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CASE REPORT

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Pemphigus vulgaris mimicking nose tumor

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ABSTRACT

Introduction: Pemphigus vulgaris (PV) is an autoimmune bullous dermatosis. PV clinical presentation is characterized by painful blisters, and skin and mucous membranes erosions. The first symptoms of PV are localized mainly in mucous, followed by the appearance of skin lesions several weeks later. Pemphigus localized as an isolated skin nasal lesion, without any prior mucosal involvement occurs rarely.

Case report: A 55-year-old patient was admitted to the Dermatology Department with the suspicion of pemphigus disease. The patient underwent the excision of a nasal tumor at the Department of Plastic Surgery a month earlier, but the lesion started to reappear. Initially, the histopathological examination suggested a diagnosis of acantholytic acanthoma, removed completely, but further diagnostics at the Dermatology Department confirmed the presence of PV. The patient was treated initially with a corticosteroid course and one month after rituximab administration was added, achieving good clinical response and tolerance.

Conclusions: The cases of localized pemphigus vulgaris, without mucosal involvement may cause diagnostic difficulties. The differential diagnosis should consider both the results of the ELISA test and direct immunofluorescence (DIF) examination to avoid misdiagnosis.

Forum Derm.

Keywords: bullous disease, nasal tumor, skin tumor, plastic surgery, direct immunofluorescence, ELISA, rituximab

INTRODUCTION

Pemphigus vulgaris (PV) is caused by the presence of autoantibodies against desmoglein 3, sometimes in combination with desmoglein 1, that target components of desmosomes, resulting in the loss of intercellular adhesion between keratinocytes and the formation of intraepithelial blistering [1, 2]. Desmoglein 3 is the major component in the mucosa and always affects the mucous membranes [2, 3]. Mucosal manifestations are usually the first symptoms of PV, followed by the appearance of skin lesions several weeks later [1–3]. The most common skin locations are the scalp, face, chest, axillae, groin, and umbilicus [1, 2]. Pemphigus vulgaris localized in the form of isolated lesions on the nose and without mucosal involvement is reported very rarely [3, 4]. PV also tends to localize around natural body orifices, the early appearance of which may be unrelated to pemphigus by dermatologists. Other locations that have been reported in the literature include the medial canthus of the eye, the auricle, the external auditory canal, the anterior nares, the lips, the nipples, the umbilicus, the anus, and the external genitalia of women and men, as well as the fingernails and toenails [5].

CASE REPORT

A 55-year-old patient was admitted to the Department of Dermatology, Venereology and Allergology in Gdańsk to extend the diagnosis of a recurrent tumor of the nasal tip. The skin lesion presented as erosion had been observed by the patient for 6 months. Initially, it affected only the left ala of the nose, where a full-thickness skin graft from the right arm was used to remove the lesion suspected of being malignant skin cancer. The procedure took place at the Department of Plastic Surgery and removed lesion was sent for histopathological examination, which resulted in

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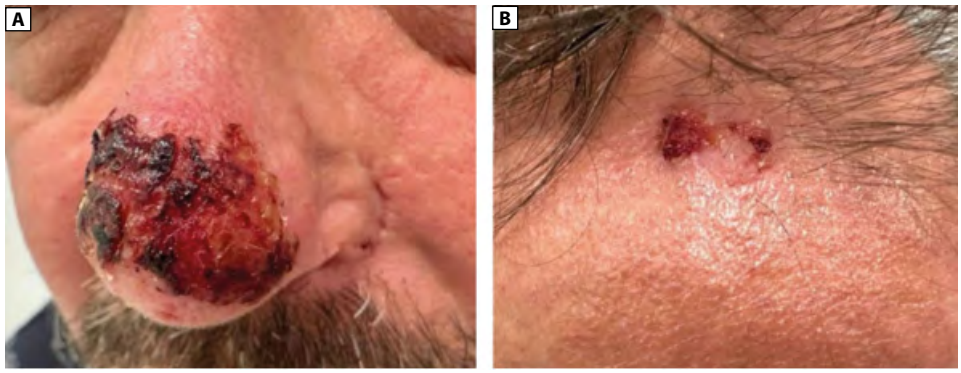

Figure 1A, B. The patient's clinical picture during the first consultation at the Dermatology Department, after the recurrence of erosions on the tip of the nose and first onset on the forehead

