Pemphigoid Diseases as a Sign of Active Psoriasis: A Case Report and Brief Review

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**Key Words**

Pemphigoid · Bullous pemphigoid · Pustular psoriasis · Psoriasis vulgaris · Psoriatic activity · Antigen-altering factors

**Abstract**

**Background**: Overlap of bullous pemphigoid (BP) with chronic psoriatic plaques (CPP) is a common condition. However, the association of BP with pustular psoriasis (PP) is uncommon. Moreover, perilesional erythema and pustular lesions on CPP are accepted as a sign of unstable psoriasis. Unstable psoriasis could be triggered by certain irritant topical treatments against psoriasis. These chemical agents could also induce a localized pattern of generalized PP. Here, we describe BP and PP collision in unstable CPP.

**Objective**: By this observation we suggest that BP could be a sign of active psoriasis. Presumably, psoriasis-induced BP is an inflammation activity-dependent condition.

**Methods**: This study is a case report and literature review.

**Results**: The dramatic response of bullo-pustular lesions to short-term methotrexate (MTX) treatment suggests the rule of ‘no psoriasis, no BP’. Presumably, MTX suppressed the active inflammatory state of the disease for the first time as early as 1929 [3]. Bullous pemphigoid (BP) is the most common associated autoimmune bullous disease. The incidence of BP in psoriatic patients is higher than in the general population. However, the etiopathogenetic relation of the two diseases is not fully understood.

**Introduction**

Pustular psoriasis (PP) can be generalized and localized. Generalized PP (GPP) involves more than two anatomical units of the body. Acute GPP, GPP of pregnancy, juvenile GPP, annular GPP, and localized pattern of GPP are different clinical variants of GPP [1]. Localized GPP often evolves during unstable phases of chronic psoriatic plaques (CPP) due to irritants like coal tar or sudden potent topical steroid cessation [1]. In BP inflammation is a predominant event compared with psoriasis vulgaris. Therefore, pustular formations on CPP and perilesional erythema are signs of the active inflammatory state of the disease [1, 2]. The co-occurrence of psoriasis and autoimmune bullous disease was reported in the literature for the first time as early as 1929 [3]. Bullous pemphigoid (BP) is the most common associated autoimmune bullous disease. The incidence of BP in psoriatic patients is higher than in the general population. However, the etiopathogenetic relation of the two diseases is not fully understood.

**Case Report**

A 77-year-old male patient was referred to the dermatology department with new pustular formations on both crura. The patient had suffered from psoriasis vulgaris for 20 years. He had a BP attack several years previously. On dermatological evaluation, CPP restricted to the knee, elbow and lumbar regions was revealed. Large, itchy psoriatic plaques were found on both medial crura with pustular formations alongside the edge of the plaques (fig. 1). The pustular lesions were restricted to the crura and did not generalize during the hospitalization period. Active erythematous lesions with less hyperkeratosis were found around the CPP. Prior to the pustular development on both crura, the patient acknowledged that he used potent corticosteroid treatment and a week previously he discontinued a topical administration. Pustular and plaque lesions of psoriasis were confirmed histopathologically (fig. 2). There were no signs of infectious diseases and suspicious drug intake, which can trigger pustular formation. Routine blood test was normal. Acute-phase reactant, albumin and calcium levels were normal. No abnormalities were found in the autoimmune markers and endocrine profile. During the hospitalization period bullous skin lesions at the base of the pustular lesions on the crura were detected (fig. 1). A skin sample taken from a bullous lesion revealed subepidermal splitting and rich eosinophil infiltration was found. On direct immunofluorescence examination dermoepidermal linear C3 and IgG deposition was detected (fig. 2). The patient was treated with methotrexate (MTX)
10 mg/week and potent topical corticosteroid. At the end of the second week the pustular and bullous formations completely healed and did not relapse following 3 months of follow-up (fig. 1).

Discussion

There are some comorbid conditions with BP such as dementia, cerebrovascular events, Parkinson’s disease, bipolar disorders, diabetes mellitus, autoimmune diseases, and psoriasis. The association of psoriasis with autoimmune bullous disease is very common [8]. The incidence of BP in chronic plaque-type psoriasis is higher than in PP. Usually, the diagnosis of psoriasis precedes BP by 20 years [8]. The opposite is rare. Bullous lesions are usually restricted to the CPP. BP in relation with psoriasis usually evolves at an early age compared with sporadic BP. Topical corticosteroids, topical anthralin, coal tar and ultraviolet (UV) radiation might be triggering factors for the development of BP in psoriatic patients [8]. In our case, bullous formation was developed without any triggering factor. Spontaneous BP development restricted to the CPP was shown in one report [9]. In figure 1, clinically double-splitting (subcorneal and directly beneath the pustular lesions), subepidermal splitting is obvious. No pustules and bullae were found on intact skin. Furthermore, the location of bullous lesions was at the same line where pustules were formed.

