Marjolin’s ulcer: malignant neoplasm arising in scars

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Summary

Malignant neoplasm arising in chronic, non-healing wounds has been known since ages and it was named Marjolin’s ulcer about one hundred years ago. This scar malignancy arises in burned, constantly injured or chronically inflamed skin. Such pathologies as osteomyelitis, decubitus ulcers, chronic fistulas, frost bite, chronic venous failure, vaccination sites, skin graft donor sites and chronically traumatized skin are numbered among the etiological factors. Despite these numerous risk factors this oncological syndrome is rarely diagnosed and commonly mistaken, thus it may often be overlooked. Marjolin’s ulcer may be defined by many pathological types of neoplasms. Squamous cell carcinoma (SCC) is the most commonly identified histological type followed by basal cell carcinoma (BCC), malignant melanoma, sarcomas (fibrosarcoma, liposarcoma, dermatofibrosarcoma protuberans, mesenchymal tumor), mixed tumors: SCC-BCC, SCC-melanoma and others. There is an agreement over the prevention methods with skin grafting of burned areas and excision with simultaneous grafting of ulcerations appearing in non-healing wounds. To date, there has not been a consensus reached over the treatment protocol. Wide surgical excision seems to be the most preferred method. Inoperable cases and recurrences may be treated with radiotherapy alone or combined with chemotherapy.

Key words skin neoplasm • burn scar • scar malignancy • Marjolin’s ulcer


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**BACKGROUND**

Marjolin’s ulcer is an often overlooked pathology arising in burned, constantly injured or chronically inflamed skin. Cancers developing in scar tissues were officially named Marjolin’s ulcer in 1903 by Da Costa [1]. In 1828 Jean Louis Marjolin, French physician, described an ulceration in scar tissue, however without stating if it is capable of malignant transformation [2]. At the same time Dypuytren presented a case where a patient, several years earlier burned with sulfuric acid, underwent amputation because of a cancer that developed in the scar tissue site [3]. Literature contains even earlier reports on scar neoplasms. Earliest from about 100 A.C. by Celsus on cancers developing in burn scars [4].

**ETIOPATHOLOGY AND HISTOLOGY**

For many years the term Marjolin’s ulcer was used as a synonym of burn scar neoplasm [5]. Nowadays the etiology of scar neoplasms has widened. There are several pathologies of skin known to be potential sites of Marjolin’s ulcer development, among them: osteomyelitis [6], decubitus ulcers [6,7], chronically traumatized skin [6], chronic fistulas [8], frost bite [9], chronic venous failure [10,11], vaccination sites [12] and skin graft donor sites [13].

There are various theories concerning the mechanism of scar malignancy development. Scar tissue is generally less resistant to injuries and it heals with difficulty, especially in sites such as the joint area. It is postulated that cells forming the scar tissues release toxins by autolysis and hetrolysis. The healing phase is therefore prolonged and groups of rapidly dividing cells susceptible to mutagens form [14]. Blood vessels and lymphatics regenerate poorly. Scar tissue than becomes an immunologically crippled site where tumor cells can escape the immunological elimination processes [15].

In most cases, histologically, Marjolin’s ulcer is a squamous cell carcinoma (SCC) – 73%, followed by basal cell carcinoma (BCC) – 10%. Malignant melanoma, sarcomas (among them: fibrosarcoma, liposarcoma, dermatofibrosarcoma, protuberans, mesenchymal tumor), mixed tumors: SCC-BCC, SCC-melanoma are less frequent (Table 1) [6,7,11,13,16,17]. The incidence of SCC and BCC in patients with Marjolin’s ulcer is inversely proportional to their occurrence in the general population. Marjolin’s ulcer develops into BCC when the injury leading to scar formation is superficial and spares the skin adnexa which are necessary to regenerate the epidermis within which the basal cells lay.

**DIAGNOSIS, PREVENTION AND TREATMENT**

There is a lag period between the development of Marjolin’s ulcer in a scar tissue and the time of injury. It has been observed that the latency is inversely proportional to the patients’ age. Malignant transformation is delayed in younger injury victims. The older the patient at the time of injury the shorter the lag period. The average latency period is 36 years and the average patients’ age at the time of diagnosis is 52. Male/female ratio is 2:1. Incidence in women is greater only in cases of malignant melanoma [6,7,10,13,16,17].

