Diagnostic difficulties in a case of a female patient with pemphigus vulgaris

Trudności diagnostyczne u pacjentki z pęcherzycą zwykłą

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SŁOWA KLUCZOWE:
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ABSTRACT

Introduction. Autoimmune blistering diseases are mediated by autoantibodies directed against structural proteins of the skin. Pemphigus vulgaris (PV) is the most common type of pemphigus. The main auto-antigen in PV is desmoglein 3, although other antigens such as desmoglein 1, desmocollins, plakoglobin and pemphaxin may also be involved. More than 50% of cases begin with oral lesions. Skin lesions on the face appear occasionally.

Objective. To present an unusual clinical manifestation of pemphigus vulgaris.

Case report. We present a case of a 54-year-old female patient with skin lesions localized on the nose, who due to suspicion of skin cancer not confirmed by histopathology was referred to us by an oncologist. Pemphigus vulgaris was suspected when erosions on the oral mucosa were observed, and this diagnosis was established on the basis of immunological tests. The patient was treated with prednisone and azathioprine, with very good results.

Conclusions. We present the case owing to the difficulties in the diagnostic process and, moreover, due to spectacular clinical improvement after the treatment.

STRESZCZENIE

Wprowadzenie. Pęcherzyca zwykła jest najczęstszą autoimmunologiczną odmianą pęcherzycy. Charakteryzuje ją obecność autoprzeciwciał skierowanych przeciwko strukturalnym białkom naskórka. Ponad 50% przypadków rozpoczyna się zmianami w obrębie błony śluzowej jamy ustnej, natomiast zmiany skórne zlokalizowane na twarzy obserwuje się rzadko.

Cel pracy. Przedstawienie przypadku nietypowej manifestacji klinicznej pęcherzycy zwykłej.

Opis przypadku. Przedstawiamy przypadek pacjentki skierowanej do Kliniki Dermatologii w Zabrzu z Centrum Onkologii w Gliwicach z podejrzeniem raka podstawnokomórkowego skóry nosa z prośbą o konsultację dermatologiczną. U pacjentki był planowany zabieg usunięcia chirurgicznego zmiany, ale ze względu na niejasny obraz histopatologiczny skierowano ją do dermatologa. Pogłębiona diagnostyka, jak również zmiany, które pojawiły się na błonach śluzowych jamy ustnej, pozwoliły na ustalenie rozpoznania pęcherzycy zwykłej.

Wnioski. Przypadek przedstawiamy ze względu na nietypowy obraz kliniczny sprawiający duże trudności diagnostyczne, a także dobry efekt terapeutyczny po zastosowanym leczeniu.

INTRODUCTION

Autoimmune blistering diseases are mediated by autoantibodies directed against structural proteins of the skin. Pemphigus vulgaris (PV) is the most common type of pemphigus in Europe and North America, with an annual incidence of approximately 1–5 per million population [1, 2]. The peak incidence of this disease occurs in patients between the 4th and 6th decades.

More than 50% of cases begin with oral lesions. Mucous membranes are involved in almost all cases, and in some patients oral lesions are the only manifestation of the disease. Painful erosions may occur in the mouth, conjunctiva, pharynx, larynx, esophagus, urethra, cervix uteri and rectal mucosa [3, 4].

Cutaneous lesions appear as flaccid vesicles of various size developing on normal skin or on an erythematous basis. The process may be localized or generalized. The scalp, axillae and groin are frequently involved. Skin lesions on the face appear occasionally. Vesicles rupture easily, producing erosions that may extend at the periphery. Also crusted verrucous lesions may develop [2].

The main auto-antigen in PV is desmoglein 3, although other antigens such as desmoglein 1, desmocollins, plakoglobin and pemphaxin may also be involved in the process [1].

The most important diagnostic test is direct immunofluorescence (DIF) of the skin or mucosal biopsy taken from tissue surrounding bullous lesions revealing linear or granular intercellular deposits of IgG, IgG4 and complement [1, 5]. Indirect immunofluorescence (IIF) on monkey or human esophagus is conducted in order to reveal antibodies specific for PV in the patient's serum [1, 5]. Acantholysis is present in histopathological examination of skin biopsy taken from a new small vesicle or from a marginal part of a larger lesion [1, 2, 5].

