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CASE REPORT

A Case of Newly Developed Pemphigus Foliaceus and Possible Association with Alternative Bee-Venom Therapy

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Bee-venom is composed of a variety of peptides, enzymes, and biogenic amines, and is demonstrated to have both anti-inflammatory and immune-stimulatory effects in human body. Pemphigus foliaceus (PF) is a variant of pemphigus, which is a rare autoimmune bullous disease presenting with erythematous scaly crusted plaques. Although the exact pathogenesis was not identified, there have been three case reports of autoimmune disorders associated with bee-venom. In this case, a 64-year-old female was diagnosed with PF, which was developed after alternative bee-venom acupuncture therapy. We assumed that the bee-venom caused the diseases through a temporal relationship and its known immunostimulatory action. Herein, we suggest that physicians recognize the possibility of bee-venom stimulating the immune system and triggering various autoimmune diseases including pemphigus. **(Ann Dermatol 33(5) 467～469, 2021)**

-Keywords-
Autoimmune diseases, Bee venoms, Immunology, Pemphigus

INTRODUCTION

Bee-venom is composed of a variety of peptides, enzymes, and biogenic amines, and is demonstrated to have both anti-inflammatory and immune-stimulatory effects in human body. Pemphigus foliaceus (PF) is a variant of pemphigus, which is a rare autoimmune bullous disease presenting with erythematous scaly crusted plaques. Although the exact pathogenesis was not identified, there have been three case reports of autoimmune disorders associated with bee-venom.

CASE REPORT

A 64-year-old female presented with a 1-month history of pruritic crust formation but no history of autoimmune disease or malignancy. The patient had been treated with bee-venom acupuncture in the way of subcutaneous injection twice a week for 2 months at an oriental medicine hospital due to back pain. The exact concentration or the entire contents of the bee-venom acupuncture were unknown. A month after starting the alternative bee-venom therapy, her skin lesions started to develop, then she stopped the bee-venom therapy. Physical examination revealed pruritic erythematous erosive and crusted patches and plaques on the scalp and trunk, which was not in accordance with the acupuncture site (Fig. 1). The oral mucosa was not affected. Laboratory findings revealed that there were no bee-venom-specific immunoglobulin E (IgE) or wasp-venom-specific IgE in her serum. Tzanck smear on trunk lesion was negative finding. A punch-biopsy specimen from the trunk revealed intraepidermal acantholysis just below the stratum corneum containing neutrophils and lymphocytes (Fig. 2A). In the dermis, perivascular infiltration of lymphocytes and histiocytes was observed. A direct immunofluorescence study showed immunoglobulin G (IgG)

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and complement 3 deposition in the intercellular space of keratinocytes (Fig. 2B). In addition, an indirect immunofluorescence study revealed IgG deposition in the intercellular space at a 1:160 dilution (Fig. 2C). Based on these clinical, histopathological, and immunological findings, the patient was diagnosed with PF. In addition, we concluded that it was most likely triggered by the bee-venom, based on correlation with the time of onset and clinical manifestations. She was treated with oral methylprednisolone (16 mg/day for 2 weeks, subsequently tapered by 4 mg per week) and azathioprine (100 mg/day); the patient achieved partial remission at 2 months after initial treatment. We received the patient's consent form about publishing all photographic materials.

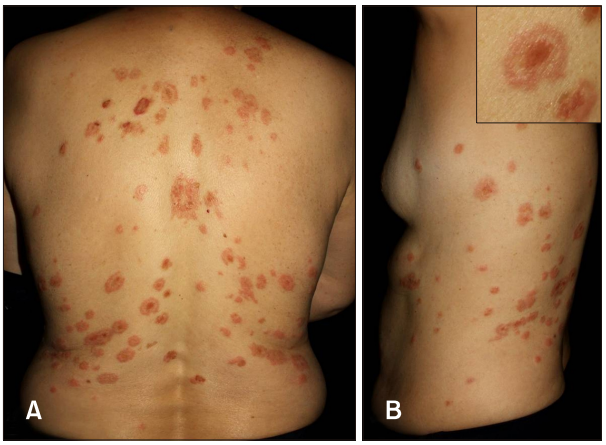

Fig. 1. Clinical features. (A, B) Annular erythematous plaques with vesicobullae on the trunk and scalp.

DISCUSSION

Pemphigus refers to a group of autoimmune diseases in which autoantibodies against desmogleins affect the skin and/or mucous membranes[1]. PF is a rare autoimmune bullous disease presenting with erythematous scaly crusted plaques, mostly in a seborrheic distribution[2]. Although the etiology of PF has not been clearly established, it seems to be induced by genetic and/or extrinsic triggers that can stimulate immune responses, such as drugs, diseases, hormonal alterations, or environmental factors[3].

