
Case Report

Marjolin's Ulcer: A Case Report and Literature Review

Yue-Chiu Su¹, Li-Ren Chang²

Marjolin's ulcer is an aggressive cutaneous malignancy, which is common in previously traumatized or chronically inflamed skin. It has high regional metastasis and fatality rates. Our patient presented with ulcer, erythema, swelling and verrucous lesions on the left leg. He had a history of tibia fracture 30 years ago with poor wound heading. Histopathological examination of the excision specimen demonstrated well-differentiated/verrucous squamous cell carcinoma (SCC) with deep dermal invasion without lymph node metastasis. The patient received amputation after taking into consideration the deep dermal invasion and the possibility of local recurrence and distant metastasis. At 9-month follow-up, the patient had no relapse or metastasis. In this report, the etiology, diagnosis, treatment and prognosis of this disease are discussed with a brief review of the literature.

Key words: Marjolin's ulcer, squamous cell carcinoma

Introduction

Da Costa was the first to coin the term Marjolin's ulcer (MU) in 1903 to describe an aggressive skin malignancy in previously traumatized or chronically inflamed skin.¹ The incidence of MUs in such lesions is reported to be 0.77%-2%.^{2,3,4} Malignant transformation occurs after a mean of 35 years, ranging from as short as 6 weeks to as long as 70 years.⁵ Various risk factors have been reported,

including toxins released from damaged tissue, immunological factors, repeated irritation, poor lymphatic regeneration, co-carcinogens, DNA mutations, and local toxins.¹ In the majority of cases, MU presents as squamous cell carcinoma (SCC). It frequently has high regional metastasis and fatality rates. Reviewing of literature showed an overall mortality rate of MU of at least 21%.³ The prognosis of patients with MUs depends on tumor stage, histology grade, regional nodal spread, local recurrence and presence of distant metastasis.

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Early recognition and aggressive treatment of MU can improve patient's outcomes. Here, we report a case of MU presenting as well-differentiated verrucous SCC to highlight this condition after bone fracture.

Case Report

A 66-year-old man presented with poor healing of a wound on the left leg and progressively painful sensation at the emergency department. Medical history included a tibia fracture 30 years ago with a non-heal-

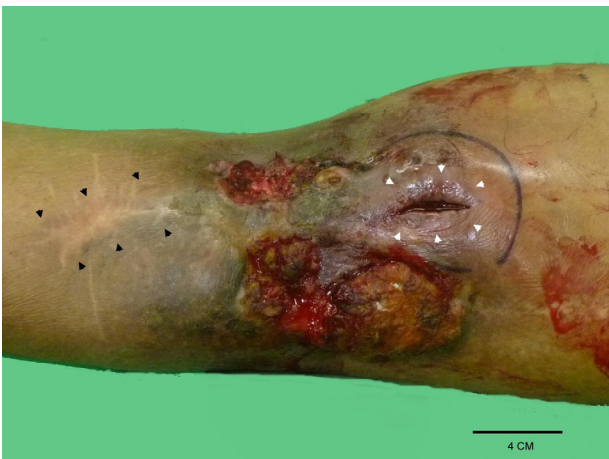


Fig. 1 Clinical presentation of a non-healing ulcer with erythema and swelling of the surrounding skin, together with two exophytic, wart-like-lesions, measuring 10.5×4 cm and 8.8×2 cm on the skin surface. Note the old fracture scar below the lesion (black arrow) and the wound from incisional biopsy (white arrow).

ing wound. He had received skin flap repair 5 years ago. On physical examination, an ulcer was noted on the patient's left leg with erythema and swelling over the surrounding skin together with two exophytic, wart-like lesions, measuring 10.5×4 cm and 8.8×2 cm on the skin surface (Fig. 1). The patient's body temperature was 36.7°C , pulse rate was 81/min, and respiratory rate was 16/min. Laboratory examination disclosed white blood cell count of $11860/\text{mm}^3$ with 51% neutrophils, 11% monocytes, 21% lymphocytes, 15% eosinophils and 2% basophils, platelet count of $449000/\text{mm}^3$, and hemoglobin concentration of 17g/dL. The levels of creatinine, glucose, and electrolytes were within normal limits. C-reactive protein (CRP) concentration was 15.7mg/L. Chest X-ray showed no abnormalities. After consultation with plastic surgeon, incisional biopsy was performed and the pathologic diagnosis was verrucous hyperplasia (Fig. 2). However, since MU was suspected clinically, wide excision of the lesion was performed. Pathological examination of the specimen showed well-differentiated verrucous SCC with deep dermal invasion (Fig. 3). Twenty-two inguinal lymph nodes were dissected without evidence of metastasis. Although positron emission tomography survey showed no abnormality, the patient received amputation after

