

Bee venom acupuncture for circumscribed morphea in a patient with systemic sclerosis

A case report

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Abstract

Rationale: Bee venom has been reported to demonstrate antinociceptive and anti-inflammatory effects in experimental studies, but there remain questions regarding the clinical use of bee venom, especially for scleroderma. This case report shows the successful outcome of bee venom acupuncture for circumscribed morphea in a patient with systemic sclerosis, which is considered to be a rare condition.

Patient concerns: A 64-year-old Korean woman had circular white areas (3 and 1 cm diameter) with severe itch in the right lateral iliac crest. Based on an initial diagnosis of systemic sclerosis (1 year prior to presentation at our clinic), she had been treated with painkillers, steroids, antitussive expectorants, and aspirin, with minimal effect on her recent skin symptoms.

Diagnoses: In this study, the diagnosis of circumscribed morphea was based on localized skin symptoms of the patient with systemic sclerosis.

Interventions: The patient visited Gachon University Korean Medical Hospital for treatment of topical skin symptoms. After being evaluated for bee venom compatibility, she was administered subcutaneous bee venom acupuncture along the margins of the patches (superficial circumscribed lesions) using the shallow surround needling method twice per week for 1 week and then once per week for the following 3 weeks.

Outcomes: Itch levels were evaluated before each treatment session: by her second visit, her itch had decreased from 8 to 3 on a 10-point numerical rating scale; by her sixth visit, her itch had decreased from 3 to 0. She did not experience adverse effects, and these improvements were maintained until the 2-month follow-up evaluation.

Lessons: Bee venom treatment demonstrates the potential to serve as an effective localized therapy for circumscribed morphea.

Abbreviations: CAM = complementary and alternative medicine, LoS = localized scleroderma, NRS = numeric scale, SSc = systemic sclerosis, TCM = traditional Chinese medicine, TKM = traditional Korean medicine.

Keywords: *Apis mellifica*, bee venom, morphea, pharmacopuncture, sclerosis

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Consent for publication: Informed consent for publication of this case report was obtained from the patient, as potentially identifying information may be included in this article.

Availability of data and material: The data are not available for public access because of patient privacy concerns, but are available from the corresponding author on reasonable request.

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1. Introduction

Scleroderma is a rare, chronic, autoimmune disease of connective tissue, associated with cutaneous, joint, and internal organ involvement. Cutaneous scleroderma is characterized by enhanced fibroblast activity, leading to hypertrophic dermal collagen. There are localized and systemic forms of scleroderma. Localized forms include morphea and linear scleroderma.^[1,2] While the association of morphea and systemic sclerosis (SSc) is considered to be a rare condition, several studies have reported their coexistence or possible coevolution.^[3,4]

There are currently no recommended curative treatments for scleroderma. Available treatments include immunosuppressants; intralesional, topical, and oral steroids; topical vitamin D; and phototherapy. There are case reports of UV-A1, UV-B, PUVA (bath and topical), and targeted phototherapies in cases of scleroderma; UV-A1 appears to be the most efficacious therapy (i.e., it is the most commonly recommended treatment).^[1] However, side effects have been reported, such as thermal skin burns, itching, and headaches, although this treatment has been shown to relieve general symptoms.^[5] Moreover, morphea with large skin rashes and morphea involving multiple anatomical regions both involve great difficulty for UV-A treatment.^[6]

Several studies have demonstrated that alternative therapies might alleviate various symptoms induced by scleroderma.^[7,8] However, these studies lacked verifiable outcome measures, and

they did not aim to clarify the distinctive role of alternative medicine.

