Bowen's disease and basal cell carcinoma in a renal transplant recipient – case report

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Abstract

The increased risk of carcinogenesis is a well-known complication in patients after transplantation. It was proved that it is mainly caused by the necessity of use of immunosuppressive drugs. The most frequent tumours are skin cancers, among which the following are the most prevalent: Kaposi's sarcoma, squamous cell carcinoma and Bowen's disease as its *in situ* form, and basal cell carcinoma. Neoplastic lesions in immunosuppressed patients are characterized by their occurrence in younger patients, mainly in males, more frequent extracephalic location and formation of large tumours. Depending on the lesion location, its size and histological type, various treatment methods are used, such as cryotherapy, local application of imiquimod or 5-fluorouracil ointment, laser excision (CO_2, Nd-YAG), photodynamic therapy and surgical excision. The prophylaxis includes education of patients, self-examination of the skin, avoiding sun exposure, photoprotection and actinic keratosis treatment. This article presents a case of a 60-year-old men who developed Bowen disease and basal cell carcinoma after the renal transplantation. Both skin lesions were surgically excised with a margin of healthy skin and the patient was educated about the importance of prophylaxis.

Key words: Bowen's disease, basal cell carcinoma, immunosuppression.

Introduction

Organ transplantation is one of the greatest achievements of modern medicine. Better and better surgical techniques and advanced immunosuppressive treatment resulted in both the increased number of transplanted organs in the whole world and life extension after the operation. The kidney is the most frequently transplanted organ, and it is the treatment of choice in the case of end-stage renal disease [1-3]. In organ transplant recipients, simultaneously many different immunosuppressive drugs are used, which is in turn related to a higher risk of adverse effects of the treatment. The most frequent adverse effects of immunosuppressive drugs include above all infections (bacterial, viral, fungal) and an increased risk of neoplastic disease development, which was proved by numerous studies [1, 4, 5]. Skin malignant cancers, such as squamous cell carcinoma (SCC), basal cell carcinoma (BCC) or Bowen's disease (*in situ* squamous cell carcinoma) and other cancers, such as Kaposi's sarcoma and malignant melanoma (*melanoma malignum* – MM), are observed in 3-10% of kidney recipients [1, 6-8]. Skin cancers in immunosuppressed patients are usually characterized by the occurrence of numerous lesions, higher invasiveness and an increased risk of recurrence after the standard treatment.

Case report

A 60-year old patient reported to the Outpatient Dermatology Department because of an ulceration on the skin of the right wing of the nostril and a tumour on the front side of the left thigh. The ulceration on the skin of the right wing of the nostril measured 0.5 × 0.8 cm, was covered with a scab and had an elevated ridge on the circumference of the lesion (Fig. 1). The tumour on the left thigh attracted attention due to its large size (2.0 × 4.0 cm) and wart-like surface (Fig. 2). The development of lesions was attributed by the patient to the second operation of kidney transplantation performed 6 years ago. In the 1970s, nephrolithi-

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asis was diagnosed in the patient, which resulted in chronic renal failure, and therefore the patient has received an allowance since 1987. After long-term dialysis therapy, the decision was made about kidney transplantation, which was performed in 2002. Since the transplant was rejected, the patient was qualified for another operation that took place in 2004. Additional diseases stated in the medical history by the patient included arterial hypertension, diabetes caused by glucocorticosteroids (administered as immunosuppressive treatment after the kidney transplantation), gastric and duodenal ulcer disease, and also hepatitis C. The patient receives the following drugs for the above diseases: bisoprolol 5 mg, furosemide 40 mg, doxazosin 4 mg, diltiazem 90 mg, short-acting human insulin (10 U at midday), premixed insulin consisting of 40% fast-acting insulin and 60% prolonged-acting insulin (16 U in the morning and 16 U in the evening), ranitidine 150 mg and allopurinol 100 mg. Additionally the patient as immunosuppressive treatment after the kidney transplantation constantly receives tacrolimus 0.5 mg (once daily), mycophenolate mofetil 250 mg (once daily), and prednisone 5 mg (once daily), and remains under the constant care of a transplantation outpatient clinic. During a consultation in the Teaching Hospital Dermatology Outpatient Clinic, specimens of the lesion from the right wing of the nostril and from the lesion on the front side of the right thigh were collected for histopathological examination. In the histological image, the lesion on the right nostril was identified as adenoid basal cell carcinoma (*Ca basocellulare adenoides*) (Fig. 3), whereas the lesion on the left thigh was identified as Bowen's disease (Figs. 4, 5). The skin lesion from the nose with a 4-mm margin of healthy skin and the lesion from the left thigh with a 5-mm margin were surgically excised under local anaesthesia with 1% lignocaine. The patient's postoperative course was uncomplicated.

