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Atypical Bullous Pemphigoid After Linagliptin Intake

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 77-year-old
Final Diagnosis: Atypical bullous pemphigoid
Symptoms: Bullous skin lesions
Medication: —
Clinical Procedure: —
Specialty: Dermatology

Objective: Unusual clinical course

Background: Bullous pemphigoid is a common pruritic skin lesion reported in elderly patients. It is caused by an immunologic reaction between autoantibodies and hemidesmosome proteins of epithelial cells. The disease is characterized by a symmetrical blister distribution on the body. Diagnosis should be suspected in elderly patients presenting with a tense blister on normal-appearing skin or on an erythematous base. In the literature, several forms of typical bullous pemphigoid after treatment with linagliptin have been reported. However, this is the first reported case of atypical nonbullous pemphigoid after linagliptin intake.

Case Report: A 77-year-old woman presented with multiple erythematous papules and nodules on the upper extremities and trunk. The patient was being treated with linagliptin for diabetes. Diagnosis was made with biopsy and histopathological studies, followed by direct immunofluorescence. The histopathological study showed a subepidermal blister with an underlying polymorphous infiltrate, mainly of an eosinophilic profile. Direct immunofluorescence showed linear IgG and C3 antibodies to hemidesmosomes at the lamina lucida of the basement membrane. Thus, the diagnosis of atypical nonbullous pemphigoid was made.

Conclusions: This report emphasizes the great variety of bullous pemphigoid presentation and the need for a greater level of awareness of the adverse effects of linagliptin. Thus, atypical nonbullous pemphigoid should be considered among the potential differential diagnoses in patients with multiple erythematous papules and nodules on the upper extremities and trunk.

Keywords: Drug-Related Side Effects and Adverse Reactions • Linagliptin • Pemphigoid, Bullous

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/932356

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Background

Bullous pemphigoid is a common cutaneous autoimmune disease [1] affecting mainly elderly patients [2,3] and is associated with high morbidity and mortality compared with a population matched for age, sex, and location [2].The disorder is due to a reaction between specific antigens in the basement membrane on the hemidesmosome of epithelial cells [4]. Diagnosis should be suspected in elderly patients presenting with a tense blister on a normal-appearing skin or on an erythematous base [5,6].

Several atypical types have been reported, including localized lesions [7] and erythematous lesions [3], similar to our case. Bullous pemphigoid can be triggered by drugs, such as diuretics [8], antibiotics, nonsteroidal anti-inflammatory drugs, antihypertensives, antiarrhythmics, antidiabetics, antirheumatics, tumor necrosis factor inhibitors, vaccines, and other agents [8]. We conducted an exploratory search in PubMed on May 20, 2021, using the following query: "atypical bullous pemphigoid after gliptin intake", "dipeptidyl peptidase-4 (DPP-4) inhibitors and atypical bullous pemphigoid", "oral gliptin" AND " atypical bullous pemphigoid". The research did not reveal any articles pertaining the topic. The reported cases of bullous pemphigoid after linagliptin intake had a typical presentation [9], and, to the best of our knowledge, this is the first case report of atypical nonbullous pemphigoid after linagliptin intake.

Case Report

A 77-year-old woman with a history of diabetes (treated with linagliptin for 2 years) and hypertension (taking verapamil for 10 years) presented with multiple erythematous papules and nodules on her upper extremities and trunk (**Figures 1, 2**). The patient had pruritis 1 month prior to the presentation. She had been treated symptomatically with topical steroids and antihistamines, under monitoring. Two months later, the cutaneous lesions resolved, except for the pruritis.

A skin biopsy was performed, and the histopathology study showed a subepidermal blister with an underlying polymorphous infiltrate, mainly of an eosinophilic profile (**Figure 3**).

Direct immunofluorescence showed linear IgG and C3 antibodies to hemidesmosomes at the lamina lucida of the basement membrane. A diagnosis of atypical nonbullous pemphigoid was made.

Subsequently, the patient was prescribed methotrexate (12.5 mg), and her lesions improved.

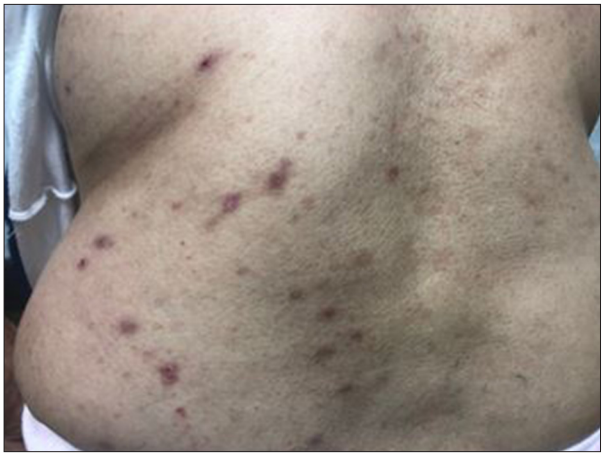

Figure 1. Papules and nodules noted on the flank.

