MARJOLIN’S ULCERS AS A CONSEQUENCE OF CHRONIC VENOUS ULCERS AND CHRONIC SKIN INJURY – CASE REPORTS

BŁAŻEJ CIESIELCZYK1, DAWID MURAWA2, PIOTR NOWACZYK1
Department of Surgery, F. Raszeja Memorial Hospital in Poznań1
Ordynator: dr n. med. W. Burchardt
1st Department of Surgical Oncology, Great Poland Cancer Center in Poznań2
Ordynator: prof. dr hab. P. Murawa

In the literature, Marjolin’s ulcers are defined as skin cancers that develop secondarily in areas susceptible to an injury, seized by a chronic inflammation or covered by scar tissue. This paper presents three clinical cases of spinocellular carcinoma, which occurred around long-standing venous ulcers or chronic traumatic skin injury within the lower limbs. All the patients had their limbs amputated. No clinical or radiological qualities of lymphadenopathy were diagnosed. The latest checkups indicated the patients’ good condition without traits of the neoplastic disease. Managing patients with chronic ulcers, regardless of their aetiology, requires that the doctor should have increased oncological alertness. In this case, one of the most important elements of diagnostics is a regular histopathological assessment of the lesion. Only this procedure enables the early and efficacious surgical treatment of potential secondary neoplastic lesions and possible saving of the limb.

Key words: Marjolin’s ulcers, squamous cell carcinoma, chronic wounds, venous ulcers, post-traumatic skin injury

Skin cancers can be divided into 2 principal groups: basal cell carcinomas (BCC, basalioma) and squamous cell carcinomas (SCC, carcinoma spinocellulare). The process of oncogenesis for both groups is complex; it concerns disorders in the regulation of expression of protooncogenes, suppressor genes or genes encoding growth factors.

Spinocellular (squamous cell) carcinoma is a skin neoplasm of much higher malignancy in comparison with basal cell carcinoma. It is characterised by invasive growth and frequently results in metastases to lymph nodes. Taking morphological features into account, two types are distinguished – ulcerating (SCC exulcerans) and verrucose (SCC vegetans). The location of lesions varies – usually it is related with the mucocutaneous borderline (genital areas), lower lip, and areas around the nose and eye sockets. The treatment consists of a surgical resection of the lesion (with a possible transplantation), deep cryotherapy or laser therapy (1). In view of modern research, carcinogenesis and development of squamous cell carcinoma within chronic venous ulcers seems to be a proven process, though it is rare and refers only to 0.21-0.4% of patients with venous ulcers (2). We have not found any reports on the occurrence of basal cell carcinoma within chronic ulcerations. There seems to be no correlation between this neoplasm and chronic venous insufficiency.

The factors predisposing patients to the development of squamous cell carcinoma within the lower limbs are: advanced varicose veins, thromboembolic disease, chronic skin damage and injuries, chronic exposure to sunlight and chronic infections (3). The ulcerating form of squamous carcinoma is very similar to ulcerations formed as a consequence of chronic venous insufficiency, which continues to be the cause of difficulties and errors in diagnosing.

In 1828, the French surgeon Jean-Nicolas Marjolin was the first to use the term ‘cance-
rating ulcerations’ (4). At present, the so-called Marjolin’s ulceration refers to any form of skin cancer that develops in areas prone to injuries, chronically inflamed or covered by scar tissue (5). The development of such ulcerations within the lower limbs and in the area of venous stasis still evokes some controversy.

Below, we present two cases of squamous cell carcinoma diagnosed in a long-standing ulceration as a consequence of chronic venous insufficiency of the lower limbs and one case being the consequence of chronic post-traumatic skin injury.

CASE REPORTS

1. Patient J.T., aged 78, case-book No. 003694/01, was admitted into the Department of Surgery, Franciszek Raszeja Memorial Hospital, Poznań on 23 April 2001 with the diagnosis: ulceratio chronicae et ostitis cruris dex. From 1999 to 2001, the patient was treated within the catchment area of her residence due to chronic venous insufficiency and a right shin ulceration. In spite of the ambulatory application of various drugs, targeted antibiotic therapy and repeated cleaning, it was impossible to reduce the ulceration area. Culture was collected many times (Streptococcus β-haemolyticus gr. G, Staphylococcus aureus, Bacteroides fragilis – Department of Laboratory Diagnostics, Health Care Centre Poznań-Jeżyce). When pressing the granulation tissue, the doctors treating the ulceration observed a suet-like substance and suspected it was thick pus. In the final period, the ulceration worsened and attacks of fever occurred. On admission, the patient had a painful ulceration in her shank, 20 cm in length and 15 cm in width. An X-ray of the right shin showed bone defects on the side of the medial tibia. An ultrasound of the groin showed no traits of metastases within the lymph nodes. The suppurative granulation and the inflamed bone structures were operatively resected (necrotic lesions comprised about a half of the volume of the tibia). Material for bacteriological and histopathological examinations was collected. The result of the bacteriological examination was: Pseudomonas aeruginosa (Department of Laboratory Diagnostics, Health Care Centre Poznań-Jeżyce). A targeted antibiotic therapy was implemented. The result of the histopathological examination was: infiltratio carcinomatosa – carcinoma planoe epitheliale keratodes G2 (Grażyna Zengte ler’s Histopathological and Cytological Unit). The right lower limb was amputated at the level of the lower third of the thigh. The post-operative course had no complications.

