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Case Report

Marjolin's ulcer: A case series

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Abstract

Background: Marjolin's ulcer (MU) is a rare but aggressive malignant transformation of long-standing scars or chronic wounds.

Case Illustration: we present three cases of MU that arise from post-traumatic scar. Two of the cases were found on the lower extremity and one on the scalp. Two lesions of lower extremities were preceded by burn injury from various causes. One lesion on the scalp was caused by non-burn trauma. Diagnosis was confirmed after tissue biopsy which revealed well-differentiated squamous cell carcinomas. Two patients underwent surgical intervention (wide excision and Mohs micrographic surgery) followed by split-thickness skin graft (STSG). In one patient, a wide excision was planned to be performed but the patient died before the surgery.

Discussion: the most frequent type of MU is squamous cell carcinoma (SCC). Extremity is the most common sites of predilection followed by the head and neck region. Marjolin's ulcer with histopathological feature of SCC is more aggressive and carries a poor prognosis with a high rate of recurrence.

Conclusion: early recognition of malignant conversion followed by comprehensive staging and early treatment, are of the utmost importance. Surgery remains the optimal treatment for MU, frequent and intense follow-up after surgery is required.

Keywords*: marjolin's ulcer, scar, squamous cell carcinoma, ulcer*

Abstrak

Latar Belakang: Ulkus Marjolin (UM) merupakan keganasan yang jarang namun bersifat agresif yang berasal dari jaringan parut atau luka kronik.

Ilustrasi Kasus: dilaporkan tiga kasus UM yang berasal dari jaringan parut pascatrauma pada masa anak-anak. Ulkus terdapat pada regio ekstremitas bawah dan kulit kepala. Dua kasus berupa lesi pada ekstremitas bawah muncul pada jaringan parut terkait luka bakar, sedangkan satu kasus berupa lesi pada skalp disebabkan oleh trauma lain. Pemeriksaan histopatologi untuk ketiga kasus tersebut menunjukan hasil karsinoma sel skuamosa berdiferensiasi baik. Tindakan bedah (eksisi luas dan bedah Mohs) diikuti penutupan defek dengan split-thickness skin graft (STSG) sudah dilakukan pada dua pasien. Satu pasien dengan lesi di skalp direncanakan untuk tindakan eksisi luas.

Diskusi: karsinoma sel skuamosa (KSS) merupakan jenis keganasan pada UM yang paling banyak ditemukan. Ulkus Marjolin paling banyak ditemukan pada regio ekstremitas, diikuti kepala dan leher. Ulkus Marjolin dengan gambaran histologi KSS lebih agresif dan memiliki prognosis yang buruk dengan risiko kekambuhan tinggi.

Kesimpulan: deteksi dini adanya perubahan ke arah keganasan, menentukan stadium kanker secara komprehensif, dan tata laksana sedini mungkin, merupakan hal yang penting. Tata lakasana utama UM adalah tindakan bedah dan diperlukan pengamatan berkala secara ketat pascabedah.

Kata kunci: *jaringan parut, karsinoma sel skuamosa, ulkus, ulkus Marjolin*

Background

Marjolin's ulcer (MU) is a rare cutaneous malignancy originating from scar tissue formed by any cause or chronic injury.[1,2] Jean-Nicolas Marjolin, a French surgeon, first discovered chronic ulcers in scar tissue caused by burns in 1828. Most MU occur in scar tissue caused by burns with an incidence of 0.77 –2%, especially in second to third-degree burns with secondary wound healing.[2,3] In addition to burns, chronic inflammatory conditions could also be a predisposition to MU, such as osteomyelitis, hidradenitis suppurativa, venous ulcers, diabetic ulcers, and anal fistulas.[2]

Marjolin's ulcer most commonly occur in the fifth decade of life with a male to female ratio of 2:1.[2] The latent period from the onset of trauma to progression into become a malignancy is generally slow, at 30-35 years.[4] The lower extremities are the most common site of MU (53.3%). The scalp region has the highest risk of bone invasion.[5,6]

Marjolin's ulcer is often misdiagnosed as an infection or chronic ulcer and leads to delayed treatment. When compared to sun exposure-related skin malignancies, scarring-related carcinomas have a risk of regional metastasis, poorer prognosis, and higher mortality.[3,5] Surgery is the main modality in the management of MU.[7,8]

We report 3 cases of a MU arising in areas of healing burn and non-burn scars. Physicians should have a high index of suspicion in chronic wounds that are recalcitrant to therapy and should remember to biopsy all suspected lesions. Early recognition and definitive treatment are the mainstays ensuring the best prognosis.

