

Marjolin's ulcer associated with ulceration and chronic osteomyelitis *

Úlcera de Marjolin associada a ulceração e osteomielite crônicas

Ermelindo Tavares ¹

José Alberto Soares ³

Luís Ferreira ⁵

Gonçalo Martinho ²

Frederico Vera-Cruz ⁴

Abstract: This report describes a 78-year old male patient with a chronic venous ulcer on his left leg for the past 24 years, complicated by a squamous-cell carcinoma. After staging of the disease, the treatment administered was amputation of the leg above the knee. Marjolin's ulcer consists of the malignant transformation of a chronic ulcerative lesion. It is a relatively rare phenomenon. The malignant tumor most commonly described in the literature is squamous cell carcinoma, followed by basal-cell carcinoma, sarcoma and melanoma. The pathogenesis of Marjolin's ulcer remains to be fully clarified.

Keywords: Carcinoma, squamous cell; Leg ulcer; Osteomyelitis

Resumo: Doente do sexo masculino, de 78 anos, portador de uma úlcera venosa crônica na perna esquerda, com cerca de 24 anos de evolução, complicada por carcinoma espinocelular. Após o estadiamento da doença, o tratamento preconizado foi amputação acima do joelho esquerdo. A úlcera de Marjolin é a transformação maligna de uma lesão ulcerosa crônica. Trata-se de um fenômeno relativamente raro. A neoplasia maligna mais frequentemente descrita na literatura é o carcinoma espinocelular, seguido do basalioma, sarcoma e melanoma. A sua patogenia permanece pouco compreendida.

Palavras-chave: Carcinoma de células escamosas; Osteomielite; Úlcera da perna

INTRODUCTION

Marjolin's ulcer was first described in the 19th century. ¹ It consists of the malignant transformation of a chronic ulcerous lesion. ² A chronic ulcer associated with scarring is the type of precursory lesion most often described in the medical literature. In the majority of these cases, the malignancy found consists of squamous-cell carcinoma, ² generally located on the extremities, particularly on the lower limbs. Latency until malignant transformation takes on average three decades. ¹ Surgery is the treatment of choice and represents the therapeutic option with the highest cure rate and best survival.

Chronic ulcers, particularly on the lower limbs, constitute one of the many comorbid conditions that affect a large number of patients in primary healthcare

units. This report discusses the complication of a chronic ulcer, the rarity of this condition, the possible catastrophic consequences for patients and some of the signs indicative of the presence of malignancy.

CASE REPORT

A 78-year old Caucasian male, a retired agricultural worker living in Santarém (Ribatejo, Portugal), was referred by his attending physician for consultation with a specialist in dermatology in July 2008 because of a chronic venous ulcer on his left leg that for the past year had been progressively growing in size, with abundant, fetid suppuration, increasing pain and expansion of the friable, exophytic area.

The patient reported that the problem had

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¹ Currently participating in the medical intern program in Dermatology and Venereology, Santarém Hospital, Portugal.

² Currently participating in the medical intern program in Orthopedics and Traumatology, Santarém Hospital, Portugal.

³ Assistant physician in Dermatology and Venereology, Santarém Hospital, Portugal.

⁴ Currently participating in the medical intern program in General Surgery, Santarém Hospital, Portugal.

⁵ Assistant physician in General Surgery, Santarém Hospital, Portugal.

begun in 1984 following an episode of thrombophlebitis on his left leg. Since then, despite the application of dressings using various different types of material, the ulcer progressed through periods of partial healing followed by periods of deterioration; however, it never healed completely. In 1995, during a suicide attempt involving a firearm, one of the bullets became lodged in the region immediately below the ulcer, near an area of the lesion, which at that time had almost completely healed. With the entry of this foreign body and its subsequent surgical removal, the condition of the lesion worsened once again. In 1996, the patient was submitted to a skin graft; however, viability was only limited. In 1998, he became lost to follow-up at the hospital.

