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Case Report

# Marjolin's ulcer: A non-frequent manifestation of a carcinomatous transformation in a chronic wound – Description of three cases and literature review

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ABSTRACT

*Introduction:* Lesion resulting from malignant transformation of a non-healing chronic wound of various etiology is referred to as Marjolin's ulcer. Histopathologically in most cases it is a squamous cell carcinoma, while basal cell carcinoma, melanoma malignum and sarcoma cases have been reported in the literature.

*Aim:* The aim of the work was to outline major characteristics of the entity and to focus on a variety of lesions which may evolve into this malignancy, based on literature review and patients operated on in the authors' department.

*Material and methods:* Four cases of malignant lesions which occurred in patients presenting chronic wounds in the period 2008–2012 were described.

*Results and discussion:* All patients presented squamous cell carcinomas which evolved in chronic post-burn wounds (two cases) and a chronic atheroma (one case). The time between the initial injury and malignant transformation was long (over 20 years in all cases). One patient died in the course of the disease.

*Conclusions:* Marjolin's ulcer is a non-frequent manifestation of a malignant neoplasm. It is an entity, which should be suspected and meticulously diagnosed and treated in all individuals presenting alerting symptoms such as chronic ulcerations of previously injured skin. It is a highly-virulent kind of malignant skin lesion in most cases due to late diagnosis and to histopathological characteristics of the entity. Surgical wide excision is a treatment of choice. In some cases, radiotherapy and limb amputation in some cases of acral localization are advocated. There is no agreement on prophylactic regional lymph node dissection.



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## 1. Introduction

A neoplasmatic lesion evolving in chronic skin wounds and scars of various etiology is widely referred to as Marjolin's ulcer. It was first described in 1828 by Jean-Nicolas Marjolin, a French anatomist and surgeon, a colleague of Dupuytren, in a section upon ulcerations in *Dictionnaire de Médecine*. He presented four cases of a type of ulcer named *ulcère verruqueux*.[20] He did not describe them as malignant nor as resulting from pre-existing chronic ulcerations.[4] It was in 1850 when Robert William Smith observed some types of ulcers that developed in post-burn scars, floggings or extensive lacerations and connected them with the ulcerations described by Marjolin.[18] The above described lesions had either metastatic potential or were locally destructive, resulting in pathological bone fractures. Next description of a carcinomatous transformation in chronic wound – in a varicose ulcer of the leg – comes from John Chalmers DaCosta from the year 1903.[5] *British Medical Dictionary* describes Marjolin's ulcer as a "squamous carcinoma developing in a chronic benign ulcer, e.g. a varicose ulcer, an old unhealed burn, or a wound scar".[11] Although it was not Marjolin who first pointed out the malignant characteristics of ulcers arising in chronic wounds and scars, it is him who these lesions have been named after.

Squamous cell carcinoma (SCC) is the most common histopathological manifestation of Marjolin's ulcer, followed by basal cell carcinoma (BCC).[15] Malignant melanoma or a sarcoma is less commonly identified.[21] SCC arising in chronic wounds constitutes approximately 2%–5% of SCC cases[19] being more frequent in men than in women (3:1), with predilegence to age over 50 years.[8] The level of malignancy is relatively high, including high local recurrence rate and metastatic potential.[21]

No univoqual data on the pathogenesis of Marjolin's ulcer exist. It has been suggested that some genetic or immunological factors may come into account.[21] Some authors suggest that traumatized and chronically inflamed and hypoxyed tissues may be more prone to carcinomatous transformation. However, most authors agree that a permanent, chronic inflammatory process and immune system deficiency play a significant role in its evolution.[3,21]

## 2. Aim

The aim of the work was to outline major characteristics of the entity and to focus on a variety of lesions which may evolve into this malignancy, based on literature review and patients operated on in the authors' department.

## 3. Material and methods

A review of the patients treated in the authors' department was made. Four cases of malignant lesions which occurred in patients presenting chronic wounds in the period 2008–2012 were described.