Case Illustration

Case 1

A 49-year-old male presented with 45-year history of scar wound on the head which developed an enlarging ulcer within 6 months. The wound was malodourous, bleed easily, and painful. In the parieto-occipital region, there was a hypertrophic scar, 10 x 8 cm in size, irregular, partly shiny surface, skin-coloured, accompanied by a 7 x 5 x 0.5 cm ulcer and alopecia (Figure 1A). The finding of dermoscopy were consistent with SCC (Figure 1B). There were no palpable enlarged lymph nodes. Histopathological examination revealed acanthosis, ulcer, infiltrative epithelial malignant tumor mass between the connective tissue stroma, and horn pearl which corresponds to well-differentiated squamous cell carcinoma (Figure 2). Chest X-ray examination and abdominal ultrasound found no signs of metastases in the heart, lungs, or intra-abdominal organs. Brain multi-slice computed tomography (MSCT) scan with contrast showed a heterogeneous suspected malignant lesion in the cutis-subcutis of the left parieto-occipital region to the left posterior neck which destroys the parieto-occipital bone and attaches to the duramater, with multiple bilateral cervical lymphadenopathies with the largest size of 1 cm. The patient was diagnosed with SCC T4NxMx as well as secondary bacterial infection. Wide excision was planned to be performed by Oncologic surgeon and Neurologic surgeon, but the patient died before the surgery.

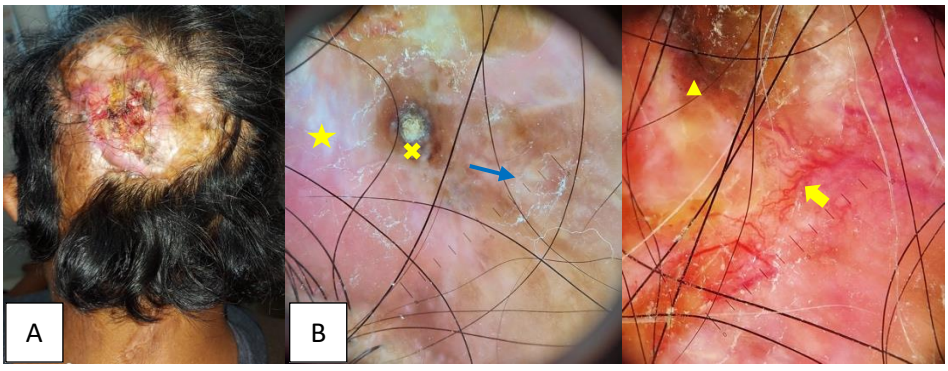

Figure 1. (A) Clinical manifestations of Marjolin's ulcer in the parieto-occipital region. (B) Dermoscopic features of white structureless areas (star), follicular hyperkeratosis (cross), scale-crust (blue arrow), polymorphous vessels