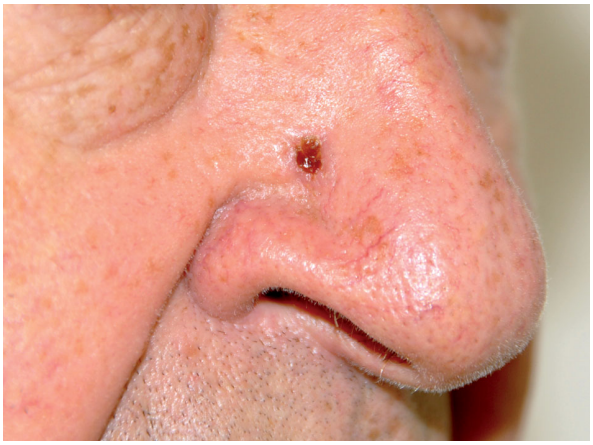

Fig. 1. Basal cell carcinoma on a wing of the nostril

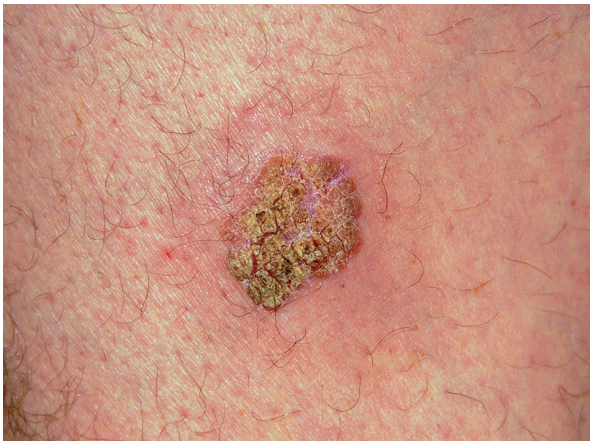

Fig. 2. *In situ* squamous cell carcinoma (Bowen's disease) on the left thigh

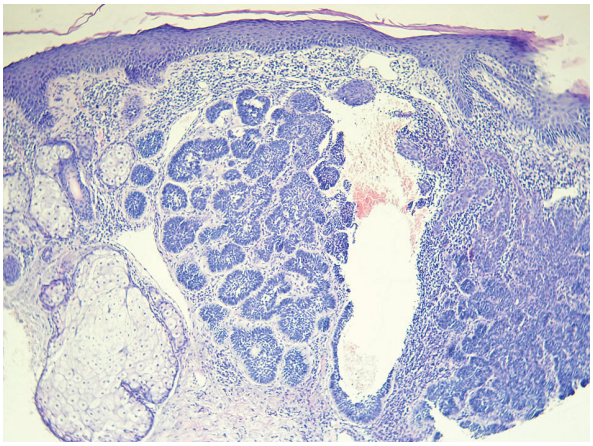

Fig. 3. Microscopy image of a fragment of basal cell carcinoma lesion on the right wing of the nostril. Well-defined lesions of cells with basophilic nuclei, palisade arrangement on the circumference, with glandular "gaps" in some places (H & E staining, 100× original magnification)

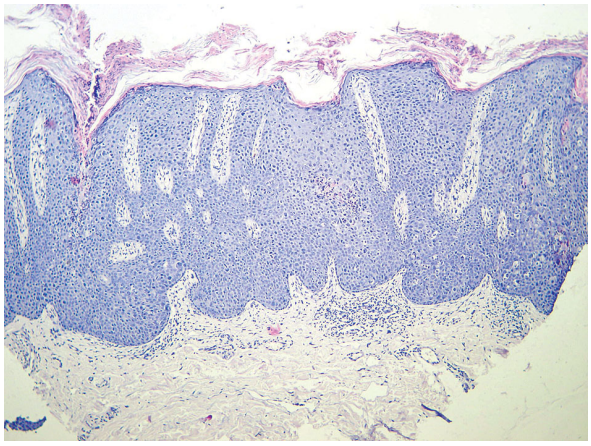

Fig. 4. Microscopy image of a fragment of Bowen's disease lesion (*ca. spinocellulare in situ*) on the left thigh. Acanthotic epidermis with wide bowenoid rete ridges and disorganized cell arrangement (H & E staining, 100× original magnification)

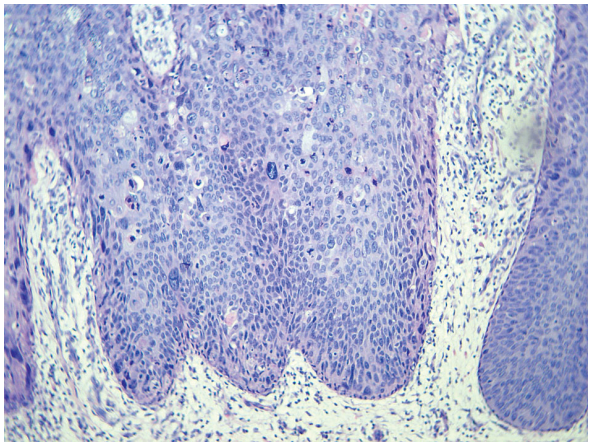

Fig. 5. Microscopy image of a fragment of Bowen's disease lesion (*ca. spinocellulare in situ*) on the left thigh. Numerous cells with atypical nuclei and dyskeratotic cells in the whole thickness of the epidermis (H & E staining, 400× original magnification)