Pharmacopuncture is a new form of acupuncture treatment in traditional Korean medicine (TKM) and traditional Chinese medicine (TCM) that involves stimulating acupoints with the injection of herbal medicines. Bee venom acupuncture is one of most commonly used pharmacopuncture treatments; it originated from bee sting therapy. Bee venom treatment has been widely used in complementary and alternative medicine (CAM) for 3000 years and has demonstrated increasing evidence for anti-inflammatory, antiapoptotic, antinociceptive, anti-fibrotic, and anti-atherosclerotic effects.^[9] With these pharmaceutical characteristics, bee venom therapy has also been used as therapy for rheumatoid arthritis, Parkinson's disease, amyotrophic lateral sclerosis, postherpetic neuralgia, Alzheimer's disease, liver fibrosis, atherosclerosis, pain, and other illnesses.^[10–12]

Bee treatment has been reported to be ineffective for relapses, fatigue, lesion burden or volume, disability, and quality of life; additionally, in CAM, it has been reported to affect multiple sclerosis (the effect has not yet been fully verified).^[13] However, thus far, there has been no report regarding the effect of bee venom therapy in patients with SSc who exhibit circumscribed morphea skin symptoms. This report describes the improvement of localized skin symptoms in a patient with SSc after 1 month of bee venom treatment.

2. Case report

The patient was a 64-year-old woman, 160 cm in height, weighing 45 kg. She had experienced itching in the right lateral iliac crest for approximately 10 days, for which she occasionally applied soothing cream; however, it was ineffective and she had difficulty sleeping at night due to sudden itching. She found circular white areas in the right lateral iliac crest (3 and 1 cm in diameter) in the mirror and visited the nearby Gachon University Gil Korean Medical Hospital. She described her itching symptoms as similar to being bitten by a worm.

Raynaud's phenomenon and joint pain had appeared over the years, and she had been diagnosed with SSc in the Rheumatology Department of Seoul National University Hospital, in February 2017. She was also diagnosed with Takayasu's arteritis in the Department of Surgery, Seoul National University Hospital, in February 2017 due to hypertension, which was not controlled by the blood pressure medication for approximately 2 years; she underwent aortic surgery in May 2017. After the surgery, she was treated with painkillers, steroids, antitussive expectorants, and aspirin.

At the time of her visit to our clinic, she expressed desire to treat the skin condition locally, due to concerns regarding the large amount of medications she was taking, as well as postoperative complications, including fatigue and weight loss. She had planned to try TKM after she recovered and had reduced her medication usage in the future. Pharmacopuncture involves stimulation of acupoints with an injection of herbal medicines in TKM and TCM; it exhibits more rapid efficacy than oral administration because the drug does not pass through the digestive system, and is frequently used for the regulation of immune balance in clinical settings.^[4,5] The patient had previous experience with bee venom pharmacopuncture due to shoulder pain. Thus, to relieve rapidly worsening localized skin symptoms by using immune regulation, we selected bee venom pharmacopuncture. After undergoing several evaluations that confirmed the patient was eligible for bee venom therapy, she provided

informed consent and was treated with diluted bee venom acupuncture. This case report is one of retrospective chart reviews under the patient's agreement to publication.

For this study, sterilized bee venom solution was prepared through aseptic processing of 1 g of dried bee venom, dissolved in 10,000 cc of water; the final bee venom pharmacopuncture solution was provided in a sealing vial by Jaseng Herbal Medicine Dispensary (an extramural facility meeting Korean Good Manufacturing Practice standards). Bee venom acupuncture was administered subcutaneously along the margins of the patches (superficial circumscribed lesions), using the shallow surround needling method. A volume of 0.02 mL of bee venom was administered into each site with a 31-gauge insulin syringe (Shinamed, Anseong, Korea) at a depth of 3 to 4 mm; the total injected volume did not exceed 0.2 mL. Bee venom treatment was administered twice per week for 1 week and once per week for the following 3 weeks.

After the first treatment, the patient's average itch and sleep disturbance scores immediately decreased from 8 to 4 and from 6 to 2, respectively, on a 11-point numeric scale (NRS 11). At the third visit, she reported that the itch had nearly disappeared after 2 treatments, but weakly reappeared intermittently. The score decreased to 0 on her third visit and was maintained at 0 until the fifth visit. On this fifth visit, she reported that she could no longer feel the itch, and that it no longer interfered with her sleep (Fig. 1). In addition to the reduction in itching, her skin condition was improved. At the 3-month follow-up evaluations, it was confirmed that the skin condition had improved to resemble normal skin (Fig. 2). Because the patient was satisfied with this outcome, she discontinued treatment for this skin symptom. There were no adverse effects during treatment, except for a slight itchiness at the site of injection for approximately one-half day following treatment.