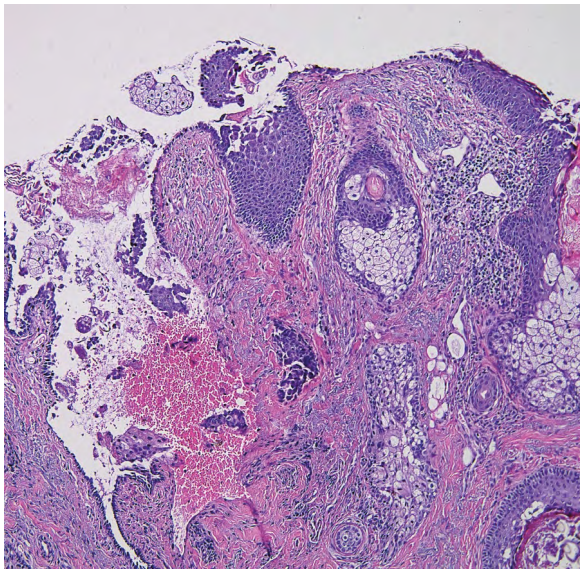

Figure 2. Histopathological image in hematoxylin and eosin staining of intraepithelial acantholysis

Table 1. Patient's direct immunofluorescence (DIF) results

Immuno-globulin	Deposits	Localization	Intensity
IgG	–	Spinous layer of the epidermis	+++
IgA	Granular	Dermal-epidermal junction	+++
IgM	Granular	Spinous layer of the epidermis Dermal-epidermal junction	+
C1q	Fine-grained	Dermal-epidermal junction	+++
C3c	Granular	Spinous layer of the epidermis Dermal-epidermal junction	+

C1q — complement component 1q; C3c — complement component 3c; IgA — immunoglobulin A; IgG — immunoglobulin G; IgM — immunoglobulin M

the acantholytic acanthoma, being removed completely. At this stage, the pathologist suggested also the possibility of pemphigus disease. After one month the patient noticed the reappearance of a lesion spreading around the tip of the nose. Also, frequent and recurrent nosebleeds occurred and the patient noticed erosions within the oral cavity. Due to the above, the patient was consulted at the Dermatology Department, where exhibited one large skin erosion on the nose covered with crusts, as well as another one on the forehead (Fig. 1). During hospitalization, a biopsy was taken for the histopathological examination (HPE). The examination revealed the presence of intraepidermal blisters caused by acantholysis, with the basal layer remaining connected to the basement membrane. Additionally, an inflammatory infiltrate consisting primarily of lymphocytes, eosinophils, and neutrophils was observed in the surrounding dermis (Fig. 2). Direct immunopathological examination (DIF, direct immunofluorescence) of a skin sample confirmed positive fluorescence for pemphigus (+++), shown in Table 1. The serum test for circulating autoantibodies (ELISA) revealed an increased titer of autoantibodies against desmoglein 3 (titer level 7.1). Biochemical blood tests were performed, without any major abnormalities apart from an increased level of antinuclear autoantibodies ANA-Hep2, in titer 1:320, granular type, and increased titer (+++) of anti-Mi2 (myositis-associated autoantibodies). General examinations such as chest X-ray, abdominal ultrasound, and tests for Lyme disease, hepatitis B and C, HIV, tuberculosis, and cancer markers were taken. The results of all the performed tests led to the diagnosis of pemphigus vulgaris.

During the patient's first hospitalization at the Department of Dermatology, the treatment with prednisone at a dose of 30 mg/day was delivered with planned rituximab treatment initiation. At a follow-up a month later, due to the patient's well general condition seen in tests, rituximab was administered at a dose of 1000 mg *i.v.* with a maintained dose of systemic steroid, achieving (after another month) good clinical response and tolerance (Fig. 3, 4).

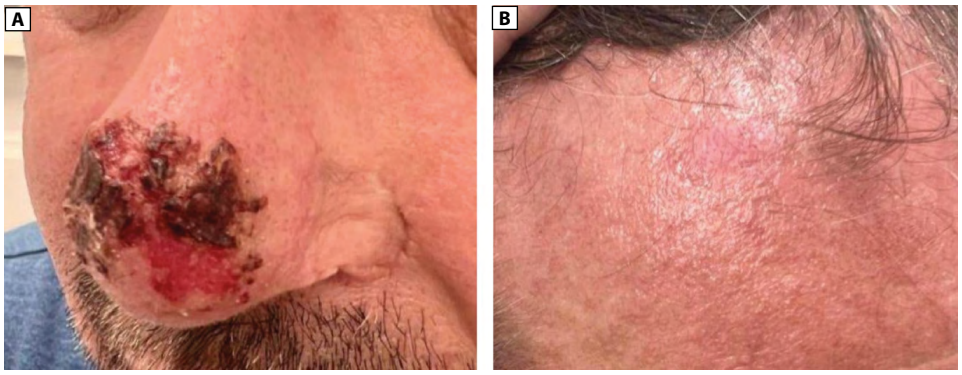

Figure 3A, B. One-month treatment follow-up with rituximab at the dose of 1000 mg *i.v.* in combination with prednisone 30 mg/day

