Case Report

Simultaneous Bullous Pemphigoid and Vitiligo Associated with Adalimumab Therapy in a Patient with Psoriasis Vulgaris

Abstract

Antitumor necrosis factors (TNFs) agents are increasingly being used for the effective treatment of diverse diseases. Due to its extensive use and longer duartion of treatment, there are a growing number of reports of the development of autoimmune conditions such as systemic lupus erythematosus, bullous pemphigoid (BP), and vitiligo associated with the use of anti-TNF agents. We describe a patient who developed BP as well as vitiligo after receiving treatment with adalimumab for plaque psoriasis. To our knowledge, this is the first case of simultaneous presentation of two diseases related to the use of adalimumab, and this highlights the importance of monitoring for more than one autoimmune event during TNF inhibition treatment.

Keywords: *Adalimumab, bullous pemphigoid, vitiligo*

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Introduction

Adalimumab, a human monoclonal tumor necrosis factor (TNF) inhibitor, is approved for the treatment of psoriasis in adult patients.[1] It is usually well-tolerated; however, several cutaneous adverse events have been reported during therapy, including immune-mediated skin lesions (e.g., vitiligo).[2] We describe a patient who developed bullous pemphigoid (BP) as well as vitiligo after receiving adalimumab for treating plaque psoriasis. Our case raises pertinent questions regarding the mechanisms leading to the simultaneous development of these two disorders after the use of adalimumab. It is also noteworthy that adalimumab is used for treatment of both BP and vitiligo.

Case History

We present the case of a 45-year-old man who had mild to moderate plaque psoriasis for 10 years, treated with adalimumab (80 mg single dose, administered subcutaneously [induction dose] and 40 mg every two weeks [maintenance dose]). The patient did not have any other associated autoimmune diseases, diabetes or metabolic syndrome. After recieving the third dose during the maintenance therapy, the patient abruptly developed multiple, pruritic, tense blisters, located on both arms and thighs, abdomen, and back. Nikolsky's sign was negative. Simultaneously, the patient developed multiple achromic macules and patches on the trunk and hands, corresponding to vitiligo. A diagnosis of BP was made based on clinical, histological and immunological criteria (linear deposits of IgG and C3 at the dermal-epidermal junction by direct immunofluorescence) [Figure 1a-c]. Titres of anti-BP180, anti-BP230, and anti-p200 antibodies could not be assessed. However, antinuclear antibodies showed a titre of 1:40 with a homogeneous pattern but anti-dsDNA antibodies were not detected. Adalimumab was withdrawn and the patient was administered oral prednisone at a dose of 0.5 mg/kg/day for four weeks which was tapered down to 5 mg every week maintaining the remission throughout. Adalimumab at a dose of 40 mg every 2 weeks was reintroduced. One week later the patient developed new lesions of BP along with development of more achromic macules [Figure 2a-d]. Adalimumab was stopped and the patient started ustekinumab.

Discussion

There have been several reports of improvement of BP and vitiligo lesions in patients receiving anti-TNF alpha (α) therapy. On the other hand, the use of these

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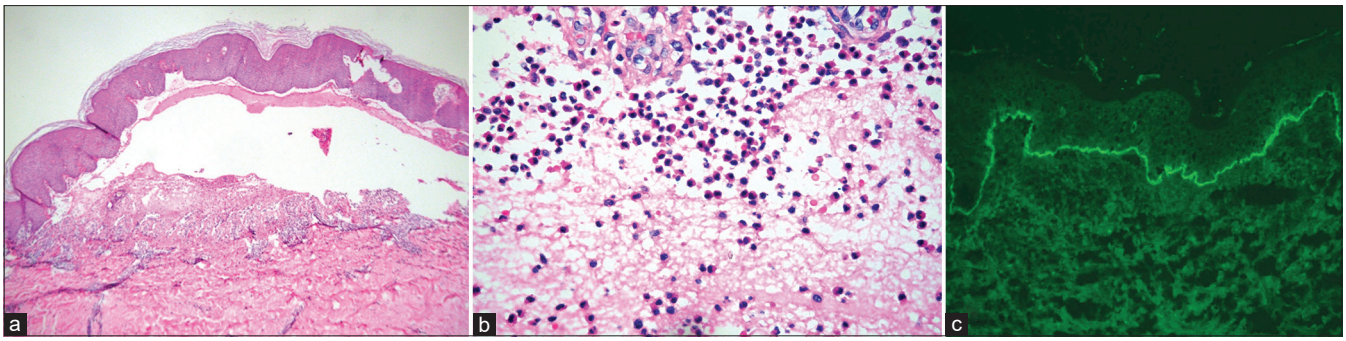

Figure 1: (a) Subepidermal blister with. (b) Dense eosinophils infiltrate in the dermis (hematoxylin and eosin, x10 and x40 respectively). (c) The basement membrane zone shows a linear staining pattern for IgG by direct immunofluorescence (x40)