3. Discussion

Morphea, also known as localized scleroderma (LoS), is a distinctive inflammatory disease involving the skin and the subcutaneous tissue, characterized by excessive collagen deposition that ultimately leads to fibrosis. In contrast to SSc, Raynaud's phenomenon, typical autoantibodies, and visceral involvement are generally absent in LoS.^[1,2] Though LoS is known as a dermatologic disease, it has also been reported in the literature as having a possible overlap with other autoimmune diseases or as a symptom of evolution toward a systemic form.^[4,14,15] Although they are distinct clinical entities, SSc and LoS present analogous histopathological findings;^[4,16–18] furthermore, the presence of autoantibodies or Raynaud's phenomenon has also been reported in LoS.^[15] Consistent with this perspective, a prior study reported coexistence or possible evolution of SSc and LoS.^[3,4] Morphea is typically asymptomatic, with occasional itching and rare pain. Morphea typically begins as a red or purple area of skin that then becomes thickened and white.^[2] In this case, the patient exhibited morphea, which became white with itching.

Previous studies have demonstrated that CAM therapies promote mental and physical health in SSc patients.^[6,19] However, the effects of these therapies on active-phase morphea in patients with SSc have not yet been reported.

The precise pathogenesis of morphea is poorly understood, and there have been few clinical or histopathological studies in Asian patients.^[20] The causes of morphea are commonly regarded as vascular endothelial damage, activation of immune and

Numerical rating scale (NRS)

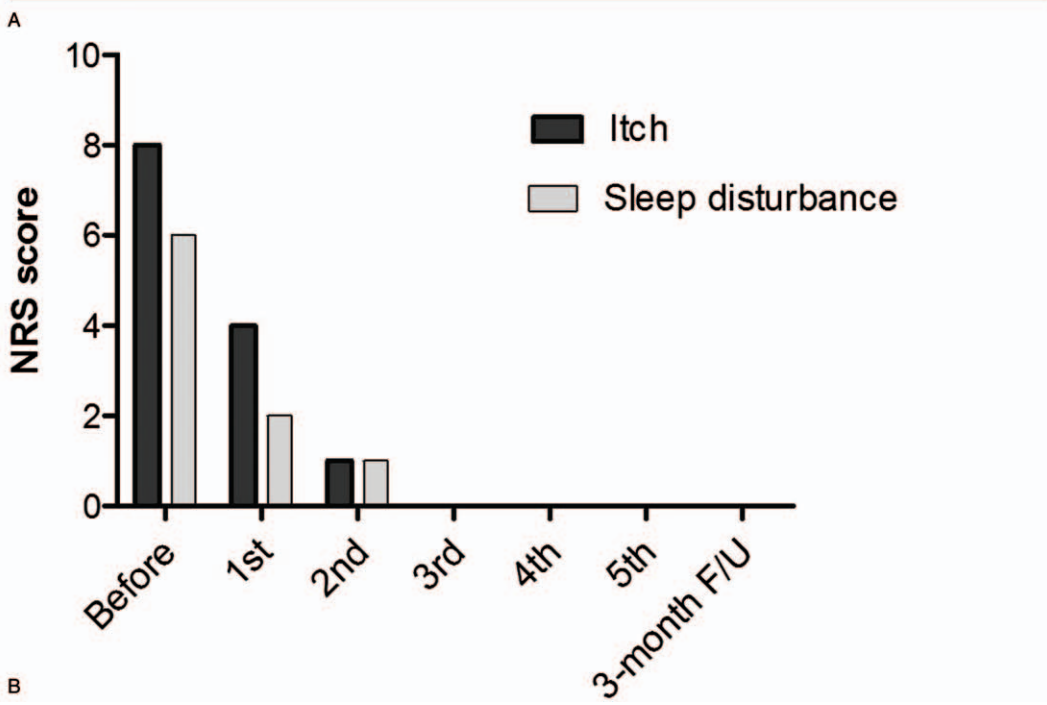
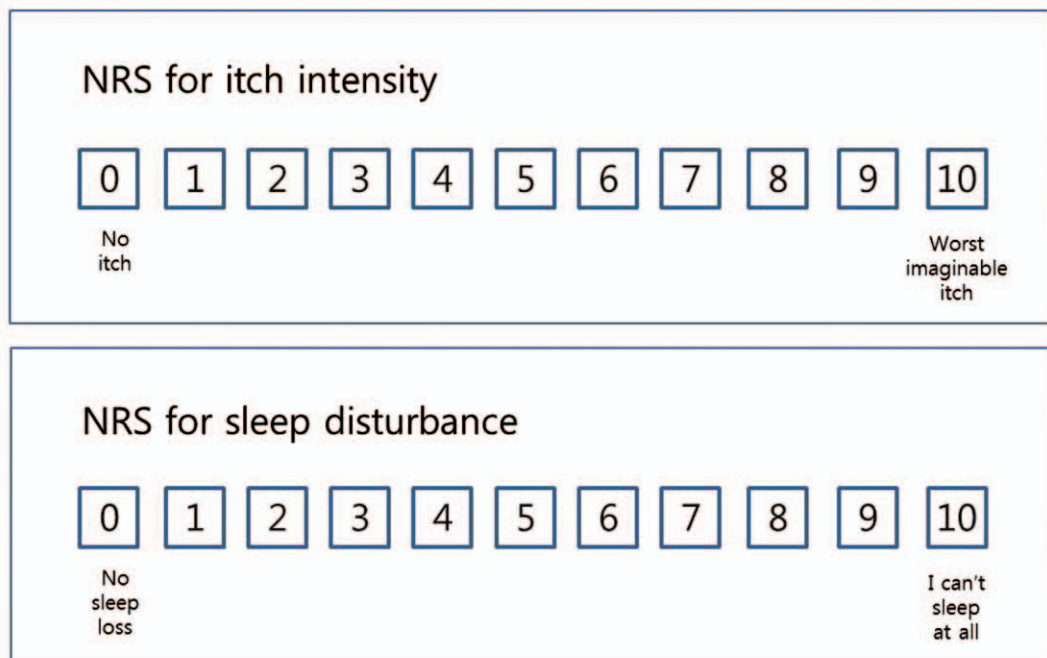