The patient is now bedridden, hospitalized and totally dependent on others for all his daily requirements. He has ischemic heart disease, had an acute myocardial infarction, and has severe depression, a full prosthesis on his right knee, chronic bronchitis, benign prostatic hypertrophy (BPH) and recurrent acute bacterial dermo-hypodermatitis on his left leg. He was being treated with 450 mg/day of aminophylline, 100 mg/day of acetylsalicylic acid and 3 g/day of paracetamol.

General examination revealed the patient to be depressed and showed crackling and stertors in both lungs. At dermatological examination, an ulcer measuring around 20 x 12 cm was found, with raised, irregular borders and a friable, exophytic area in the upper portion, which was also hardened, with exposure of the bone in the lower segment. There was a purulent, fetid and extremely abundant exudation (Figures 1 and 2). Peripheral adenopathies were not found either in the popliteal fossa or in the left inguinal region.

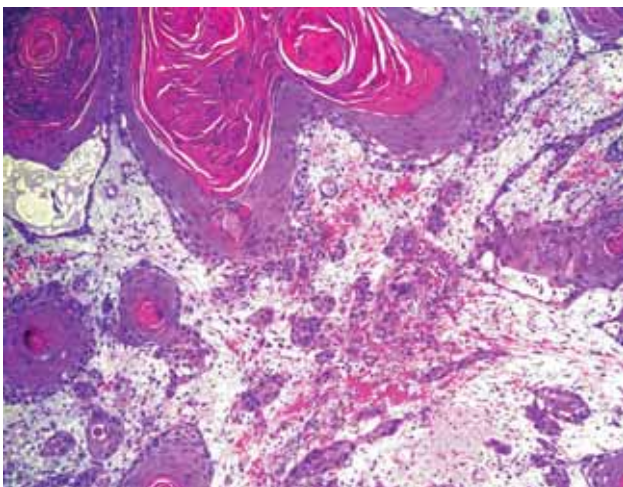


FIGURE 1: Well-differentiated squamous-cell carcinoma

The principal diagnostic hypothesis was a malignant tumor over the chronic ulcerous lesion, i.e. Marjolin's ulcer.

Laboratory evaluation (full blood count, glucose levels, kidney and liver function) was normal. The expansion, sclerosis and bone destruction shown in the x-ray of the left leg was compatible with a process of chronic osteomyelitis of the tibia (Figure 3). No nodular opacity was found at chest x-ray. Computed tomography of the abdomen and pelvis added no further information. Histology performed on the tissue fragment removed from the upper region of the ulcer permitted definitive diagnosis to be made of a well-differentiated squamous-cell carcinoma with deep invasion of the dermis (Figure 4).

Amputation above the left knee was the treatment of choice, taking into consideration the patient's comorbidities, the chronic osteomyelitis and the extent of the tumor invasion. Histological examination of the subcutaneous adipose tissue, the muscle and the periosteum, with no neurovascular invasion.

The patient progressed favorably during hospitalization. In the first month following surgery, the surgical stump healed and there was no recurrence of the tumor. At the 6-month follow-up visit, no inguinal adenopathies were detected, either at physical examination or by ultrasonography. Laboratory evaluation remained unchanged. Abdominal ultrasonography and chest x-ray showed no secondary deposits in the liver or lungs, respectively.