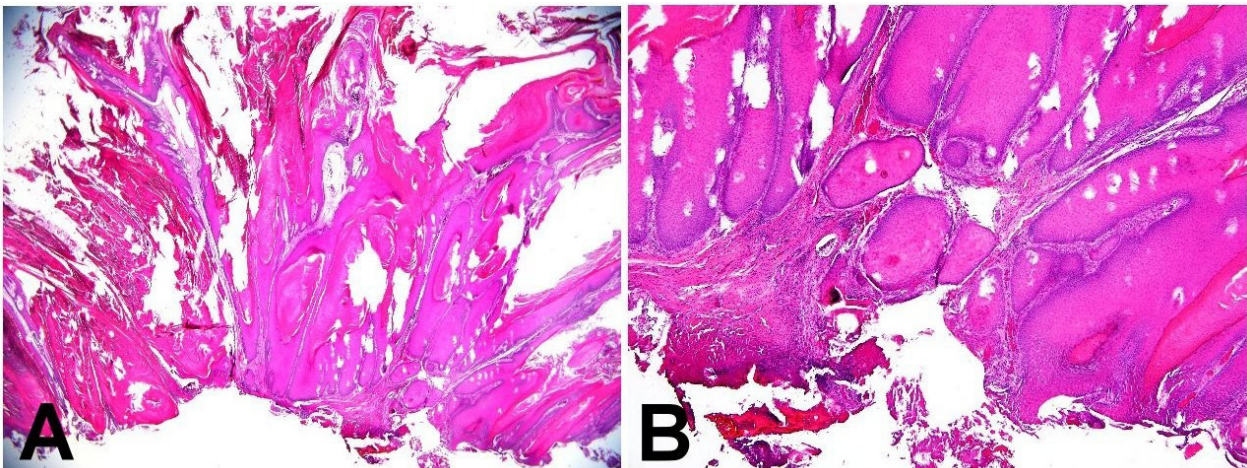


Fig. 2 Incisional biopsy of one of the exophytic lesions showing verrucous hyperplasia with minimal cellular atypia on (A) low-power (12.5X), and (B) high-power (40X) magnification.

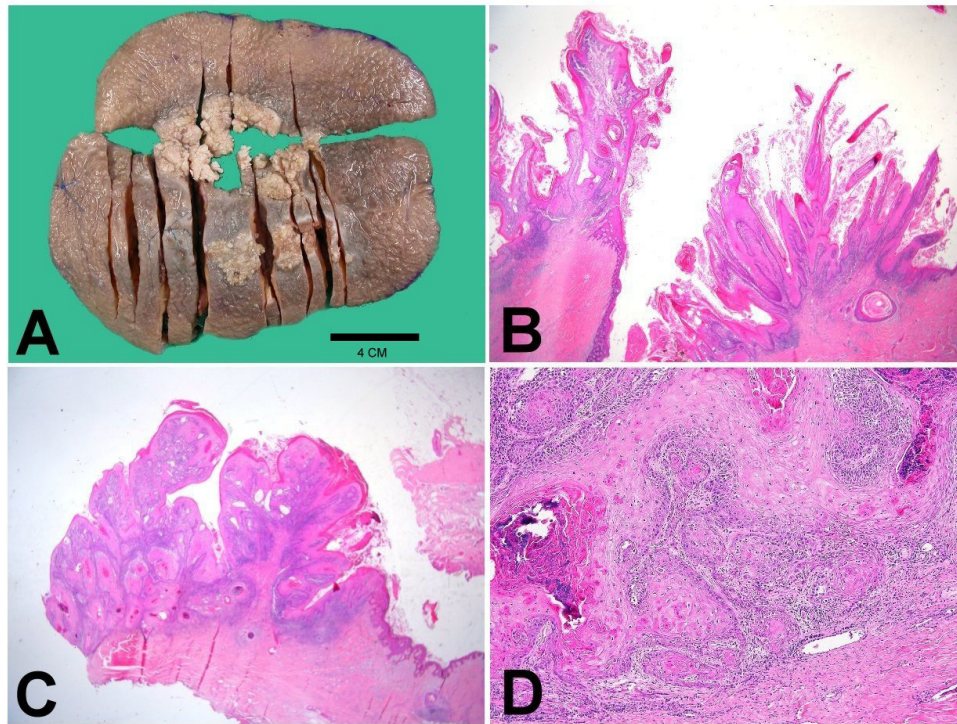


Fig. 3 (A) Gross specimen from wide excision showing verrucous hyperplasia of skin. Low-power magnification (12.5X) demonstrating (B) Verrucous hyperplasia component consistent with that of previous incisional biopsy, and (C) Squamous cell carcinoma (SCC) component of the lesion with invasion of reticular dermis (tumor thickness 6 mm) (D) High-power magnification (200X) showing keratinocytic atypia and stromal invasion without lymphovascular and perineural invasion or necrosis. Mitotic counts were 1-2 per 5 HPF.

being informed of the finding of deep dermal invasion and the possibility of local recurrence and distant metastasis. At 9-month follow-up, no relapse or metastasis was noted.

