C A S E R E P O R T S
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Giant exophytic Marjolin's ulcer of the lower leg after a gunshot wound

Gigantski egzofitični Marjolinov ulkus na potkolenici posle sklopetarne povrede

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Abstract

Introduction. Marjolin's ulcer is a skin malignancy that occurs on a scar or chronic wound. It most commonly occurs on a burn scar. Squamous cell carcinoma is the most common type of this tumor in more than 90% of cases. The rate of this rare malignant transformation is 1–2%. Marjolin's ulcer is more aggressive than other skin cancers. Wide excision is the treatment of choice. Recurrences are common. We present a large exophytic carcinoma of the lower leg as a rare form of this tumor according to the size and type together with reconstruction results. **Case report.** A 52-year-old man was presented with a large exophytic tumor on the left lower leg. The tumor was located at the site of the previous gunshot injury. The latent period was 22 years. Tumor size was 14 × 12 cm. Wide excision was performed (2-cm surgical margin), including the deep fascia, and the defect was closed by a split-thickness skin graft from the opposite thigh. Histology showed well-differentiated squamous cell carcinoma. There were no regional or distant metastases. One year after surgery, there was no recurrence of the tumor. **Conclusion.** Early diagnosis of Marjolin's ulcer and wide excision are mandatory. Surgical margins for excision should be 2 cm, and excision should include deep fascia. Multiple and repeated biopsies of chronic wounds are advised. There is no consensus on the staging of Marjolin's ulcer and lymph node dissection.

Key words:
burns; carcinoma, squamous cell; cicatrix; leg; reconstructive surgical procedures; wounds, gunshot.

Apstrakt

Uvod. Marjolinov ulkus je maligni tumor kože koji se javlja na ožiljku ili na hroničnoj rani. Najčešće se javlja na ožiljku od opekotine. Najčešći tip tumora je skvamocelularni karcinom koji se javlja kod više od 90% slučajeva. Učestalost te maligne transformacije je 1–2%. Marjolinov ulkus je agresivniji od drugih karcinoma kože. Metoda izbora u lečenju je široka ekscizija. Recidivi su česti. Prikazujemo veliki egzofitični karcinom potkolenice, retku formu tumora u odnosu na veličinu i tip tumora, sa rezultatom nakon radikalne operacije i rekonstrukcije. **Prikaz bolesnika.** Prikazan je muškarac, star 52 godine, sa velikim egzofitičnim tumorom na levoj potkolenici. Tumor je bio lokalizovan na mestu prethodne sklopetarne povrede. Latentni period je iznosio 22 godine. Dimenzije tumora bile su 14 × 12 cm. Urađena je široka ekscizija (2 cm od ivica tumora) zajedno sa fascijom, a defekt je pokriven transplantatom delimične debljine kože, uzetim sa suprotne natkolenice. Histološki nalaz je pokazao da se radilo o dobro diferentovanom skvamocelularnom karcinomu. Nisu bile prisutne regionalne ili sistemske metastaze. Godinu dana posle operacije nije bilo recidiva tumora. **Zaključak.** Osnove lečenja Marjolinovog ulkusa su rana dijagnoza i široka ekscizija. Ekscizija treba da bude 2 cm od ivica tumora sa uklanjanjem duboke fascije. Preporuka je da se kod hroničnih rana periodično sprovode multiple biopsije. Stavovi oko stadijuma Marjolinovog ulkusa i disekcije limfnih žlezda nisu usaglašeni.

Ključne reči:
opekotine; karcinom, planocelularni; ožiljak; potkolenica; hirurgija, rekonstruktivna, procedure; rana vatrenim oružjem.

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Introduction

Marjolin's ulcer (MU) is a term used for skin malignancy arising from a scar. This malignant transformation, which is rarely seen, is named after French surgeon Jean-Nicolas Marjolin. Initially, the term referred to squamous cell carcinoma (SCC) that occurs on a burn scar many years after the injury. Later, it was noticed that other types of skin malignancy can occur and that the tumor can occur not only on the scars from the injury but also on the chronic wounds and the sites of chronic inflammation [1]. MU is more aggressive than other skin cancers, with a metastasis rate of 27.5% [2]. The latent period or transition time is about 26 years [3]. Burns are the most common cause of malignant degeneration (68%). SCC occurs in 94% of cases [4]. MU is more common in less developed countries. The most common localization is the lower extremity in half of the patients. Men are more commonly affected than women (2 : 1). MU is most commonly seen at the age of 55 years [5]. The diagnosis of MU is based on anamnesis, clinical presentation, and histological findings after biopsy. Venous ulcers, pressure sores, and chronic hidradenitis are most often mentioned in the differential diagnosis. Different sizes of MU have been reported. Treatment is primarily surgical, with wide excision and skin grafting. Radiotherapy and chemotherapy are usually adjuvant or palliative treatments for advanced cases of MU. Recurrence occurs in about 16.7% of patients [6].