2. Patient H.M., aged 83, case-book No. 009704/03, was admitted into the Department of Surgery, Franciszek Raszeja Memorial Hospital, Poznań on 30 September 2003. For 50 years, she had had symptoms of chronic venous insufficiency in the form of venous thrombosis of the lower limbs and ulcerations of both shanks. In 1993, she underwent an amputation of the right lower limb at the thigh level due to squamous cell carcinoma. For 10 years, she had had ulcers on the left shin. For about one year, the state of the ulceration had worsened. Specimens were collected in an ambulatory way and the histopathological result was carcinoma planoe epitheliale keratodes G2 (Grażyna Zengteler’s Histopathological and Cytological Unit). Initially the patient did not agree to operative treatment and radiotherapy was applied without success (total dose 20 Gy).

On admission, within the medial surface of the left shin, she had a persistent, oozing, fetid ulceration sized 10 x 8 cm (fig. 1), secreting a suet-like substance (of thick pus character) when pressed. An ultrasound of the groin

Fig. 1. Patient H.M., ulceration of the left calf
did not show metastatic lesions within the lymph nodes. The limb was amputated at the level of the lower third of the thigh. The post-operative course had a complication caused by an infection in the stump. After draining and implementation of targeted antibiotic therapy, the infection regressed. After the stump had healed, the patient was discharged in good general condition on 24 October 2003. At present, the patient is in good general condition without traits of the neoplastic disease. The latest check-up was on 12 October 2006. The patient is sedentary due to her age and condition after the amputation of both limbs.

3. Patient J.J., aged 53, case-book No. 002250/07, was admitted into the Department of Surgery, Franciszek Raszeja Memorial Hospital, Poznań on 21 February 2007 with the diagnosis: carcinoma planoephiteliale G2 of the left foot (Grażyna Zengteler’s Histopathological and Cytological Unit). In 1975, the patient suffered a foot injury while working at a construction site (the foot was crushed by a beam falling from a height). After an unsuccessful reconstruction attempt (necrosis around the toes), the patient underwent an amputation at the forefoot level. Due to the insufficient amount of skin, the front of the stump was covered with skin transplants (the healing process lasted 11 months). After complete healing of the stump in 1977, for half a year there were attempts to use special orthopaedic footwear – without success (it caused injuries and provoked the opening of the wound). The stump around the transplants was very susceptible to minor injuries. Wounds repeatedly appeared around it and healed spontaneously. From 2004, the patient had a chronic ulceration within the forefoot stump, which would not heal. In December 2006, a swab was collected from the ulceration – S. aureus (“Labo-Med” Medical Diagnostics Centre). Targeted antibiotic therapy was applied, however it brought no effect. In that period, the patient began to complain about strong pain within the foot and left shank. When the granulation was pressed, an outflow of suet-like contents was observed. In January 2007, the patient observed a tumorous growth on the ulceration, which was resected. Specimens were collected from the ulceration. The result of the histopathological examination was as above. On admission, within the stump of the forefoot, there was an ulceration sized 5 x 6 cm (fig. 2).

An ultrasound of the groin showed no metastatic traits within the lymph nodes. The patient underwent an amputation of the left lower limb at the upper third of the shin. The operative specimen was sent for a histopathological examination. The final result was: carcinoma planoephiteliale keratodes infiltrans G2 (Grażyna Zengteler’s Histopathological and Cytological Unit). The post-operative course showed no complications. The wound healed. The patient had a prosthesis applied and is undergoing rehabilitation. He was discharged on 23 March 2007.

DISCUSSION

In recent years in the diagnostics of secondary proliferative lesions, in view of chronic venous insufficiency of the lower limbs, there has been an attempt to identify pathogenetic factors and molecular changes responsible for the process of carcinogenesis. Examinations of infections in venous and neoplastic ulcerations (ca planoephiteliale) have shown that HPV virus is absent from cells with neoplastic lesions. Nearly one third of patients with venous ulcerations showed positive PCR to DNA HPV in the material from the lesion, which indicates an expulsion of venous ulceration cells infected with HPV by neoplastic cells (6). Also, expression of p21WAF1/CIP1, p53, bcl-2 and Ki-67 in venous ulcerations and squamous cell carcinomas resulting from ulcerations was examined. It was proven that all the samples from the venous ulcerations were negative as far as expression of p53, p21 and bcl-2 was concerned, and expression of Ki-67 was visible only

Fig. 2. Patient J.J., ulceration of the forefoot stump
in some areas of the ulceration. No expression of p53 and p21 were proven around the lesion, which points to a different process of carcinogenesis than in the case of carcinomas induced by UV radiation (7). Impola et al. also observed a change in the expression pattern of cytoplasmic metalloproteinases within chronic ulcerations of the lower limbs (8).