Discussion

MU represents a malignancy arising from posttraumatic scars and chronic wounds. Malignant transformation occurs after a mean period of 35 years, ranging from as short as 6 weeks to as long as 70 years.⁵ The most common histologic type is SCC (71%), followed by basal cell carcinoma (12%), melanoma (6%), sarcoma (5%), squamobasal cell carcinoma (1%), SCC-melanoma (1%), and other rare neoplasms (4%).³ A variety of rare tumours may emerge in the post-burn wounds and scars and these include fibrosarcoma, liposarcoma, dermatofibrosarcoma protuberans,

and mesenchymal tumors.^{3,4,6}

Although malignant transformation of chronic wounds requires further clarification, various factors have been implicated, including toxins released from damaged tissue, immunological factors, repeated irritations, poor lymphatic regeneration, co-carcinogens, DNA mutations, and local toxins.¹ Lower limbs constitute the most frequent site of MUs. The other sites reported to be affected, in order of reducing frequency, include head and neck region (i.e., face, scalp, neck), upper limbs and other body parts.^{3,4,6}

The diagnosis of MUs is based on the clinical findings in the patient's history, detailed examination of the ulcer and its draining nodal basin, and the histology of the lesion. Macroscopically, MUs have been reported to exist in two forms which are of prognostic importance: (1) exophytic form characterized

by prolonged and relatively benign course and low probability of distant metastasis; and (2) infiltrative form characterized by rapid formation of ulceration, poor prognosis, and high probability of metastatic spread.⁷ Once the biopsy confirms the diagnosis of MU, determination of the local extent of the lesion and staging is needed. Magnetic resonance imaging (MRI) or computed tomography (CT scan) is performed to determine the local extent of the lesion and invasion of any underlying structures. Given the aggressive nature of MU, distant metastases should be ruled out with metastatic work-up that includes chest CT scan, abdominal ultrasonography and positron emission tomography (PET).

SCCs originating from these lesions are more aggressive than other primary SCCs. MU has a higher tendency for local recurrence and distant metastasis via the lymphatic system.⁸

At presentation, regional lymph nodes are involved in 20%-66.7% of the patients.^{3,5} Distant metastases are reported in 14% of the patients.³ Although metastatic spread is primarily to the regional lymph nodes, metastasis to organs such as the liver, lung, brain, kidney may also occur.⁵

The treatment of MUs requires multidisciplinary teamwork. Treatment strategies for MUs include wide local excision, dissection of the regional nodes, amputation for advanced lesions of limbs, radiotherapy and chemotherapy.⁶ Adequate surgical resection is most important to prevent local recurrence and a horizontal clearance margin of 2-5 cm has been advocated.⁹ Use of frozen sections has been reported for intraoperative diagnosis and evaluation of surgical excision safety margins.¹⁰ Amputation is indicated when wide local excision is not possible due to deep invasion, bone or joint involvement, infection, hemorrhage, or when excision would cause major functional disability.⁷

Sentinel lymph node biopsy should be performed regardless of the presence of

enlarged lymph nodes. Regional lymph node dissection is indicated when nodes are clinically palpable except proven metastasis.

Radiotherapy and chemotherapy are indicated in patients with poor prognostic factors or distant metastasis. The indications for chemotherapy are not well-established. It is often instituted for patients whose lesions cannot be surgically removed, those with distant metastasis, recurrent disease, and those who refused surgery. Chemotherapy is usually based on 5-Fluorouracil with a combination of cisplatin, methotrexate and bleomycin. It may be in the form of adjuvant or neoadjuvant therapy.⁵

Review of literature, showed an overall mortality rate of MU of at least 21%.³ The prognosis of patients with MUs depends on tumor stage, histology grade, regional nodal spread, local recurrence and presence of distant metastasis.

In conclusion, a high index of suspicion is required in the management of chronic non-healing ulcers that are recalcitrant to therapy and all suspected lesions should be biopsied. Early recognition and aggressive treatment of MUs and close follow-ups are critical for improving patient's outcomes.

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