We present a large MU of the lower leg at the site of a previous gunshot injury, with giant proportions for the exophytic form of MU in this region.

Case report

A 52-year-old male patient presented with a large fungoid soft tissue mass on the posteromedial part of the left lower leg. The tumor was located at the middle and distal 1/3 of the lower leg, measuring 14 × 12 cm (Figure 1). The patient had a gunshot injury at the same site 22 years earlier, and the wound healed by secondary intention. The growth of the tumor was slow, accompanied by bleeding and infection. The pain was of medium intensity. There was no distal neurovascular deficit. Inguinal nodes were not enlarged. Radiography showed a great number of metal foreign bodies with no bone damage (Figure 2). *Pseudomonas aeruginosa* was isolated, and the patient was treated with amikacin. In general anesthesia, a wide tumor excision was performed, using margins of 3 cm. Underlying deep fascia was included. The defect was closed by a split-thickness skin graft from the opposite thigh (Figure 3). Histological analysis showed well-differentiated invasive SCC, with histological grade I and nuclear grade I (Figure 4). There were no tumor elements at the edges of the resection, and no tumor cells were found in excised muscle samples. No distant metastases were found either on additional examinations. The skin graft was well

Fig. 1 – Exophytic tumor on the left lower leg, measuring 14 × 12 cm.

Fig. 2 – X-ray of the left lower leg, with a great number of foreign bodies after a gunshot injury.

Fig. 3 – Split-thickness skin graft two weeks after surgery.

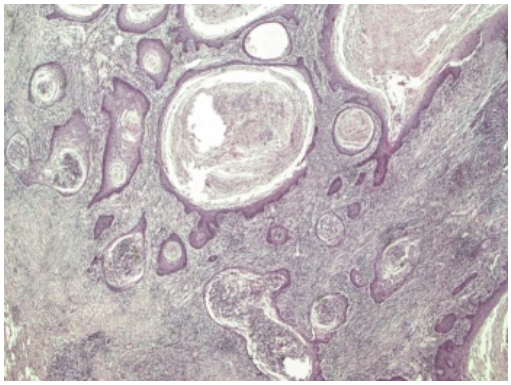

Fig. 4 –Well-differentiated squamous cell carcinoma with incomplete and complete keratinization in the form of horn pearls [hematoxylin and eosin staining, ×200].

consolidated, and the donor site healed well without complication. One year after the surgery, there was no recurrence of the tumor, and there was no regional and systemic metastasis.

Discussion

MU was named after the French doctor Jean-Nicolas Marjolin, who described an ulcer on a burn scar in 1828. In addition to the burn scar, which is the most common cause of MU (in 68% of cases), it can also occur at scars from other injuries, surgeries, chronic ulcers (vascular, pressure sore), chronic osteomyelitis, site of the previous frostbite, scars from skin grafts, donor sites of skin grafts, vaccine scars, fistulas (including AV fistulas), sinuses, chronic suppurative hidradenitis, radiodermatitis, discoid lupus erythematosus, pemphigus, herpes zoster, leprosy ulcer, etc. [4]. In general, MU occurs on scars from wounds that have healed by secondary intention, on chronic wounds, and on the skin with chronic inflammation with frequent disruption of the skin. There is a case of MU that was developed on the surface of the pleura several years after the treatment of empyema with the Eloesser flap [7].

The incidence of MUs is estimated to be 2% in post-burn scars and 1.7% in chronic wounds. It occurs more commonly in older age and is two times more common in men. In a study by Xiang et al. [8], among 140 patients with MU, the initial injury or disease was at the age of 1–75 years, and MU developed at the age of 15–85 years, averaging 53.3 years. The latency period is 11–41 years, with an average of 28.8 years. The age of the patient at the time of injury is in negative correlation with the length of the latency period. MU most often occurs on the lower leg (62%). Other sites are the head (16%), upper extremity (12%), and trunk (10%) [9]. SCC is found in more than 90% of patients with MU. Other malignant tumors are less common: basal cell carcinoma, melanoma, verrucous carcinoma, sebaceous cell carcinoma, fibrosarcoma, angiosarcoma, liposarcoma, leiomyosarcoma, osteosarcoma, dermatofibrosarcoma protuberance, malignant solitary fibrous tumor, etc. [10]. Rare localization and types of MU have been described, such as sebaceous cell carcinoma of the eyelid, 16 years after a chemical burn in a 68-year-old woman [11].