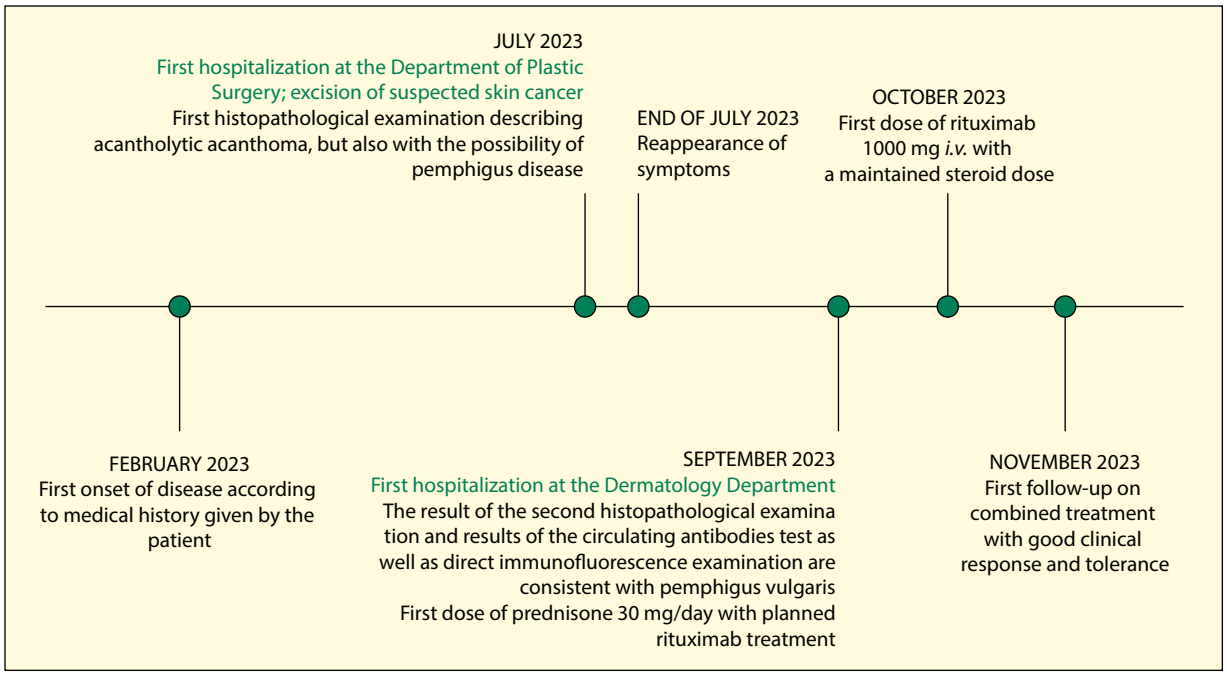

Figure 4. Timeline of a disease progression and provided health care

DISCUSSION

According to the literature, the present patient's case is an uncommon example of PV with an initial localization on the nose, which persisted for 6 months without mucosal involvement, and to that the lesion was probably treated surgically at first. Acanthomas are benign tumors of epidermal keratinocytes, that present with a wide range of histological patterns including epithelial acantholysis, and present as an asymptomatic keratinizing papule or nodule, that clinically documents a tendency for older patients, localized predominatingly on the trunk [6]. It is important to consider acantholytic acanthoma typically appears as a solitary, hyperkeratotic papule, in contrast to acantholytic dermatoses such as pemphigus [7].

In the present case, histopathological examination (HPE) was conducted twice. The first one was performed following the surgical excision. At the Dermatology Department, a second HPE was carried out, complemented by direct immunofluorescence (DIF) and ELISA tests. Although HPE is not typically required for diagnosing bullous diseases according to standard diagnostic protocols, it is often helpful in suggesting atypical cases like ours. Standard tissue staining with hematoxylin and eosin in cases of bullous diseases does not reveal the characteristic features to the pathologist.