DISCUSSION

In 1828, Jean-Nicholas Marjolin, a French surgeon, first described the malignant transformation of chronic healing processes resulting from burn



FIGURE 2: Exophytic, friable area (greatest magnification)



FIGURE 3:
Chronic
osteomyelitis
of the tibia



FIGURE 4:
Ulcer with
exophytic area
(left or upper
region) and
area of
exposed bone
with the pres-
ence of puru-
lent exudate
(right or lower
region)

injuries. In 1923, DaCosta first coined the expression “Marjolin’s ulcer” to describe malignant tumors forming over burn injuries. Currently, the term is used to refer to any type of malignant tumor located over a chronic sore; however, these lesions most commonly involve burns and chronic fistulae, which, when taken together, constitute around 80% of cases.¹ Less commonly, venous and decubitus ulcers, vaccination scars, chronic osteomyelitis,¹ hidradenitis suppurativa, pilonidal cyst and discoid lupus erythematosus may be involved.³

Osteomyelitis is a well-known precursor of squamous-cell carcinoma. The incidence of Marjolin’s ulcer in chronic osteomyelitis is difficult to evaluate; however, Hobart and Miller reported that Marjolin’s ulcers developed in 1.5% of all cases of chronic osteomyelitis.¹ With respect to the present patient, the following question needs to be answered: was osteomyelitis a precursor of the malignancy? We believe that the probability of the chronic osteomyelitis having been the precursor of the tumor is slight, and that the hypothesis of it being a late sequela of an ulcerous lesion is more likely.

The type of carcinoma most commonly associated with these lesions is squamous-cell carcinoma, which constitutes 75-90% of all cases. Other histological types such as melanoma, sarcoma and basal-cell carcinoma are rare. Most tumors are located on the extremities, particularly the lower limbs. Malignant transformation occurs after a mean of 43 years; however, this period may vary from 10 to 70 years.⁴ Tenopyr and Silverman reported that the time of progression of an ulcer has to be at least three years for

malignant transformation to be considered; otherwise, the hypothesis of a primary lesion causing the ulcer should be raised.⁵

Malignant transformation of a chronic sore is a dynamic process that remains to be fully clarified; however, various factors such as repeated trauma, immunodeficiency, growth factors present in the exudate and changes in tissue vascularization and genetic predisposition may contribute. The onset and/or intensification of pain,¹ fetid suppuration of abnormal volume,¹ exophytic and friable areas, an increase in the size of the lesion, hardening and a tendency to hemorrhage¹ are signs that are strongly indicative of malignant transformation.

Definitive diagnosis is made by histological examination of the lesion. Various biopsies should be made, including tissue from the central portion of the ulcer (sarcomas have this type of distribution) to reduce the probability of false-negative results, since even when tissue is collected from a large area, it may be difficult for the pathologist to differentiate between pseudoepitheliomatous hypertrophy and squamous-cell carcinoma.²

According to some studies, treatment depends on factors inherent to the patient (age, comorbidities) and to the tumor itself (site, extension and the presence or absence of metastases) and must therefore be individualized.⁶ Because of the advanced stage of the tumor at the time of diagnosis, the treatment of choice for most patients consists of radical resection with or without lymph node removal or irradiation, leaving a surgical margin of no less than 1 cm. Amputation is indicated in cases of deep dermal invasion, bone

involvement, hemorrhage, extensive infection and chronic osteomyelitis,^{7,8} as was found in the present case.

Other forms of treatment such as cryotherapy, radiotherapy and chemotherapy were not found to be effective and are reserved for palliative use in patients for whom surgery is contraindicated. With respect to conservative surgery, the question is related to the maintenance of organ function at acceptable levels and effective treatment of the malignancy and of the

infection. This type of surgery generally involves complex and lengthy procedures, the functional results of which are often disappointing with, at times, recurrence of the tumor.^{2,4}

In the medical literature, prognosis in cases of Marjolin's ulcer estimates a three-year survival rate of 65-75%, which increases in cases of well-differentiated carcinomas.² The presence of distant metastases is obviously indicative of poorer prognosis with a 3-year survival rate of 35-50%.² □

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MAILING ADDRESS / ENDEREÇO PARA CORRESPONDÊNCIA:

Dr Ermelindo Tavares
Rua Alexandre Herculano, Nº 26, 2º direito
2005-188 Santarém, Portugal
e-mail: tavares.ermelindo@gmail.com

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