In spite of no specific diagnostic criteria, the low availability of molecular diagnostics to diagnose early forms of cancer and the indefinite time after which a neoplasm can be expected in an untreatable ulceration, each chronic venous insufficiency and all complications resulting from it should be carefully analysed by the doctor in charge. The right diagnosis is the most difficult element in the treatment of carcinomas that develop on the basis of chronic ulceration. Long-standing treatment of ulceration causes lower oncological alertness. The patient is frequently treated by various physicians (general surgeon, vascular surgeon, dermatologist), who may not observe the process of change in the character of the ulceration. While periodical culture collection from the wound belongs to routine ambulatory practice, the collection of subsequent histopathological specimens (especially in the case of an initial non-neoplastic diagnosis in the first result) is rarely used. Failure to do so may result in a serious diagnostic error. It must be remembered that chronic ulceration (venous, ischemic or inflammatory) is a place of carcinogenesis. We have observed that ulcerations with a rapid growth of granulation, which when pressed, secrete a suet-like substance of the thick pus character, are particularly suspicious.

Patients after the sixth decade of life should be given the greatest care (3, 9) because the occurrence of neoplasm is most frequent in this age group. Clinical squamous carcinomas resulting from chronic ulcerations develop above all on the sides of the ulceration and rarely occur in its centre. Their shape may adopt the form of a wart, erosion, nodule or a cauliflower-like form (3). Although research says that the average time span between the formation of ulceration and cancer diagnosis is about 25 years and no cancer has been diagnosed in ulcerations aged less than 3 years (2, 10, 11), each ulceration that does not improve, worsens or is atypical should be an indication for a biopsy (9). Early diagnosis is very important.

Baldursson et al. examined a group of 25 patients selected from the Swedish Inpatient Register and the Swedish Cancer Register, all of whom had SCC that developed secondarily to venous ulceration. They analysed specimens from the neoplastic lesions and defined the cancer grading once again. They found that while the patients had venous ulceration diagnosed on average at the age of 56.4 and cancer in the ulceration diagnosed on average at the age of 78.5, their survival median was about 1 year and the prognosis was related to the degree of histological malignancy of the neoplasm (9, 12).

It is assumed that squamous carcinomas, which form secondarily in areas exposed to chronic irritation, an injury or inflammation, are more aggressive than primary neoplasms and that they have a higher tendency to local relapse and distant metastases (5). The treatment of well-differentiated tumours should include a resection with a wide margin and the covering of the defect with a transplant. In the case of moderately and poorly differentiated tumours (G2 and G3), it is necessary to take amputation into account (9, 13), which some consider to be the treatment of choice (12) and in some cases, it is even necessary to take hemipelvectomy and hemicorpectomy into account (13). Regardless of the method of treatment, a check-up is always necessary in order to exclude local relapse and metastases in the lymph nodes as well as distant metastases (there are reports on the presence of metastases in the lungs) (3). For example, Lifeso and Bull recommended preventive resection of regional lymph nodes or radiotherapy of the regional lymph flow in all patients treated due to Marjolin’s ulcers (12). This procedure arouses great controversy, however. Nevertheless, more recent publications on the subject also assume radiotherapy (13) or resection of inguinal lymph nodes (11) as some of the therapeutic possibilities. An interesting alternative seems to be the biopsy of the sentinel node in order to exclude the presence of metastases in local lymph nodes. Eastman et al. made an intraoperative identification of the sentinel node (the colloid and dye method) in 6 patients with Marjolin’s ulcers (squamous cell cancer) formed on the base of burn scars and without clinical lymphadenopathy. The sentinel node was identified in 5 patients. In 4 of the patients, histopathological micrometastases of squamo-
us cell cancer within the collected nodes were found (4).

The presented patients did not undergo lymphadenectomy because the result of the ultrasound of the groins did not evoke any suspicion.

Similar to other authors (9, 14), we think that the treatment of Marjolin’s ulcers should not include radiotherapy. This type of treatment does not guarantee effective eradication of the tumour and may be the cause of formation of a chronic wound (9). Patient H.M., due to her initial disagreement to operative treatment, had radiotherapy, but without success.

To sum up, it is necessary to stress the role of early diagnosis of neoplastic lesions. This enables potential treatment and saving a limb, which is a great advantage to the patient. Perhaps early diagnosing and differentiation of neoplastic and non-malignant lesions will be possible soon due to the spreading of methods of molecular diagnostics. It is necessary to remember to collect several specimens if the ulceration does not react to treatment, its state is worsening or its morphology evokes our suspicions in any way.

REFERENCES


Received: 7.05.2007 r.
Adress correspondence: 61-312 Poznań, ul. Glebowa 17