(yellow arrow), ulceration (triangle), and mixed background

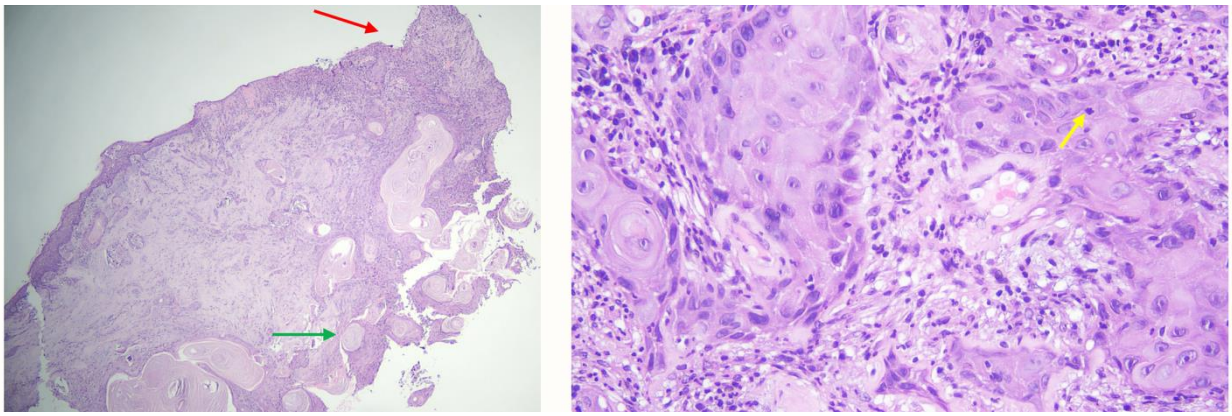

Figure 2. Well differentiated squamous cell carcninoma: ulceration (red arrow), acanthotic epidermis, keratin pearls (green arrow), pleomorphism and mitotic figures (yellow arrow).

Case 2

A 48-year-old male with long lasting, painful, chronic ulceration on burn scar on the left upper leg. The wound started as a small lesion and progressively enlarged within 2 years. The lesion had grown into 22 x 14 x 0.5 cm exophytic, raised edges, well-circumscribed, and malodorous ulcerated lesion (Figure 3A). Dermoscopy of the lesion showed polymorphous vessels, white circles, rosettes, white structureless areas, scale-crust, and mixed background (Figure 3B). Painless, mobile lymph nodes enlargement with 1.5 – 2 cm in size were palpated on the left inguinal. Skin biopsy results showed atypical mitosis, horn pearl, and dense inflammatory cells of lymphohistiocytes, eosinophils, and plasma cells in the dermis which corresponds to well-differentiated squamous cell carcinoma. MRI examination of the lower extremities indicated a malignant mass in the cutis to medial subcutis to the posterior side of left femoral region without muscle, bone, or neurovascular involvement, with left inguinal and external parailiac lymphadenopathy. Diagnosis of SCC T3NxMx with secondary bacterial infection was established. The patient underwent wide excision and dissection of inguinal lymph nodes performed by surgical oncologist. A defect was reconstructed with split-thickness skin graft (STSG) by plastic surgeon. The incision edges were tumor-free, no lymphovascular invasion was found. The entire lymph nodes were also tumor-free. There was no recurrence reported.

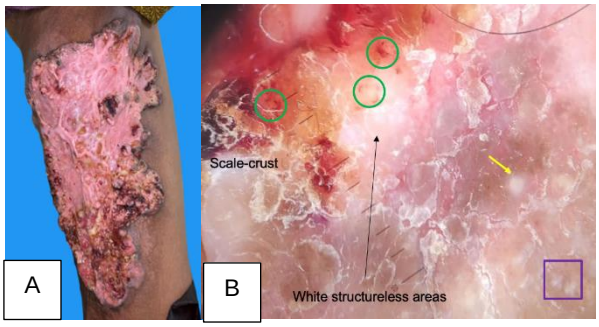

Figure 3. (A) Clinical manifestations of Marjolin's ulcer on the left upper leg region. (B) Dermoscopic features of polymorphous vessels (green circles), white circles (yellow arrow), rosettes (purple square), white structureless areas, scale-crust, and mixed background.

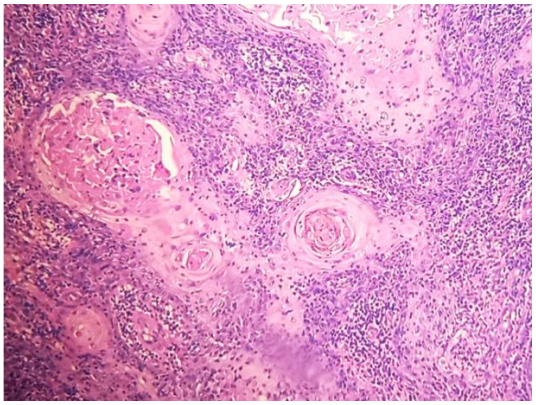

Figure 4. Well differentiated squamous cell carcinoma**:** atypical mitosis, horn pearl, and dense inflammatory cells of lymphohistiocytes, eosinophils, and plasma cells in the dermis.