## 4. Results

### 4.1. *Case 1*

A 60-years-old-patient was referred to Clinic due to large ulcerations of right gluteal crease, perineal region and posterior left upper and lower leg with a positive biopsy for *carcinoma planoepitheliale keratodes G1* (well-differentiated neoplasm-low grade of malignancy). At the age of 3 years he suffered from a thermal injury caused by clothes which caught fire. He was treated with split thickness skin grafts and the burns healed completely. He first presented at the Clinic at the age of 19 due to a large ($25 \times 12$ cm$^2$) non-healing ulceration of the posterior surface of his left upper leg and a cicatricial contracture of his left popliteal region. The contracture was released and the wound was covered by a split thickness skin graft. Some focal skin graft necrosis occurred in the postoperative course. The patient remained asymptomatic until his 60s, when a positive biopsy for *carcinoma planoepitheliale keratodes G1* was made from a non-healing wound in left gluteal and inguinal region, which corresponded to prior thermal injury site (Figs. 1 and 2). Ultrasound exam of both inguinal regions revealed several reactively enlarged lymph nodes. A wide excision of the lesion with a 2-cm margin was performed and the defect was covered with a split thickness skin graft (STSG) (Fig. 3). The histopathological exam presented *carcinoma planoepitheliale spinocellulare keratodes G2* (moderately – differentiated neoplasm – intermediate grade of malignancy), the resection margins were clear. The patient returned to our attention 6 months later due to an ulceration on the medial margin of the skin graft in the perineal region and a large ($5 \times 15$ cm$^2$) non-healing wound covered focally with necrotic tissue on the posterior surface of right upper leg. Again, the lesions were excised with wide margins and the defects were covered with STSG. Postoperative course was uneventful. The patient returned to the operating room after another 3 months due to a rapid growth of a tumor (of diameter of 5 cm) in perineal region (Figs. 4 and 5). The tumor was excised and the defect was covered by STSG. Postoperative course was complicated by partial skin graft necrosis, which resulted in need for reoperation. First histopathological exam revealed *carcinoma planoepitheliale spinocellulare keratodes G1* with clear margins, while wound biopsy performed at the time of reoperation

**Fig. 1 – Patient 1 – ulceration in the perineal area – frontal view.**

**Fig. 2 – Patient 1 – ulceration in the perineal area and gluteal crease – posterior view.**

**Fig. 3 – Patient 1 – after resection of the lesion and coverage of the defect with STSG.**

**Fig. 4 – Patient 1 – recurrent lesion in the perineal area – frontal view.**

**Fig. 5 – Patient 1 – recurrent lesion in the perineal area – posterior view.**

turned out to be free of neoplasmatic changes. The patient returned to our attention 6 months later presenting local recurrency in the operated area, moreover a large tumor in his right inguinal region was noted (Fig. 6). Needle biopsy of the enlarged lymph node revealed carcinoma planoepitheliale cells. The patient was referred to the oncological department for further treatment. Radiotherapy was applied. Due to embolytic complications the patient died 6 months after discharge from Department of Plastic Surgery.

### 4.2. *Case 2*

A 66-year-old patient presented at our outpatient service with a large tumor of the neck (Fig. 7), which has been developing in a chronically inflamed atheroma for over 35 years. There has been a rapid growth of the lesion in the last few years. It was a $20 \times 15$ cm$^2$ large, cauliflower-like lesion with foul odor, presenting sero-purulent exudate. Patient's medical and family history were uneventful. The patient was admitted to the Plastic Surgery Department. An X-ray exam of cervical spine was performed, it showed no pathological bony involvement. The tumor was resected with a margin of 2 cm. The defect was covered with a split-thickness skin graft. The postoperative course was uneventful. Histopathological exam revealed *carcinoma planoepitheliale keratodes G1 invasivum*.

**Fig. 6 – Patient 1 – metastatic inguinal node.**

**Fig. 7 – Patient 2 – the lesion on the neck.**

Resection margins were clear. The patient is being observed basing on an outpatient clinic.