Pemphigus vulgaris is a chronic and recurrent disease that requires regular assessment of the effectiveness of treatment and possible side effects [1, 2, 5]. First-choice therapy is prednisone or prednisolone 1.0–1.5 mg/kg when skin and mucous membranes are affected and in localized and less severe processes the doses can be lower (0.5–1.0 mg/kg). If after 2 weeks of treatment the disease is not controlled, doses can be increased to 2 mg/kg. In patients with severe lesions or those with higher risk of side effects of chronic use of corticosteroids, immunosuppressants should be introduced earlier. The first-choice immunosuppressant is azathioprine at a dose of 1–3 mg/kg/day. Second-choice treatment includes mycophenolate mofetil, monoclonal antibodies (rituximab), intravenous immunoglobulins (IVIG), cyclophosphamide and dapsone [1, 5].

Occasionally the clinical image of PV may mimic other dermatoses, including skin cancer. Currently, melanoma and non-melanoma skin cancer (NMSC) are the most common types of cancer in white populations. Of the two types of NMSC, basal cell carcinoma (BCC) accounts for approximately 75% to 80% of cases and cutaneous squamous cell carcinoma (CSCC) accounts for 20% to 25% of cases [6]. Non-melanoma skin cancer occur commonly in the sun-exposed head and neck region (80% to 90%) [7]. Basal cell carcinomas are most frequently found on the nose. The typical lesion is a small, pearly (waxy) nodule with a central depression and elevated border containing dilated blood vessels. It might have a history of ulceration, crusting or bleeding.

OBJECTIVE

Presentation of a PV case in which skin lesions suggested basal cell carcinoma, but after several laboratory tests the proper diagnosis was established.

CASE REPORT

We present a case of a 54-year-old female patient with suspected skin cancer referred to our clinical department by an oncologist. Skin lesions were localized on the nose. Crusts and small ruptures had been present for 5 months (fig. 1). The patient was treated with several topical medications without any improvement, and due to continuous progression of the process the general practitioner referred her to the Oncology Department, where a skin biopsy was carried out. The biopsy was non-diagnostic, and the patient was referred for dermatological consultation. She was hospitalized in the Dermatology Department in February 2014. Several laboratory tests were performed – all blood test values were within normal limits, and bacteriological smear and myco-

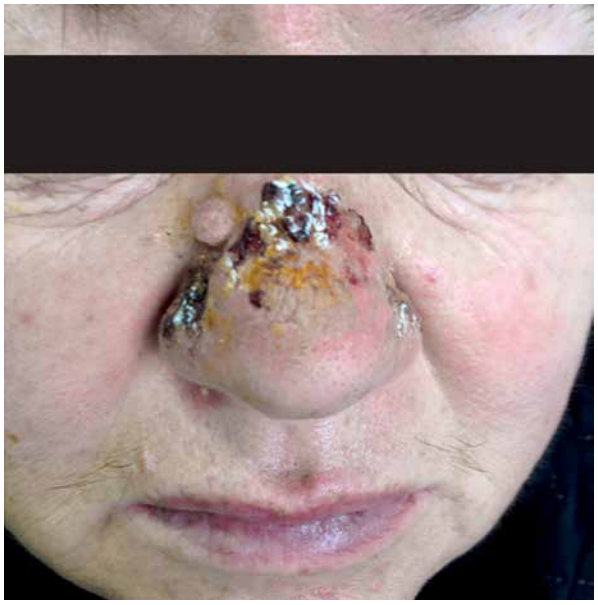

Figure 1. Skin lesions before treatment
Rycina 1. *Zmiany skórne przed leczeniem*

logical examination were negative. The second lesional biopsy was performed and revealed bands of collagen with leucocytic infiltration, spongiosis with dyskeratotic keratinocytes and inclusion bodies. This picture was difficult to establish a clear diagnosis – Herpes simplex infection was suspected (fig. 2). The patient was given topical and systemic antibiotics and anti-viral medications, but no improvement was observed. In April 2014 the patient also presented small ulcerations localized on the oral mucosa. An immunological examination was performed and revealed a very high level of antibodies against desmoglein (> 1 : 1000). The patient was treated with

