Milia within resolving bullous pemphigoid lesions

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Abstract

Bullous pemphigoid is an autoimmune blistering disease that is characterized by pruritus, cutaneous urticarial plaques, and tense bullae, with mucosal involvement. On histopathology, a subepidermal blister is predominantly evident with eosinophilic inflammatory infiltrates in the upper dermis. In a few bullous dermatoses, milia can manifest at the scar of blistering lesions or in non-lesional skin. Milia are classically associated with epidermolysis bullosa acquisita, porphyria cutanea tarda, and mucous membrane pemphigoid. We report a case of bullous pemphigoid with milia manifesting within healing blistering lesions.

Keywords: bullous, bullosa acquisita, epidermolysis, milia, pemphigoid, pemphigus

Introduction

Bullous pemphigoid (BP) is a prevalent autoimmune blistering disease that is characterized by pruritus, cutaneous urticarial plaques, tense bullae, and occasionally blisters in the mucous membranes. Histopathological section of subepidermal blister is predominantly evident of eosinophilic inflammatory infiltrates within the blister cavity of upper dermis [1]. Bullous pemphigoid is associated with human leukocyte antigen and environmental factors [2,3]. In certain bullous dermatoses, milia can be evident on scar of blistering lesions, or in non-lesioned skin [4]. Milia is classically associated with epidermolysis bullosa acquisita, porphyria cutanea tarda, and mucous membrane pemphigoid [5-7]. Lately, the number of case reports demonstrating milia in association with BP is increasing, yet it remains a relatively uncommon clinical finding in this context [1]. Herein, we present a case of BP patient manifesting milia within healing blistering lesions.

Case Synopsis

A 55-year-old woman presented to the dermatology clinic complaining of multiple tense blisters over an inflammatory base mainly over the trunk for the duration of two months. Medical comorbidities were type two diabetes mellitus and hypertension. Physical examination showed normal vital signs. Dermatological examination demonstrated multiple generalized crusted erosions with tense serous fluid filled bullae on a background of inflammatory erythema over the anterior trunk, and large erosions over genitalia. There was no mucous membrane involvement. Nikolsky and Asboe Hansen signs were negative.

Laboratory tests showed a significant increase in white blood cell count (13.8×10^9/l, normal 3.4-9.6×10^9/l), absolute neutrophil count (9.85×10^9/l, normal 1.5-8.0×10^9/l), platelet count (454×10^9/l, normal 150-400×10^9/l), erythrocyte sedimentation rate (44mm/h, normal female ≤20mm/h, C-reactive protein (6.6mg/l, normal 0.3-1.0mg/dl), mild anemia (hemoglobin 11.4g/dl, normal female 12.1-15.1g/dl),

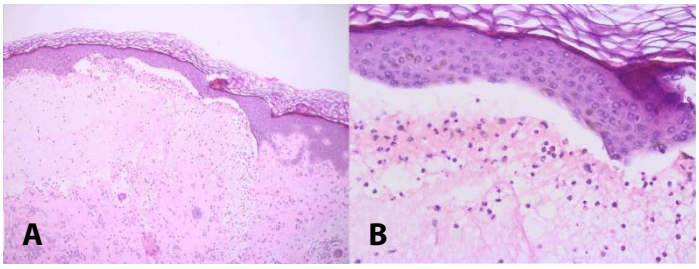

Figure 1. *H&E histopathology obtained from the leg showing subepidermal blistering with eosinophils most consistent with bullous pemphigoid,* ***A)*** *10×;* ***B)*** *10×.*

hypoproteinemia (serum albumin 32g/l, normal 34-54g/l), and low absolute eosinophil count (0.09×10^9/l, normal $0.5\text{-}1.5\times10^9$/l). ELISA for anti-BP180 and anti-BP230 antibodies were not available.

Skin punch biopsies, one for routine hematoxylin and eosin and one for direct immunofluorescence, showed subepidermal blistering disorder with eosinophil predominant inflammatory infiltration and linear C3 and IgG deposition along the dermis-epidermal junction in an n-serrated pattern, respectively (**Figure 1**). The clinico-pathological correlation was most consistent with BP.

Clobetasol cream was started for two weeks with prednisolone 20mg daily for 7 days. At follow-up examination after two months, the patient worsened and developed new tense bullae with underlying tense erythema over upper and lower extremities. Mucous membranes were spared. Prednisolone 40mg daily for 14 days and amoxicillin/clavulanic acid 1g (875mg amoxicillin and 125mg clavulanic acid) twice daily for 7 days were started. Topical treatment consisted of muprocin ointment, clobetasol cream, and paraffin gauze dressing. At follow-up examination after two weeks, the patient improved and prednisolone was tapered to 35mg daily for two weeks with close monitoring of blood sugar. After two weeks, all active lesions resolved. Prednisolone was tapered to 25mg daily, and azathioprine 50mg each day was started. Prednisolone was tapered to 5mg and was continued for 5 months then stopped; azathioprine 50mg daily was continued.