Case 3

A 40-year-old female patient presented with a mass on the right lower leg which arises from long-standing burn scar. An irregular, ulcerated mass lesion with an approximate length of 8 x 5 x 1 cm was observed (Figure 5A). The dermoscopic examination revealed the presence of dotted vessels, hairpin vessels, hemorrhage, white structureless area, and mixed background (Figure 5B). There was no palpable enlargement of the lymph nodes. Histopathologic examination showed the features of acanthosis, ulceration, horn pearl, and dense inflammatory cells of lymphocytes, neutrophils, and keratinocytes proliferation with atypical nuclei, consistent with well-differentiated squamous cell carcinoma in the dermis. Immunohistochemical examination showed positive results for AE1/AE3 and CK5 staining. Staining with Ki67 was also positive in 30% of the tumor cells. No intra-abdominal or lymph nodes organ metastasis was found from abdominal and inguinal ultrasound examination. Right lower leg MRI showed a mass with characteristics of malignancy in the cutis of the posterolateral region of the right cruris, infiltration to the subcuticular fat, and no muscle involvement. Patient was diagnosed with SCC T3N0M0 as well as secondary bacterial infection. Mohs micrographic surgery and STSG surgery was conducted. Seven months following the surgery, we observed a recurrent lesion manifested as a single ulcer measuring 5.2 x 4 x 0.5 cm at the identical anatomical site. The patient underwent a second Mohs micrographic surgical procedure. A subsequent STSG was conducted by a plastic surgeon.

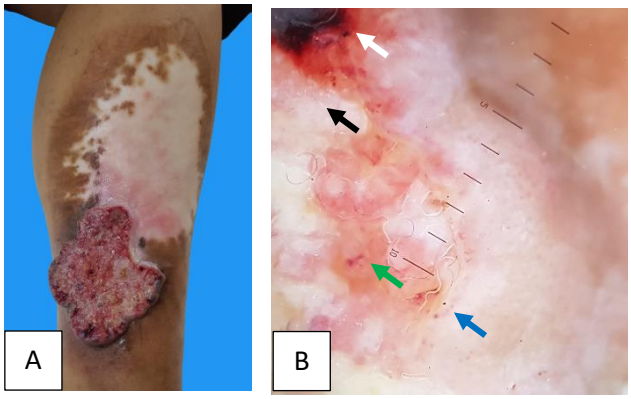

Figure 5. (A) Clinical manifestations of Marjolin's ulcer on the right lower leg. (B) Dermoscopic features: dotted vessels (blue arrow), hairpin vessels (green arrow), hemorrhage (white arrow), white structurless area (black arrow), and mixed background

Table 1. Differences in Characteristics of Marjolin's Ulcer Cases

	Case 1	**Case 2**	**Case 3**
Gender	Male	Male	Female
Age	49-year-old	48-year-old	40-year-old
Etiology of scarring	Wound infection	Burn injury	Burn injury
Location	Scalp	Upper leg	Lower leg
Age of trauma	4 years	6 years	10 years
Latent period	45 years	42 years	30 years
Onset of the disease	6 months	2 years	6 months
Secondary infection isolates	*Acinetobacter spp*.	*Pseudomonas aeruginosa*	*Escherichia coli*
Diagnosis*	SCC T4NxMx	SCC T3NxMx	SCC T3N0M0

SCC: squamous cell carcinoma. *According to National Comprehensive Cancer Network (NCCN) guideline in 2022.[9]