Bee-venom therapy involves the application of bee-venom into the body, which has been utilized as a traditional alternative medicine for therapeutic purposes such as pain control or treating inflammatory diseases[4]. The active components of bee-venom include a variety of peptides, enzymes, and biogenic amines[5]. Several studies have demonstrated the anti-inflammatory, anti-nociceptive, and immunotherapeutic effects of bee-venom[6,7]. Hamedani et al.[8] reported that bee-venom has both immunosuppressive and immunostimulatory functions depending on the dose pattern, stimulatory potency at low doses (0～0.05 μg/ml) and inhibitory effects at high concentrations (0.05～0.2 μg/ml). In addition to its suspected immunostimulatory action, there have been three case reports of autoimmune disorders associated with immunostimulatory effects of bee-venom. Rho et al.[9] reported a case of systemic lupus erythematosus that developed after bee-venom therapy for arthralgia. Ghoreschi et al.[10] reported a case of rheumatoid arthritis after subcutaneous immunotherapy with bee-venom in a patient without a history of arthritis. Gül et al.[11] reported a case of newly developed pemphigus vulgaris (PV), before which the patient had been stung by hundreds of honeybees.

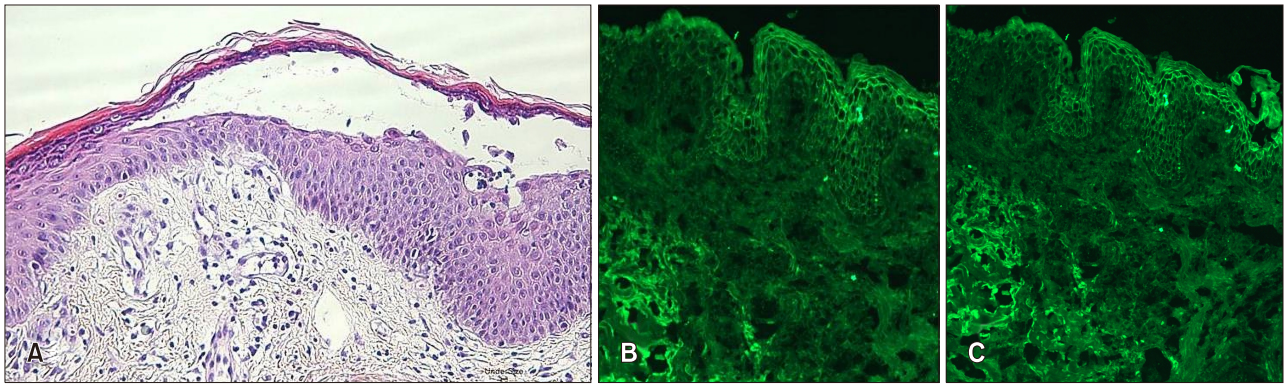

Fig. 2. Histological features. (A) Intraepidermal acantholysis just below the stratum corneum containing neutrophils, eosinophils, and lymphocytes, and perivascular infiltration of lymphocytes and histiocytes in the dermis (H&E, ×200). (B) Direct immunofluorescence study revealing immunoglobulin G (IgG) deposition in the intercellular space of keratinocytes. (C) Indirect immunofluorescence study of normal skin showing IgG deposition in the intercellular space at a 1:160 dilution.

The authors first considered the possibilities that the PV was caused by immune stimulation, by microorganisms introduced via the bees, or by another unknown mechanism. They then deduced that the bee stings were a trigger of the PV, given that the lesions first appeared at the site of the bee stings a month after the patient was stung. In our case, the patient was not stung by bees, but rather bee-venom therapy seemed to induce skin lesions a moth after initial application, which is similar to the PV case. In addition, to the best of our knowledge, this is the first case of pemphigus after bee-venom therapy.

A previously reported review and a case report gave reference to that phospholipase A2 of bee venom exerts a main role in anti-inflammatory and anti-nociceptive effects by regulating cytokines including interleukin (IL)-1, IL-2, IL-6, tumor necrosis factor, CD4+, IL-10 and affecting regulatory T cell polulation[6,9]. And the immunostimulatory effect of bee venom occurs by increasing the level of matrix metalloproteinase, interferons and affecting Th2 immunity[8,9]. Although we could not identify the exact mechanism of pathogenesis or clarify the association between bee-venom and the PF, we assumed that the bee-venom caused the diseases through a temporal relationship and known immunostimulatory action, probably associated with T cell immunity including changed regulatory T cell population or level of cytokines. In conclusion, it should be recognized that bee-venom can stimulate the immune system and trigger various autoimmune diseases including pemphigus.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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