

Koebner phenomenon in pemphigus vulgaris patients



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INTRODUCTION

Pemphigus vulgaris (PV) is a rare autoimmune mucocutaneous blistering disease characterized by epidermal acantholysis, flaccid bullae, and erosive lesions in the skin and mucosa.¹ The Koebner phenomenon (KP) is defined as the appearance of new, typical skin lesions on areas of injury in otherwise healthy skin.^{2,3} KP is described in several skin disorders, including psoriasis and lichen planus, but it remains questionable in PV.³ It is important to differentiate KP from Nikolsky's sign. Nikolsky's sign is defined as the appearance of bullous lesions on normal-appearing skin immediately after lateral pressure is applied to the skin. In contrast, for the appearance of new blisters at the trauma site to be characterized as KP, there should be a lag time between the trauma and the blister formation.⁴ KP is rarely reported in pemphigus, either because of its low incidence in this disease or the rarity of the disease itself. Here we report 2 cases of PV presenting at the site of physical trauma due to KP.

CASE 1

A 48-year-old man presented to our outpatient clinic with a 4-week history of erosions and crusted patches on the scalp. The patient underwent hair transplantation 2 months before his visit. He noticed the erosive lesions initially at the site of donor punch grafts from the posterior occipital scalp and then at the recipient site on the crown of his scalp. Results of direct smear and culture of the wound were negative. The lesions had spread and gradually involved the oral mucosa, trunk, axillary, and inguinal regions. Clinical examination found erosion and crusts at the sites of donor and recipient grafts on the scalp

Abbreviations used:

KP: Koebner phenomenon
PV: pemphigus vulgaris

(Fig 1, A and B), trunk, and axillary and inguinal regions. Nikolsky's sign was positive. Few erosions were noticed on the buccal and palate mucosa of the oral cavity. Histologic evaluation of the scalp lesions found suprabasal acantholytic blisters. Direct immunofluorescence found intercellular deposition of IgG and C3 in the epidermis. The laboratory examinations were within normal limits. The levels of antidesmoglein 1 and 3 were both more than 200 U/mL (normal value, <14 U/mL). According to these findings, the diagnosis of PV was confirmed. The patient was treated with prednisolone (100 mg/d) and mycophenolate mofetil (2 g/d). The skin lesions regressed to a great extent, and no new lesions developed until the time of writing of this report, which was 3 months after the first presentation of the disease.

CASE 2

A 46-year-old man came to our outpatient clinic complaining of 4-month-old bullous lesions on his scalp, trunk, and extremities and in the oral mucosa. Crusty and erosive lesions were found on his back, where hijama (wet cupping) had been done 10 days before his visit (Fig 2, A). Further, a crusted erosion was noticed on the ventral side of the left forearm, where a tuberculin test had been carried out about 2 weeks earlier, which was positive, with a dimension of 19 mm (Fig 2, B). Results of the laboratory

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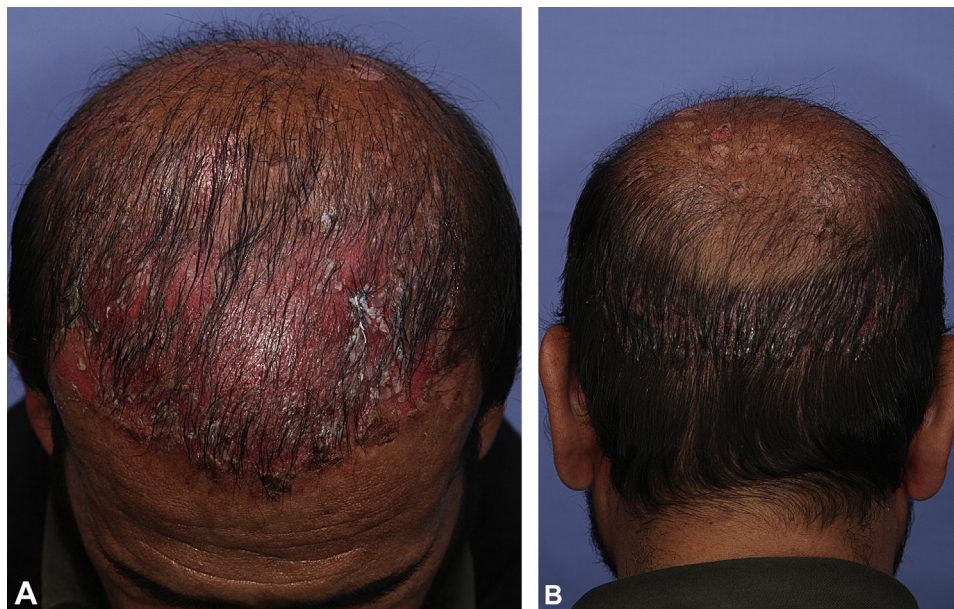


Fig 1. **A**, Erosion and crust at the graft recipient site. **B**, Erosion and crust at the graft donor site.

