion of patients offered palliative therapy in our study patients. Fifteen patients with post-operative margin positive, close margins, high-grade lesions, and residual disease have received adjuvant radiotherapy.

MUs with well-differentiated histology are less aggressive and likely to have a better prognosis than poorly differentiated histology. In some series, local recurrence was seen up to 50 % of cases[8,11] and lower extremity locations, high-grade lesions, lymph node, and distance metastasis caries poor prognosis.[5] The 3 overall survival (OS) is 65–75% and 10 years OS is 38% only. The effect of prior skin injury on survival, prognosis, toxicity, and appropriate management of MUs is yet to be well established, and more studies are required.[2,3]

Limitations of the study

Our study is single institutional and retrospective in nature, so patients may not be representative of the entire population.

CONCLUSION

Ulcers refractory to basic wound care, chronic in nature and recent change of character of long-standing scar or wound, and diagnosis of MU should be ruled out by biopsy. The management of MUs should be supervised by a multidisciplinary tumor board and more research is needed in the areas of epidemiology and treatment.

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SD, CB, AD- Conceptualization, methodology, data collection, data interpretation, statistical analysis, and reviewing of the final manuscript;
SM, SB- Conceptualization, methodology, data collection, data interpretation, reviewing of the statistical analysis, and final manuscript..

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