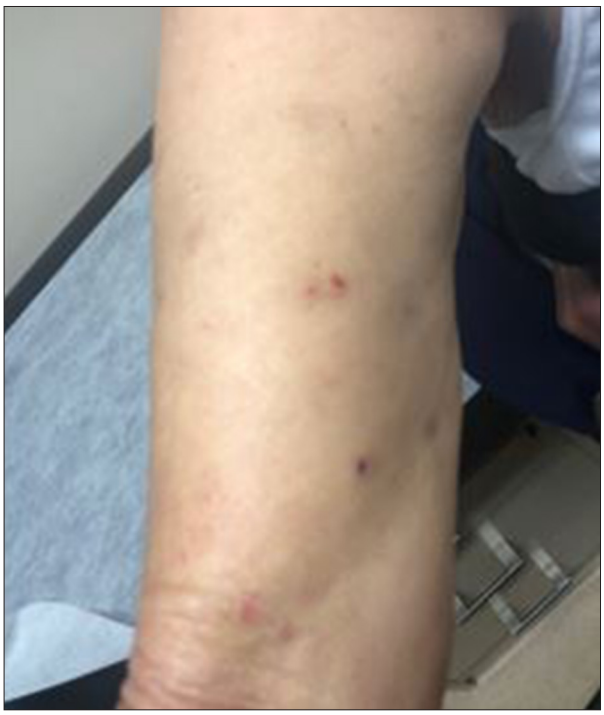

Figure 2. Papules noted on the upper extremity.

Discussion

The incidence of bullous pemphigoid is estimated to be between 0.2 and 3 per 100 000 person-years [4]. It is due to an immunological reaction between antibodies directed against bullous pemphigoid antigen 180 (BP180 or BPAG2) or 230 [2]. Atypical bullous pemphigoid is characterized by nonbullous or nonspecific [3] skin lesions and is reported in 20% of patients with bullous pemphigoid [10]. Early lesions resemble many skin disorders, which hinders the diagnosis [3]. They can manifest as polycyclic or targetoid, nodular, lichenoid, and vesicular lesions [3] and mimic prurigo simplex subacuta or a pruritic variant of atopic dermatitis [11]. Thus, it is warranted to

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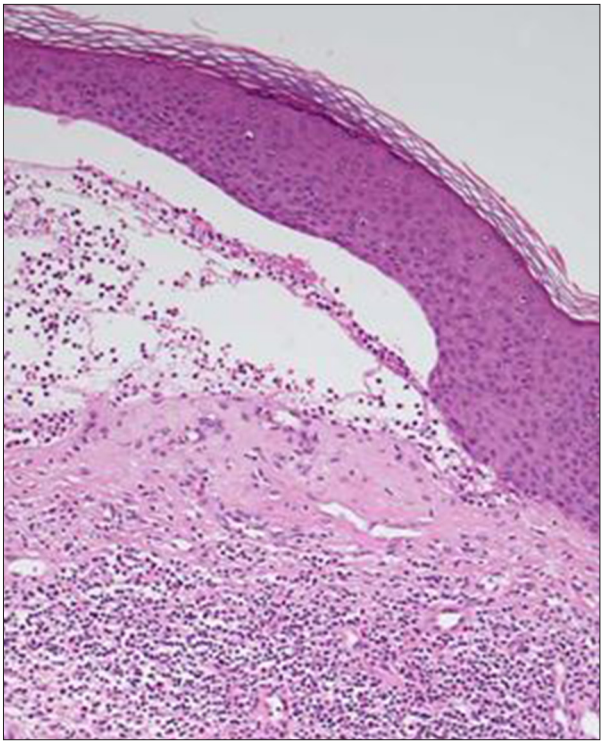

Figure 3. Subepidermal blister along with underlying polymorphous infiltrate, mainly of an eosinophilic profile.

formulate a new guideline for bullous pemphigoid that covers these histological findings of atypical bullous pemphigoid [12]. Compared with classical bullous pemphigoid, drug-induced bullous pemphigoid has an earlier age of onset [13], and mucosal lesions, if involved, are usually mild [14].

Drug-induced bullous pemphigoid is classified into 2 groups based on the resolution of the symptoms upon discontinuation of the drug: drug-induced bullous pemphigoid proper, in which symptoms resolve after discontinuation of the drug, and, drug-triggered bullous pemphigoid, in which symptoms persist after discontinuation of the drug and manifest as classic bullous pemphigoid [13].

Patients with bullous pemphigoid are usually more at risk to develop chronic conditions, including diabetes, which is among the first 3 co-morbid conditions in bullous pemphigoid [15]. To date, few articles have assessed the association between atypical bullous pemphigoid and linagliptin intake. However, as reported by Ganapathineedi et al, atypical presentation of bullous pemphigoid occurred in a patient taking cephalexin for a urinary tract infection; the patient had one blister and a diffuse symmetrical erythema on his body, sparing the face and oral mucosa [16].

The diagnosis of the disease is made clinically and through laboratory examination. Laboratory findings are identical in typical and atypical bullous pemphigoid [3]. Laboratory examination results show eosinophilia [17], and skin biopsy results show inflammatory infiltrates with an eosinophilic profile [4]. Direct immunofluorescence detects a complex of IgG and C3 deposited linearly on the basement membrane [14]. The IgE levels can be elevated in atypical bullous pemphigoid [11] and in typical bullous pemphigoid [18]. Notably, identifying the offending drug is challenging since patients with bullous pemphigoid are usually prescribed many medications [14]. Bullous pemphigoid has a poor prognosis and high risk of recurrence and a leads to a decreased patient quality of life [2,19].

Conclusions

This case report describes an adverse effect of a diabetic drug causing atypical nonbullous pemphigoid, which presented with an unusual clinical picture. Physicians should be alert to the diversity of clinical presentation of this entity, which can lead to misdiagnosis. This report emphasizes the need for a greater level of awareness of the adverse effects of linagliptin.

Declaration of Figures Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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