Discussion

Marjolin's ulcer is a cutaneous malignancy that occurs in scar tissue or chronic wounds with the most clinical manifestations in the form of chronic ulcers. The average age of onset of MU is 52.1 years.[10] Based on its latent period, MU is classified into acute and chronic. Acute ulcer is defined as malignant changes that occur within one year after the initial injury. Malignancies that occur for more than one year are called chronic ulcers.[11] All three patients in this case report were ≥40 years old and had a history of post-traumatic scarring that occurred at the young age with a latent period of MU of more than 30 years. Patients in case number 2 and 3 had a history of burns in the lower extremities. The most common etiology of MU is scar tissue caused by burns (82.5%), however, MU can also occur in chronic wounds and non-burn-related scars.[12] A cohort study by Xiang F, et al. in 2018 conducted on 140 patients with Marjolin's ulcers, showed that the most common location of MU lesions was the lower extremities (42.1%) followed by the head, face, and neck (34.5%).[6] The prevalence of bone invasion in patients with MU in the head, face, and neck regions is higher than MU lesions in other parts of the body.[6] In case 1, from the examination results of the brain MSCT scan with contrast, malignant lesions appear to destroy the occipital-parietal bone.

The pathogenesis of MU is still not fully understood. Scar tissue is suspected to lose immune cells that play a role in skin physiology. Thus, malignant cells can evade the immune response and become more aggressive. Cicatrisation of burn wounds can cause obliteration of lymphatic vessels leading to an impaired physiological immune system and increased risk of neoplastic growth.[13] Recent theories suggest an association between MU and genetic factors associated with human leukocyte antigen (HLA) DR4 and mutations of p53 and/or FAS genes.[11] Ultraviolet radiation (UV) also plays a role in the pathogenesis of MU because it can reduce the number of Langerhans cells that interfere with the function of the immune system and cause mutations of the p53 genes.[13] The patient in case 1 had a history of chronic sun exposure due to the patient's occupation as a motorcycle driver for more than 5 years. Whereas in the other two patients, it may be due to post-burn cicatrisation which causes lymphatic disorders and immune system disorders.

Squamous cell carcinoma is the most common histologic variant of MU (81.32%), followed by malignant melanoma (7.69%), basal cell carcinoma (4.40%), and osteosarcoma (2.20%).[14] Dermoscopic examination can help to distinguish the type of malignancy from MU and rule out the possibility of a chronic infection diagnosis. In all three patients, dermoscopic features in the form of ulceration, polymorphous vessels, scale-crust, white structureless area, and mixed background which corresponds to squamous cell carcinoma were found.[15] Histopathological examination is the gold standard to diagnose MU. Although the histopathological features in all three cases were well-differentiated SCC, but based on the National Comprehensive Cancer Network (NCCN) guidelines for SCC, all three patients were categorized as high-risk category based on location (head) and size (more than 4 cm).[9]

At the time of the initial visit, all three patients had secondary bacterial infections and had received definitive antibiotic therapy according to the results of culture and resistance tests. The management of patients in case 2 and 3 was wide excision and Mohs micrographic surgery followed by STSG. The patient in case 1 was planned for extensive excision by a Neurosurgeon and Oncologist surgeon because on examination there was a suspicion of invasion to the skull bone. This is in accordance with the NCCN guidelines for the management of high-risk SCC, namely Mohs micrographic surgery and wide excision with an incision limit of 2–4 cm followed by reconstruction with skin graft or local flaps. Radiotherapy is recommended for patients for whom surgery is not feasible or for cases of recurrence.[7,9] One patient (case 3) had local recurrence. Marjolin's ulcer has a recurrence risk of 20–50% and a metastatic risk of 27.5–40%. Tumor size greater than 10 cm increases the risk of distant metastasis and the risk of recurrence is higher in moderately poorly differentiated SCC or lymph node involvement.[7,10]

Conclusion

Marjolin's ulcer, a cutaneous malignancy that occurs in scar tissue, is most commonly caused by burns, and generally has a slow latent period. The most common histologic variant is SCC, while the most vulnerable area of invasion is the skull bone. Biopsy of any suspicious lesion should not be delayed to rule out malignancy. Dermoscopic examination can help to distinguish the type of malignancy of MU and surgery is the main therapy of MU. Close follow-up for the years ahead is necessary to ensure the patient's well-being.

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None

Author Contribution

All authors contribute equally to this project in the study preparation, data collection, case analysis and the writing of the manuscript

Conflict of interest

The authors report no conflicts of interest.

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