Therefore, it's important to highlight the accuracy of the HPE results depends on close collaboration between an experienced clinician and a skilled pathologist. As demonstrated by the present case, it is worth remembering the

presence of acantholysis is not exclusive to bullous diseases [8]. The recurrence of skin lesions noticed by the patient after the surgery suggested Nikolski's sign, triggered by the procedure, which prompted the diagnosis of pemphigus disease and was later confirmed by DIF examination. However, it should be added that the DIF test results showed in this case are not characteristic of pemphigus vulgaris.

The differential diagnosis of the present patient should take into consideration the results of other autoantibodies and immunopathological examination [9]. In the case of dermatomyositis (DM), antiMi-2 autoantibodies have low specificity and are present in a range from 2% to 38% of adult patients. This disease is often characterized by suggestive clinical views including Gottron's nodules (pathognomonic), scarf symptoms on the neck, and general symptoms such as fever and weakening of muscle strength, mainly of the shoulder and hip girdle [10]. In the present patient (apart from autoantibodies anti-Mi-2) nothing clinically indicates the diagnosis of DM. A similar situation occurs in the suspicion of systemic lupus erythematosus (SLE), which requires (according to EULAR/ACR criteria) the presence of not only an ANA-Hep2 autoantibody titer > 1:80 but also at least 1 out of various clinical symptoms, that the study patient did not present. It is reported the medications can also cause elevated ANA titers, so pseudo-SLE induced by the therapy, should be excluded [11]. Due to the literature, rare cases of coincidence of dermatomyositis and pemphigus vulgaris have been reported, but there is no evidence of a statistically increased co-occurrence [12]. However, it should be remembered that autoimmune skin diseases often co-exist together [12, 13]. Taking into account the localization of symptoms on the head and the increased titer of ANA and anti-desmoglein 3 antibodies, the possibility of Senear–Usher syndrome should be considered. This syndrome is a subtype of pemphigus foliaceus, also known as pemphigus erythematosus, characterized by plaques and hyperkeratosis on the sun-exposed skin or even lupus-like malar lesions. However, due to the literature, in this disease autoantibodies against desmoglein 1 are more often elevated rather than desmoglein 3 [14].

The first-line treatment for PV contains systemic corticosteroids at a dose of 0.5–1.5 mg/kg/day [1]. The main goal is to control blister formation, facilitating the healing of existing blisters, as well as prolonging remission by using a minimal dose of systemic steroids. Among other drugs azathioprine, cyclophosphamide, methotrexate and dapsone may be used individually or with oral steroids to reduce the dose in cases of high risk of adverse reactions. Dose reduction should be based on response to treatment, as relapse may occur in approximately 50% of patients. In less severe cases, topical calcineurin inhibitors may be used [1, 3, 15]. Rituximab is an intravenously administered monoclonal antibody indicated for the treatment of various autoimmune general diseases, as well as in pemphigus vulgaris in moderate to severe stage. Rituximab can be used alone giving good clinical effect, or in more severe cases, in combination with glucocorticosteroids. This drug combination gives great long-lasting clinical results with a short-term low dose of steroids and also improves the patient's DLQI (Dermatology Life Quality Index). During rituximab treatment, dermatologists need to remember to monitor the progress by testing for autoantibodies against desmoglein 3 in an ELISA test. It is reported that a persistent antibody concentration over 6 months of rituximab treatment indicates a rapid relapse of the disease [15].

CONCLUSIONS

— The cases of pemphigus vulgaris with an unusual location and without mucosal involvement may cause diagnostic difficulties.
— The diagnostic process should include results of serum tests for circulating autoantibodies (ELISA), as well as immunofluorescence (DIF) examination to avoid misdiagnosis.
— Rituximab may be used in unusual cases of pemphigus diseases achieving remission of skin lesions with good tolerance.

Article information and declarations

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Author contributions

Writing: original draft, data curation, conceptualization — MB, MK; data curation — AZ; supervision — RN; writing: original draft, supervision, conceptualization — IK; preparing and assessment of histopathological examination — EGD. All authors contributed to the article and approved the submitted version. All authors had full access to all of the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis. No medical writing or editorial assistance was received in the preparation of this manuscript.

Conflict of interest

The authors report no competing interests.

Ethics statement

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Supplementary material

None.

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