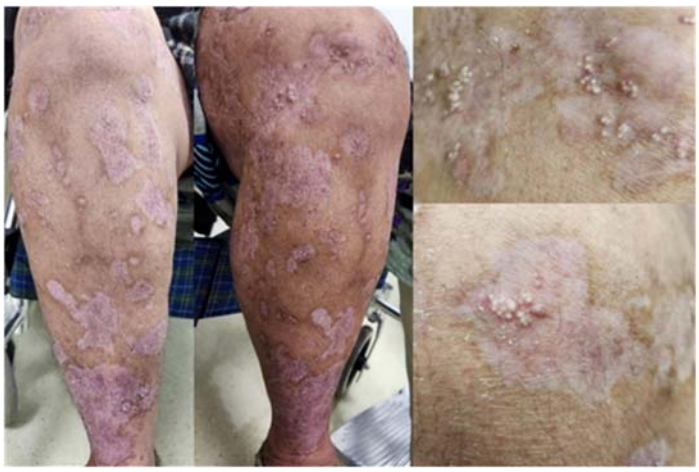

Figure 2. *Multiple grouped tense white papules were evident over healed bullous pemphigoid scars.*

At follow-up examination after three months, the patient developed new white papules over the scars of BP lesions. On examination, multiple grouped dome shaped tense pearly white papules ranging from 1-3mm were evident over healed BP scars (**Figure 2**). Clinical impression was milia and skin punch biopsy was obtained for confirmation (**Figure 3**). As the patient did not express any cosmetic concerns, the decision was made not to treat the milia.

Case Discussion

Milia are common benign superficial keratinous cysts that can be primary in origin or secondary to different dermatological diseases, medications, or trauma. Milia have been observed previously in and acquired bullous dermatoses, particularly,

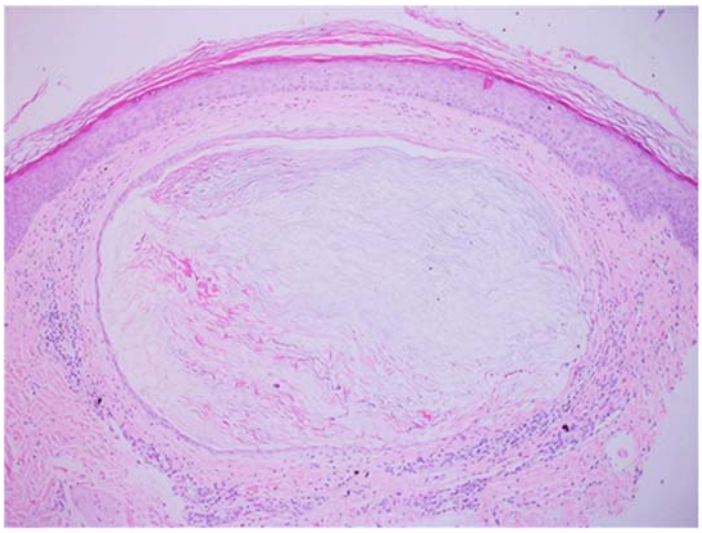

Figure 3. *H&E histopathology obtained from the leg showing milium within a scar demonstrating miniature infundibular cyst, containing walls of stratified squamous epithelium, 10×.*

epidermolysis bullosa acquisita, porphyria cutanea tarda, and mucous membrane pemphigoid. [8]. However, milia are infrequently associated with BP, a fact substantiated by the scarcity of documented cases in the literature [9]. Furthermore, numerous experts view the occurrence of milia formation as a helpful feature to distinguish epidermolysis bullosa acquisita from other acquired blistering dermatosis [3]. A global estimated prevalence of milia among BP patients is lacking, yet Vernal et al. have reported a prevalence of 7.8% in a Brazilian sample consisting of 102 BP patients [1].

Although the exact mechanism underlying milia formation in the context of BP remains incompletely understood, it is plausible that the regenerative processes of disrupted sweat glands or hair follicles play a role [9]. Moreover, Uchida et al. have suggested that an immunological predisposition as well as abnormal interactions between hemi-desmosomes and the extracellular matrix components beneath them might be related to the formation of numerous milia during the healing phase [10].

It is not clear if milia formation in BP patients is linked to disease activity and the severity of the inflammation along the dermo-epidermal junction, or not. Nonetheless, notably, three reported cases of BP patients who developed secondary milia have demonstrated high anti-BP180 titers and recalcitrant response to conventional treatments which may explain how disease activity and the need for higher doses and longer courses of prednisolone were needed to control BP in our case [3,11].

Milia manifesting within healed BP lesions might resolve spontaneously; nonetheless, it exerts a cosmetic concern to patients. It can be managed with excision and curettage, electrocautery, dermabrasion, topical retinoid, and photodynamic therapy [12]. On the other hand, Beutler et al [13]. have reported milia erupting after treatment with cryotherapy for actinic keratosis. Similarly, cryotherapy creates a sub-epidermal blister similar to our case; the localized immune compromised status post-cryotherapy may induce a secondary dermatosis-like milia.

Conclusion

We reported a case of BP that healed with numerous milia formation. Further research is required to gain a comprehensive understanding of the underlying association of milia formation in the setting of BP. Additionally, it is essential to investigate whether milia can serve as an indicator of disease activity or hold prognostic significance.

Potential conflicts of interest

The authors declare no conflicts of interest.

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