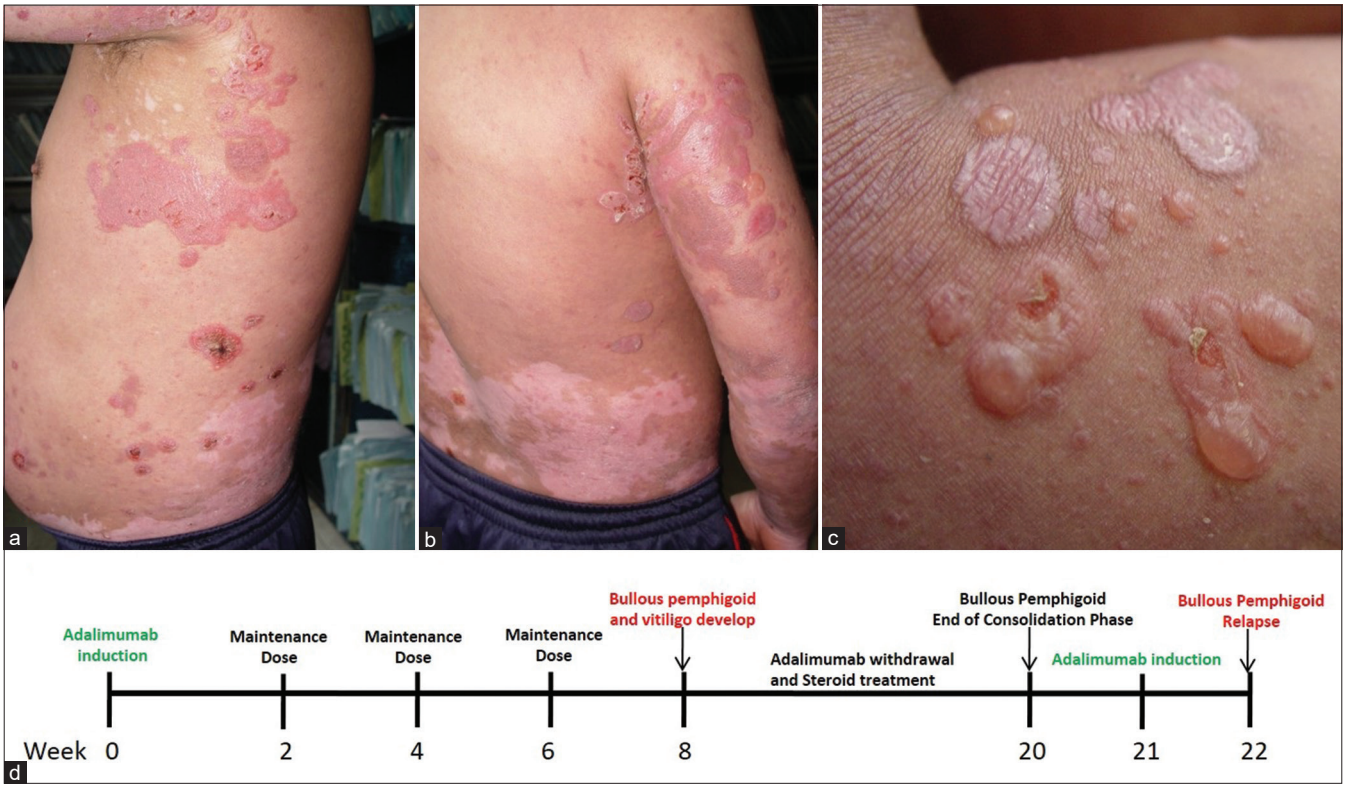

Figure 2: Timeline events during adalimumab therapy. (a-c) Skin lesions after 8-week adalimumab treatment at a maintenance dose of 40 mg subcutaneously. (d) The green color indicates the time in weeks where the induction dose of adalimumab was administered while the red color indicates the time in weeks in which the adverse event was noticed

biologics have been associated with the development of several immune-mediated diseases including vitiligo and BP. The role of anti-TNFα inhibitors in the development of immune-mediated diseases has not been completely elucidated. Several hypotheses have been proposed to explain the mechanisms underlying the development of autoimmunity during the treatment with anti-TNFα inhibitors. *In vivo*, nucleosome numbers (major autoantigens released during apoptosis) increase in patients receiving anti-TNFα therapies. This could lead to an increase in autoantibody production.[3] An alternative theory explains that there is an unbalanced cytotoxic T-cell response, hence autoreactive B cells are no longer efficiently suppressed.[4]

Although BP and vitiligo may have occurred spontaneously, the development of both diseases for the first time in this patient during adalimumab therapy and the relapse of BP and vitiligo after re-administering adalimumab suggests a nonincidental relationship.

The titers of antinuclear and anti-double stranded (ds) DNA antibodies should be routinely measured during adalimumab use to rule out the development of any autoimmune reaction. Further studies are needed to elucidate the mechanisms by which adalimumab can induce immune-mediated skin diseases.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/

her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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