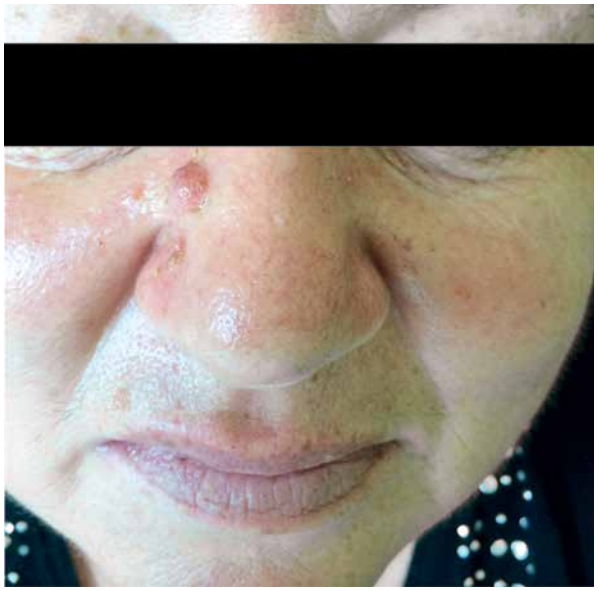

Figure 3. Skin lesions after 3 weeks of treatment
Rycina 3. *Zmiany skórne po 3 tygodniach terapii*

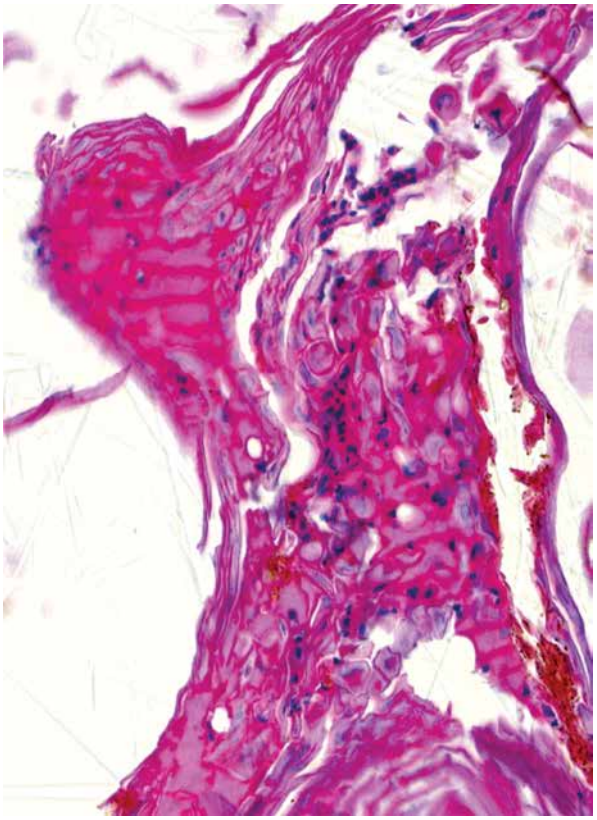

Figure 2. Histopathological examination
Rycina 2. *Badanie histopatologiczne*

systemic corticosteroids (prednisone 50 mg *p.o.* for 3 weeks with gradual reduction of the dose to 30 mg after 2 months and azathioprine 50 mg *p.o.*). The tolerance of therapy was very good, and clinical improvement, visible after the first week of treatment in the nasal region and also on the mucosa, was spectacular (fig. 3). The patient was treated for 6 months, with no further recurrence of lesions. She is still under observation in our department.

DISCUSSION

Pemphigus vulgaris is an acantholytic bullous disease with a potentially fatal course. The laboratory diagnosis is based on direct immunofluorescence showing the presence of *in vivo* bound IgG in intercellular spaces of the epidermis. To determine the clinical subtypes of pemphigus, serum studies allowing characterization of target antigens are obligatory [8, 9]. Pemphigus vulgaris is a rare cause of skin and oral ulceration. In the present case an unusual dermatological manifestation and lack of efficacy of topical treatment were the reasons that the oncologist considered surgical removal of the lesion, but he decided to consult a dermatologist first. The clinical picture could suggest basal cell carcinoma or squamous cell carcinoma, but the biopsy did not

give a clear diagnosis. The unclear clinical and histopathological image could have been caused by long-term inflammatory infiltration and earlier treatment [3]. A second biopsy, histopathological examination, as well as direct and indirect immunofluorescence studies were necessary for definitive diagnosis and the choice of proper treatment. By performing additional studies and establishing the diagnosis of PV we saved the patient from invasive surgical treatment and most likely from a skin graft. If such invasive procedures had been applied, they could have provoked generalized skin lesions and probably lack of response to immunosuppressive therapy.

CONCLUSIONS

We present the case owing to the difficulties that occurred during the diagnostic process and, moreover, due to spectacular clinical improvement after treatment. In every case of skin lesions with unusual presentation and lack of efficacy of therapy, it is advisable to supplement the diagnosis with immunological tests.

Conflict of interest

The authors declare no conflict of interest.

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