MTX is a one of the effective treatment options in chronic plaque-type psoriasis. However, MTX is not a drug that is commonly relied on for BP treatment, despite some reports suggesting MTX administration in BP management. On the other hand, MTX administration shows good results in psoriasis and BP overlap conditions. Localized GPP demonstrate an excellent response to MTX treatment, while other GPP demonstrate a moderate-to-good response [10]. In this patient, it was astonishing to see how the bullo-pustular lesions disappeared following treatment with two doses of MTX 10 mg/week. We can speculate that MTX probably inhibited active inflammation in unstable CPP and suppressed the recently flared hyperinflammation, which consequently led to the vanishing of pustular and bullous lesions. In other words, bullo-pustular lesions faded away secondarily following the suppression of active inflammation in the psoriatic base by MTX administration – no psoriasis, no BP. Therefore, by the above-mentioned speculation, we should acknowledge that the occurrence of BP and psoriasis is probably not coincidental but, rather, that psoriasis is a triggering factor for BP. Presumably, BP was an additional sign of the active hyperinflammatory state of CPP besides pustular lesions and perilesional erythema. In this case, probably due to the sudden cessation of potent topical corticosteroid usage and local rebound effect, stable CPP flared and pustules emerged as a sign of inflammation flare. Due to the hyperinflammatory state of CPP, the basement membrane (BM) was affected and BP antigens...
were altered. As a result, BP evolved. It is well known that during the unstable period of CPP perilesional active erythema and pustular lesions evolve as a sign of psoriatic activity. In this context, we should think about BP as a sign of CPP activation phenomenon besides perilesional erythema and pustules.

We suggest that the clinical overlap of BP and psoriasis corresponds to the pathogenetic overlap of the two conditions. However, in the literature there are many reports regarding BP development in psoriatic patients by certain triggering factors such as some topical drugs, systemic steroids and UV radiation. These therapeutic agents could induce BP by changing the antigenic features of the BM of the psoriatic base as well as intact skin in genetically predisposed individuals. In the literature, there are a few reports regarding BP development in patients who received phototherapy against nonsoriatic dermatosis [11]. Therefore, BP can evolve in any genetically predisposed individual who has been exposed to triggering factors which can alter the antigenic characteristics of BM. Those antigen-altering factors (AAF) could be the intake of drugs, UV radiation, some irritant topical drugs, malignancy, vaccination, infections, thermal or electrical burns, surgical procedures, or organ transplantation [12]. Psoriasis could also be included on the list of AAF of BP. Several AAF can be combined in genetically predisposed individuals and can cause BP. In psoriatic patients, psoriatic inflammation itself and the above-mentioned AAF can alter the antigenicity of BM – separately or in combination. Therefore, the incidence of pemphigoid diseases in psoriatic patients is extremely high. AAF can be found in only 15% of BP patients [12]. In our case, the BP triggering factor was psoriasis itself, presumably. In this context, we can say that bullous lesions in psoriatic patients may be restricted to the psoriatic base or could involve both intact skin and lesional area, depending on the types and combinations of AAF. In our case, the AAF was, presumably, the hyperinflammatory state of psoriatic ground due to sudden topical steroid cessation. It is likely that the type of autoimmune subepidermal blistering disease (ASBD) that evolves in psoriatic patients depends on which antigen altered in the BM. Up to now, seven ASBD have been identified according to different autoantigenic profiles. The most common ASBD associated with psoriasis are BP and anti-laminin γ-1 pemphigoid (ALG1P) [13]. This means that psoriasis more commonly alters bullous pemphigoid antigens (BPAG1 and BPAG2) and laminin-γ1 antigens of the BM. However, in the literature, mucous membrane pemphigoid, linear IgA dermatosis and dermatitis herpetiformis-associated psoriasis cases have also been reported. The last-mentioned association evolved at the background of coeliac diseases. Pemphigoid gestations is not a relevant ASBD in this context; other ASBD are probably somehow induced by psoriasis itself. AAF can alter several BM antigens and induce a variety of ASBD in the same psoriatic patient. Autoantibodies against laminin-γ1, BPAG1 and BPAG2 were found in 1 erythrodemic psoriasis patient with bullous lesions [14]. In another case, concomitant ALG1P and mucous membrane pemphigoid were demonstrated in a patient with psoriasis [15].

Unfortunately, we were unable to separate BM by salt split technique in order to reveal the type of ASBD. BP in this case was diagnosed according to classic BP diagnostic criteria: two major criteria in addition to an obligatory criterion.

In conclusion, psoriatic patients can be exposed to multiple above-mentioned AAF. Therefore, ASBD, and especially BP, incidence in psoriatic patients is extremely high. Pemphigoid itself is presumably one of the AAF. At the active phase of CPP, bullous lesions may evolve as a sign of inflammatory activity besides perilesional erythema and pustules. Inflammation and AAF can alter the antigenicity of BM and can induce any type of ASBD depending on which antigen is altered. The most common type is BP. In this case, BP was diagnosed by classic diagnostic criteria. It was restricted to the site of CPP where inflammation was active. The dramatic response of bullo-pustular lesions to MTX treatment was probably due to the rule of ‘no psoriasis no BP’. Therefore, we suggest that the occurrence of these two diseases in this patient were not coincidental but, rather, that active psoriasis induced BP and psoriasis-induced BP was a sign of psoriasis activity.

Disclosure Statement

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References


Bullous Pemphigoid as a Sign of Psoriatic Activity

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