Lower extremities are the most commonly affected sites – 36% of the cases in our study. Next is the head region (with face, scalp and neck), followed by the upper extremities and the trunk (Table 1.) [6,7,10,13,16,17].

Marjolin’s ulcer is commonly mistaken for an infected ulceration occurring at the scar tissue sites. Changes such as the appearance of flat, non-healing ulcers enlarging in circumference with elevated and indurated borders, foul-smelling, painful with exudate and bloody drainage suggest a malignant transformation. Quite often, additional X-ray may show bone destruction. Surgical biopsy performed in multiple sites is recommended to confirm the neoplasmatic conversion [10,18,20].

Most researchers agree that the best prevention of these scar malignancies is primary skin grafting of the burn sites. Chronic ulcerations appearing in non-healing wounds should be excised and also skin grafted [17,18,19,20]. Unfortunately diagnosis is often delayed. As a result approximately 30% of the cases have enlarged lymph nodes with possible metastasis [6,18,20]. 449 cases reviewed in this article confirmed the highly metastatic potential of Marjolin’s ulcer. Available data showed lymph node invasion in 19% of the cases and 13% had distant metastases (Table 1) [6,7,11,13,16,17]. Compared to the general population, malignant melanoma confirmed high metastatic potential among skin malignancies.

Treatment of Marjolin’s ulcer should be multidisciplinary. Although there has not yet been a
consensus reached over the management protocol, we agree with most of the researchers that surgery is the primary treatment. First of all, excision should be performed with cautery (which is believed to be safer as it may prevent metastasis by preventing tumor cells from being washed into the blood and lymph systems) with the addition of a small margin, for the skin, performed with a surgical scalpel for better healing [18,20]. Excision of ulcers should include a 3–4cm margin of normal skin with muscle and fascia due to the high metastatic potential and recurrence tendency [6,18,20]. If there is a clinically palpable lymphadenopathy, lymph node dissection is recommended [5,6,17,18,20] with an exception for malignant melanoma, where the sentinel lymph node biopsy should be performed regardless of the presence of enlarged lymph nodes. In cases where surgery is impossible or inadequate, radiotherapy alone or combined with chemotherapy should be performed [6,16,17]. Chemotherapy is usually based on 5-Fluorouracil with a combination of Cisplatin and Methotrexate [17].

**Conclusions**

Review of literature suggests that Marjolin’s ulcer is an infrequent lesion. In general this disorder is rarely diagnosed although its etiology is well known. Unfortunately the diagnosis and treatment are usually delayed. Therefore burns, especially full thickness burns, should be skin grafted. Non-healing wounds, fistulas and chronically inflamed skin must be properly treated. Any suspicious lesions that arise within affected areas should call for multiple biopsies as a gold standard. Patients suffering from burns or other skin pathologies leading to the formation of scar tissue or fistulas must have greater vigilance and receive medical help immediately when their fragile scars ulcerate.

**References:**


<table>
<thead>
<tr>
<th>Incidence of Marjolin’s ulcer</th>
<th>Number (%)</th>
<th>Lymph node invasion number (%)</th>
<th>Distant metastases number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histopathology:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>329 (73)</td>
<td>81 (24)</td>
<td>55 (17)</td>
</tr>
<tr>
<td>Basal cell carcinoma</td>
<td>48 (10)</td>
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<tr>
<td>Malignant melanoma</td>
<td>24 (6)</td>
<td>7 (29)</td>
<td>5 (21)</td>
</tr>
<tr>
<td>Sarcoma</td>
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</tr>
<tr>
<td>Other</td>
<td>16 (4)</td>
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<tr>
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<td>6 (1)</td>
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<tr>
<td>Squamous-melanoma</td>
<td>5 (1)</td>
<td>unavailable data</td>
<td>unavailable data</td>
</tr>
<tr>
<td>Total</td>
<td>449 (100%)</td>
<td>87 (19)</td>
<td>60 (13)</td>
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| Location:                                          |            |                                |                               |
|---------------------------------------------------|------------|                                |                               |
| Lower extremities                                 | 162 (36)   |                                |                               |
| Upper extremities                                 | 130 (29)   |                                |                               |
| Head                                              | 81 (18)    |                                |                               |
| Trunk                                             | 76 (17)    |                                |                               |
| Total                                              | 449 (100%) |                                |                               |

**Table 1. Pathology and localization of Marjolin’s ulcer [6,7,11,13,16,17].**

Ochenduszkiewicz U et al – Marjolin’s ulcer
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