Discussion

Pharmacological impairment of cellular and humoral immunity as a result of using immunosuppressive drugs enables proper functioning of the transplanted organ and causes an increased incidence of complications, such as infections and tumours. The most frequently observed infections include infections with human papillomavirus (HPV), infections with herpes simplex virus (HSV), and then fungal infections, mainly with lipophilic candida-like fungi (*Pityrosporum ovale*) in the picture of tinea versicolor, with *Candida* spp., whereas bacterial infections are less frequent [1]. Neoplastic disease may result from the following mechanisms: transfer of an undiagnosed tumour together with a transplanted organ (which happens occasionally), recurrence of a previous disease or a *de novo* proliferative process [9]. Obviously, the process of carcinogenesis consists of genetic, environmental and iatrogenic factors, and the latter ones seem to be the most important in patients undergoing immunosuppressive treatment after organ transplantation.

Skin cancers are the most prevalent cancers in the population of persons over 65 years of age. According to the literature, basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) account for over 90% of all skin cancers, and the peak in incidence is in the 70^{th}-79^{th} year of life, while the ratio of their prevalence rates is 4 : 1 [1, 10-12]. Also in patients who have undergone kidney transplantations, skin cancers are the most frequent malignant tumours, and the risk of their development is related to the degree of immunosuppression [13, 14]. Despite the ratio of prevalence of BCC to SCC of 4 : 1, in the population of patients after kidney transplantation the ratio increases and changes in favour of SCC [1]. Skin cancers are observed in the course of immunosuppressive treatment in most transplant recipients of mainly the kidneys, liver, heart, lungs and pancreas. It should also be emphasized that the risk of skin cancer metastases is higher in transplant recipients. The risk factors of skin cancers in patients who have undergone organ transplantations are: advanced age, skin phototype I-III according to the Fitzpatrick Classification Scale, long-term pharmacological immunosuppression, many years of exposure to ultraviolet radiation (UV) and presence of numerous actinic keratosis lesions (*keratosis actinica* – KA) [1, 15, 16]. The kidney is the most frequently transplanted organ. In Poland in 2009, kidneys were transplanted to 785 patients, of whom 762 recipients obtained kidneys from deceased donors, while the other 23 patients obtained kidneys from living donors. The most frequent reasons for end-stage renal disease that requires organ transplantation are primary glomerulopathies, interstitial nephritis, polycystic kidney disease and diabetic and hypertensive nephropathy [17]. The most frequent tumours in patients who have undergone kidney transplantation include Kaposi's sarcoma (2.9%), and then SCC (1.5%) and BCC (0.7%) [10]. The average latency period between kidney transplantation and the development of a malignant skin cancer is 6.5 months for Kaposi's sarcoma, 3 months for SCC and 8.5 months for BCC [10].

In patients treated with cyclosporine the risk of skin cancer is 6-8% and it is higher than in the case of other immunosuppressive drugs, such as azathioprine, for which it is 2.2-5.5% [1, 18]. Basal cell carcinomas in patients who received pharmacological immunosuppression in comparison to BCCs occurring in the rest of the population exhibit some differences, such as occurrence in younger patients, more frequent extracephalic location, more frequent occurrence in males and formation of large tumours. Differences in the histological picture consist in a higher incidence of the infiltrating type than the nodular type [19]. The literature provides descriptions of cases of so-called giant BCCs that reach a size from more than a dozen to several dozen centimetres [20-23]. Giant basal cell carcinomas are usually characterized by so-called local malignancy that results in the destruction of tissues and organs due to tumour infiltration. Additionally, giant BCCs are usually observed in debilitated, chronically ill or homeless patients, although they may also occur in patients subjected to long-term immunosuppression [20-23].

The treatment of skin squamous carcinomas depends on the histological type, size and location of the lesion. The treatment of basal cell carcinomas with a clinically low risk of recurrence and of *in situ* carcinomas includes cryotherapy, local application of imiquimod or 5-fluorouracil ointment, laser excision (CO_2, Nd-YAG) and photodynamic therapy (PDT), when laser light of a selected wavelength selectively destroys the population of cancer cells subjected to the effect of a photosensitizing agent [24]. Basal cell carcinomas with a clinically high risk of

recurrence are surgically excised with a margin of healthy tissue. Satisfactory cosmetic effects with high probability of removal of the whole lesion are obtained owing to the use of Mohs micrographic surgery. The method consists in mapping of a specimen in relation to the surrounding tissues, histological examination of the whole border of the excised lesion and possible further skin resection in case of presence of cancer cells within the margin of the collected material [25].

Conclusions

Development of malignant skin tumours is a well-known complication after kidney transplantation. The prophylaxis includes education of patients by recommending skin self-examination, avoiding sun exposure, using photoprotection and treatment of KA lesions. Regular use of photoprotective preparations may prevent further development of KA and the invasive form of SCC and to a lesser degree BCC in non-immunocompetent persons. Also regular skin examination by a dermatologist is recommended. In addition, the role of transplantologists in the prophylaxis and early diagnosis of skin cancers in patients who report to them for follow-up visits after organ transplantation operations should be noted. It should also be emphasized that immunosuppression should be performed using the lowest effective dose that ensures proper functioning of a transplant.

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