### 4.3. *Case 3*

A 51-year-old patient with uneventful medical and family history was admitted to the Plastic Surgery Department due to a non-healing ulceration of left popliteal region (Fig. 8), which evolved in a post-burn scar. Patient suffered from a thermal injury when he was 1 year old. The ulceration has been developing over last 12 months. It was $18 \times 15\ cm^2$ large, presented both ulcerated and verrucosus tissue, was covered with crusts and exudate. It was located in the area of maximal tension point over a contracture scar. The tumor was excised with a 2-cm margin of macroscopically healthy tissue. The defect was covered with a split-thickness skin graft. Post-operative course was complicated by a hematoma which evolved under the skin graft. The defect healed partially *per secundam intentionem*. Histopathological exam showed *carcinoma planoepitheliale spinocellulare keratodes G1 invasivum*. Resection margins were clear. The patient presented at the outpatient department with a granulating wound covering

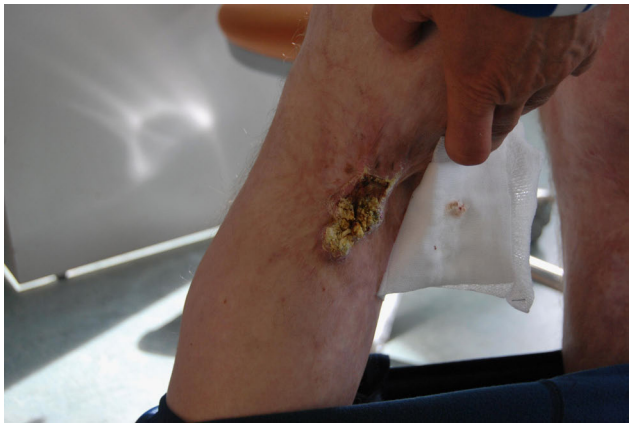

**Fig. 8 – Patient 3 – ulceration in the post-burn scar in popliteal region.**

over 2/3 of the skin graft surface 2 months after the surgery. He is planned for reoperation (covering wound with STSG).

## 5. Discussion

Marjolin's ulcer is not a common clinical manifestation of a malignant skin lesion. Although first described in 1828, it is not a common diagnosis – even if referred by specialists. It occurs in individuals presenting chronic skin ulcerations of various etiology, most commonly a long time after the primary injury. The most common primary lesions to develop Marjolin's ulcer are post-burn scars (83.7%), followed by varicose ulcerations (5.4%), postrtraumatic lesions (4.6%), fistulae in osteomyelitis (4%), pressure sores (0.8%), post-surgical wounds (0.6%), hydradenitis (0.6%) and lupus lesions (0.3%).[21] According to a review of 443 patients presenting Marjolin's ulcer, described in literature performed by Kerr-Valentic et al.,[10] neoplasmatic transformation occurs most frequently in burn scars (76.5%), followed by traumatic scars (8.1%), venous stasis ulcers, osteomyelitis and pressure sores. Other, less frequently occurring lesions leading to development of Marjolin's ulcer are myelomeningocele,[6] surgical scars,[15] posttraumatic scars,[14] chronic wounds such as fistulas,[12] gunshot wounds, dog bites, open fractures and punctures,[1] as well as minor trauma repeated frequently, which were thus not allowed to heal fully.[17] Analysis of lesions location confirms that it may occur in virtually any part of the body. It is most frequently located in the limbs (85.3%), head (8.7%) and trunk (6%),[3,21] which correlates with the observations of the authors of this article. According to Kerr-Valentic et al.,[10] most frequent locations are: lower extremities (53.3%), followed by upper ones (18.7%), trunk (12.4%). There are reports of nose,[3] cheek,[7] neck,[17] elbow,[14], and mons pubis[15] involvement.

Although it was Virchow, who pointed out that chronic mechanical or solar irritation may lead to carcinomatosus evolution, the exact mechanism of malignant transformation in chronic wounds remains unclear. In chronic wounds and scars, especially those causing contractures, there is an altered distribution of abnormally high tension forces. This may lead to extensive mechanical stimulation. On the other

hand, scar tissue seems to be immunologically compromised due to hypoxia and local anemia. Chronic reparative mechanisms lead to elevated exposure to growth factors, which also have a prooncogenic action. Barr et al.[1] described an interesting hypothesis of cocarcinogens acting as a complimentary factor in neoplasmatic transformation in a chronic wound. They described a patient presenting Marolin's ulcer on a hand previously suffering from a burn injury, which was, after a certain period of time, exposed to chemical irritating agent.