The histological finding of a well-differentiated type is characterized by islands of squamous cells with minimal cellular and nuclear atypia and rare pathological mitoses. Intercellular bridges are present, with emphasized keratinization. In the center of the tumor islands, lamellar concentric keratin masses-horn pearls are presented. Peritumoral and intratumoral stromal lymphocytic infiltrate is pronounced. Granulomatous formations around the foreign body are common in response to the presence of keratin. There are some differences between classic SCC of the skin (non-MU SCC) and SCC in MU (MU SCC). MU SCC occurs three times more often in men and at a slightly younger age (52 years), most often on the lower leg. Non-MU SCC is 1.1–1.7 times more common in men, usually occurs at the age of about 66 years, and most often on the head and neck, which is explained by exposure to UV radiation. Metastases in non-MU SCC occur less frequently (3–23%), and five-year survival is higher (61.5–94.6%). In one-third of patients, the tumor affects the muscle or bone (36%). The rate of lymphadenopathy is 23.6%, but metastases in lymph nodes are present in only 7% [9], which can be explained by a significant degree of inflammation and infection in the tumor region and obliteration of lymphatic channels by scar tissue. Metastases of MU can be lymphatic or systemic, most often in the lungs. The highest frequency of metastases in MU is noted at pressure sore (61%) [12]. Overall 3-year survival is 65–75% and 35–50% in metastatic MU [2].

Many authors have emphasized the process of malignant transformation in MU: reduction of circulation, obliteration of lymphatic channels, weakened epithelium cell junctions, epithelial implantation, releasing of local toxins, genetic interactions, and constant irritation by exogenous factors [13]. No theory has been confirmed, and the pathogenesis of MU is likely multifactorial. Many factors reduce immunological control, with increased potential for carcinogenesis. Reduction of circulation, obliteration of lymph vessels with scar tissue, and reduced activity of Langerhans' cells are significant in the development of MU. Toxic substances released by scar tissue may have mutagenic effects. A mutation in the p53 and fas genes was detected in MU, which is important in the regulation of cell apoptosis and homeostasis. Recent research has indicated the role of biomarkers as indicators for invasivity of MU [14]. It has been noted that there is an imbalance of molecules that regulate cell adhesion (claudin-1, E-cadherin, and desmoglein) due to which cell separation and biochemical transformation of cells are promoted. With the existing epithelial-mesenchymal transition (EMT) and increased production of extracellular components of the matrix (ECM) (increased expression of matrix metalloproteinases − MMPs), the so-called favorable tumor microenvironment (TME) can be developed. The invasion of tumor cells is also accelerated by certain molecules of cell signals (epidermal growth factor receptor, focal adhesion kinase, etc.) [14]. Li et al. [15] showed that survivin, a member of the apoptosis inhibitor protein family, plays a significant role in the formation of MU.

There are two clinical forms of MU, infiltrative and exophytic. The infiltrative type is formed easily, the degree of metastasis is high, and the prognosis is poor. Exophytic form grows slower, and the frequency of metastases is lower [16]. In a study performed on 56 cases of MU, Chalya et al. [17] described the presence of pain in 93% of patients and tumor infection in about 90% of patients. Tumor size ranged from 2 to 15 cm.

The largest infiltrative MU on the lower leg was described by Sakellariou et al. [18], which was 19 × 11 cm in diameter. The largest MU, in general, was described by Saraiya [19] as an ulcerative infiltrative form, measuring 43 × 23 cm. The MU we described in the paper was 14 × 12 cm in size, which ranks it as one of the largest exophytic MU compared to those described in the available literature.

Treatment of MU is primarily surgical: wide excision or amputation in advanced cases of MU in extremities. Because of the tumor size and the margins of excision, direct closure

is seldom possible. Skin graft covering is preferred. Local skin flaps are not advised, except in defects with exposed underlying tendon or bone. Split-thickness skin graft offers a good assessment of tumor recurrence. Lymph node dissection is controversial but can be considered with positive lymph nodes on physical or ultrasound examination. According to Metwally et al. [20], recurrence was noted as early as 3 months and as late as 25 years and can be associated with distant metastasis in some patients. Predictors of recurrence were age, nodal status, and type of defect reconstruction [20]. Adjuvant radiation and chemotherapy are indicated if surgical resection is not possible [4].

Conclusion

Early diagnosis, radical excision with adequate reconstruction, lymphadenectomy in case of enlarged regional lymph nodes, and adequate oncological protocol are the bases of the treatment of MU. Skin grafting of large and deep burns is mandatory. Periodic multiple biopsies are required in patients with chronic wounds, such as lower leg ulcers. We advise wide excision of MU, up to 2–3 cm from the tumor edges, together with the fascia and appropriate reconstruction and therapeutic dissection of lymph nodes in case of malignant lymphadenopathy. Radiotherapy and chemotherapy may be additional therapeutic procedures in metastatic MU.

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