Figure 1. Patient's assessment of the intensity of itch and sleep disturbance with an 11-point numeric rating scale (NRS) ranging from 0 to 10 for itching and sleep disturbance.

inflammatory responses, fibrosis, and/or nodularization due to extracellular matrix metabolism disorders. UV-A1 is studied the most among phototherapies for scleroderma; UV-A1 radiation is suspected to increase collagenase gene expression and protein expression by fibroblasts,^[5-9] resulting in an anti-inflammatory effect.

Bee venom is a very complex mixture of natural products extracted from honey bees, which contains various pharmaceu-

tical properties related to peptides (e.g., melittin, apamin, adolapin, and mast cell degranulation peptide), enzymes (e.g., phospholipase A2), and nonpeptide components (e.g., histamine, lipids, and carbohydrates).^[21,22] The use of bee venom in specific acupoints is so-called bee venom therapy, bee venom acupuncture, or pharmacopuncture in TKM.^[9] Bee venom has been reported to have effects on vascular endothelial growth factor activity, anti-inflammatory processes, anti-cancer outcomes,

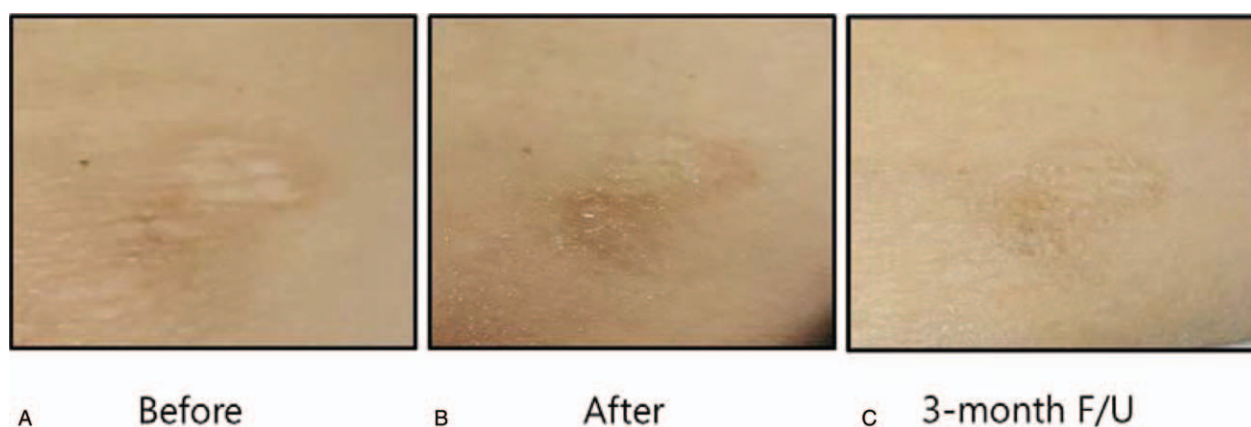


Figure 2. Skin lesion of morphea seen at the waist at first visit (A). The softened and decreased sized patch after bee venom acupuncture for 4 weeks (B) and at 3-month follow-up (C).

immune regulation, and fibrosis.^[21–24] The efficacy of bee venom may be related to the aforementioned causes of morphea. Although it is widely used, several cases have reported that bee venom therapy might cause adverse effects, such as local itching or swelling.^[11]

In this study, we chose the shallow surround needling method to target circumscribed morphea, which is localized to the skin and the subcutaneous tissue. Bee venom acupuncture was administered subcutaneously along the margins of the patches (superficial circumscribed lesions). For large patch, we used the shallow surround needling method (quintuple needling or surrounded needling); for small patch, only one point was selected. This needling method is an ancient needling method used for skin problems; it involves administration to the center of a point, with additional needling anterior, posterior, right, and left to the center of the point to treat widespread pathogenic factors.^[9] There is also a possible treatment effect of acupuncture needling on skin symptoms (circumscribed morphea).

This case report can be meaningful for several reasons. First, it differs from other case reports because there is little clinical evidence of bee venom treatment for LoS; further, the association of morphea and SSc is considered to be a rare condition. Although the number of bee venom studies on animals has been increasing, there have been few clinical reports regarding bee venom therapy for humans.^[12] This case showed improvement of local skin symptoms associated with sleep disturbance and itching through bee venom treatment for LoS in a patient with SSc. In the future, bee venom therapy may be considered as an alternative therapy for treatment of morphea, with or without SSc; it may involve the use of recommended doses, as well as the needling method of bee venom acupuncture for morphea. Second, the patient's local skin symptoms with sleep disturbance and itching were significantly improved after 5 treatments per month, an outcome maintained until the 3-month follow-ups. Although the natural resolution of morphea may be a confounder in the present case, because the patient had a plate that became white with severe itching in less than 1 month, which showed improvement within a short treatment period, such confounding is unlikely.

This case study has limitations in that the result of a single case cannot be generalized due to the insufficient number of subjects and lack of a control group. In addition, we only observed improvement of local skin symptoms, without histopathological

observation. Nonetheless, this case study could help to broaden the scope for using bee venom pharmacopuncture to treat circumscribed morphea with SSc. Although the main scale of itching measurement in patients with morphea is the NRS, or visual analogue scale (with regard to the degree of sleep disturbance), further measurements regarding quality-of-life may have been useful in analyzing changes related to symptoms of morphea symptoms because the perception of itching is subjective. It is possible that the improvement could have been reported because the bee venom was injected into morphea-related acupoints as well. Further research should be conducted to elucidate the optimal modality of bee venom treatment. In the future, we will examine the effect on overall patient condition by applying Korean medicine treatments to improve skin symptoms and other symptoms related to SSc.

4. Conclusion

Bee venom acupuncture demonstrates the potential to serve as an effective localized therapy for circumscribed morphea. Further research should be conducted to elucidate the optimal modality of bee venom treatment. In the future, we will examine the effect on overall patient condition by applying Korean medicine treatments to improve skin symptoms and other symptoms related to SSc.

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