Zieliński et al.[21] describe a case of a patient presenting SCC in a massive posttraumatic scar of the lower leg 30 years after a road accident. He suffered from large granulating wounds on his lower leg, which were covered by split thickness skin grafts resulting in partial wound closure, with residual wounds healing by secondary intention. Over the next 20 years small ulcerations appeared, which healed after conservative treatment. Twenty three years after the initial injury three ulcerations suspected of malignancy were excised and diagnosed as SCC. The lesions resulted is not being excised radically. Due to this fact and the multi-focal character of the disease, radiotherapy was implemented. It was complicated by circumferential lower leg skin necrosis, managed by split thickness skin grafts coverage. Due to further recurrent SCC lesions, which could not be radically addressed by surgical methods, the patient was informed of the necessity to amputate the limb. He did not agree for this procedure to be performed.

Kerr-Valentic et al.[10] described 10 cases with Marjolin's ulcer treated in their institution. Most of the patients treated at the University of Utah presented with Marjolin's ulcer resulting from burn injury,[5] traumatic wound,[18] pressure sore[4] and laceration.[20] Most of the lesions were located on the upper extremity and trunk (both 4 cases), scalp and legs (both 1 case). No patient had any symptoms of metastatic disease or died as a result of the treated neoplasmatic disease.

According to some authors, lesions located on the limbs are more likely to result in metastases than those located on the head or trunk. Moreover, this tendency is much more visible in lower than upper limbs (53.80% vs 34.80%, respectively).[13] In their studies Hahn et al.[9] and McCally and Dockerty[12] diagnosed 32% and 22% of their patients respectively as presenting disseminated neoplasmatic disease already at the point of primary diagnosis of Marjolin's ulcer. Barr et al.[1] observed two cases of death due to metastatic disease in patients treated with wide tumor excision ($n=16$) and three such cases in patients who were treated by amputation ($n=18$).

Surgical excision is the treatment of choice in Marjolin's ulcer.[21] The advised excision margin is 2 cm.[16] There is always a question of whether to perform an extremity amputation in case of a lesion located on the limb. It is said that the degree of the resection should be balanced in order to both obtain maximal radical effect and fulfill patient's expectations as far as cosmetical and functional results are concerned. Amputation should be taken under consideration if extension of the neoplasmatic process does not enable a salvage procedure, if osseous structures are involved and in cases of multiple recurrencies.[14,21] Radiotherapy is a valuable complimentary method of treatment both for multiple lesions as for lymph node metastases. There has been no agreement for lymhpdenectomy in Marjolin's ulcer so far. Some authors advocate this procedure in all patients, others suggest it only in case of acral localization.[2,13] Barr et al.,[1] basing on a review of 37 patients presenting Marjolin's ulcer, do not find prophylactic lymph node dissection necessary.

Most of the cases presented in this article evolved in post-burn scars a long time after initial injury. In one case Marjolin's ulcer developed in a chronically irritated lesion (atheroma). Also in this particular case the time gap between the initial lesion and neoplasmatic evolution lasted over 30 years. In two cases (post-burn lesions) there was a high rate of local recurrences and healing aberrations resulting in reoperation need, whereas one of the patients developed lymph node metastases and died due to general thrombosis.

## 6. Conclusions

Basing on the material presented by the authors, following conclusions may be made.

1. Due to high invasiveness, metastatic potential and not uncommon fatal outcome in its natural history and treatment results, Marjolin's ulcer is an entity, which should be suspected and meticulously diagnosed and treated in all individuals presenting alert symptoms such as chronic ulcerations of previously injured skin, not responding to conservative treatment, which present purulent, foul-odor exudate, elevated borders, and verrucous surface.
2. Marjolin's ulcer is a highly-virulent kind of malignant skin lesions due to late diagnosis postponed by false-benign identification of a chronic non-healing wound and to histopathological subcharacteristics of the entity. Fatal outcome is not infrequent and may result from distant metastases or embolytic complications.
3. There is a wide spectrum of morphological and histological forms of Marjolin's ulcer and they may appear at any time distance from the primary injury.
4. In case of surgical treatment there is a high recurrence rate. Therefore the patient should present at regular check-up visits followed by histological verification of new lesions suspected of malignancy whenever it is necessary.
5. Even small lesions suspected of malignant character should not be neglected.
6. Surgical wide excision is the treatment of choice in case of Marjolin's ulcer. In some cases, radiotherapy and limb amputation are advocated. There is no agreement upon prophylactic regional lymph node dissection.

## Conflict of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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