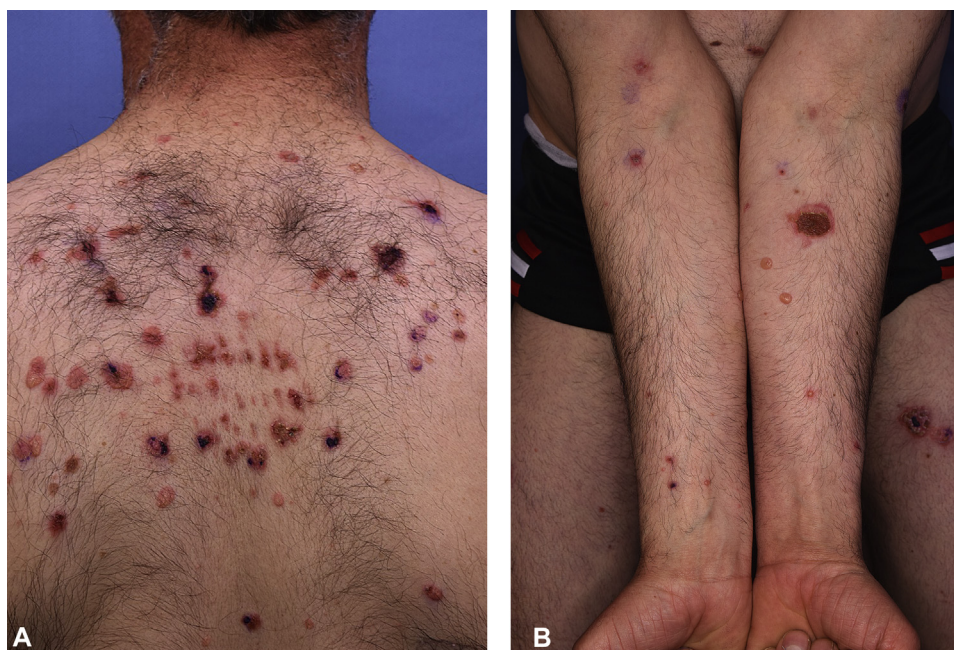


Fig 2. **A**, Erosion and crust at the site of wet cupping. **B**, Crusty erosion at the site of a skin tuberculin test on the ventral side of the forearm.

investigations were within normal limits. Results of a smear and culture of the blister fluid were negative; Nikolsky's sign was positive. The histologic examination from these lesions found suprabasal epidermal blister with acantholytic keratinocytes. Direct immunofluorescence found intercellular deposition of IgG on the cell surface of epidermis

keratinocytes. The levels of antidesmoglein 1 and desmoglein 3 were more than 200 U/mL (normal value, < 14 U/mL). Based on these results, a diagnosis of PV was made, and the patient was treated with prednisolone (60 mg/d) and azathioprine (150 mg/d). Clearing of most of the lesions was noticed in the 2-month follow-up.

DISCUSSION

In 1877, KP was first described by Heinrich Koebner in psoriatic patients as the appearance of psoriatic lesions in uninvolved skin caused by trauma. KP has since been described in numerous diseases but is still not well defined in pemphigus.³ In the literature, reports on KP in PV have included the stimulation of PV lesions by ionizing radiation, surgical procedures, burns,¹ and chemical peels.⁵ Mehregan et al⁴ reported a case of PV appearing in the area of a surgical site after rhinoplasty and hair transplantation, similar to that of case 1 in our study. Daneshpazhooh et al¹ reported on 2 patients with PV lesions at the site of hijama, as observed in our case 2. To the best of our knowledge, no previous report has shown the induction of PV at the site of a skin tuberculin test, as in our second case.

Certain procedures can trigger the onset of new lesions, which can either be limited only to the trauma site or subsequently spread to other areas.⁶ Similar to results from previous reports, in our 2 cases, the lesions were not limited only to the site of trauma,⁴ and the patients showed other skin and mucosal lesions consistent with PV.

The lag period between the exposure to trauma and the koebnerization of typical lesions is generally between 10 and 20 days, but it may be as short as 3 days or as long as a few years.^{3,6,7} In most previous cases of KP in PV, the lesions appeared within 2.5 months after the trauma.¹ In our cases, the intervals to koebnerization was 2 months, 2 weeks, and 10 days, respectively, which is in concordance with previous reports on variations in the lag time to koebnerization.

The exact mechanism by which KP occurs is as yet unknown and may involve a multifactorial interaction between individual genetic factors, environmental triggers, immunologic factors, and the healing process at the trauma site.⁴ Trauma that disturbs the dermoepidermal junction in the skin or mucosa might overexpress epidermal antigens and lead to the epitope spreading phenomenon, resulting in enhanced antigen presentation and blister formation.^{4,8-10} Another theory, proposed by Ruocco and Pisani,¹¹ is the modification of sulfhydryl groups of pemphigus antigens, which can cause epidermal

acantholysis. In addition, a traumatized epithelium makes it possible for small amounts of pemphigus antigens to cause a reaction despite the low titer of antibodies, which could not have caused epidermolysis in intact skin because of the lower expression of these antigens.¹¹ Furthermore, the healing process itself constitutes an obstacle to the normal differentiation of keratinocytes, making them more vulnerable to the low titer of autoantibodies.¹¹

CONCLUSION

KP of PV should be included in the differential diagnosis of poorly healing wounds. Skin biopsies may be necessary for a definite diagnosis and optimal management because PV may first manifest at the site of skin trauma.

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