

Efficacy of ON101 cream, a Topical Macrophage-Regulating Cream, against Chronic Burn Wounds

— *A Case Report and Literature Review*

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Background:

Individuals with flame burns experience long-term morbidity, and delayed wound healing has both physical and mental repercussions. Various strategies are used in the treatment of chronic wounds; however, no consensus has been achieved regarding the optimal approach to such treatment. ON101, a topical cream comprising *Plectranthus amboinicus* and *Centella asiatica*, has recently emerged as an alternative therapeutic option for chronic wounds. This cream regulates macrophage subtypes and exerts anti-inflammatory effects. Although numerous studies have reported the healing effects of ON101 on diabetic wounds, few studies have investigated its effects on burn wounds.

Aim and Objectives:

A 26-year-old woman presented to our clinic with a chronic burn wound behind her left ear. She sustained the wound during a chemistry experiment. Despite receiving wound care for more than six months, the patient could not achieve complete wound healing. We prescribed ON101 cream and monitored the wound closely. This case report

and literature review aims to present the therapeutic impact of ON101 cream on chronic burn wound of a 26-year-old female who was flame burned during an experiment.

Materials and Methods:

The patient independently performed wound dressing at home for 3 weeks. Her recovery was documented through photographs taken during the treatment and throughout the follow-up period.

Results:

Treatment with ON101 cream resulted in wound healing without any side effects. The patient was satisfied with posttreatment aesthetic outcomes.

Conclusion:

Our report, coupled with a literature review, highlights the therapeutic benefits of ON101 cream for patients with chronic burn wounds. ON101 may be used as a topical agent for such patients. (J Taiwan Soc of Plast Surg 2024;33:199~206)

Key words: ON101 cream; burn wounds; steroid; case report

Introduction

Chronic wound formation is a common complication in response to skin injuries, such as burns or trauma. Apart from cosmetic concerns, these chronic wounds can be painful and may sometimes lead to infection or even movement restriction, particularly when joints of extremities are involved. Among the different types of skin injuries, flame burns account for about 20% of patients within the burn population, and severe flame burns may lead to morbidities such as chronic wounds¹. The prevalence of chronic wounds is on the rise globally and is associated with a variety of condition, such as vascular disease, diabetes and old age. The delay of wound healing poses serious effects on patients' quality of life. Recent increases in understanding of immune response to wound healing shows that the alterations in immune cells could be an important contributor to chronic wound formation. The understanding of immune cells alteration may serve as a potential target for new therapies.

Skin wound repair is integral to the restoration of skin integrity. The repair process involves three dynamic phases, namely, the inflammatory, proliferation,

and remodeling phases. Smooth wound healing is dependent on an optimal level of metalloproteinases (MMPs) and balanced regulation of macrophage subtypes. MMPs strengthen the extracellular matrix of the wound area with type I collagen and promote the migration of cells, particularly keratinocytes, for epithelialization. Because of their proteolytic ability, MMPs, when present in high levels, promote the degradation of growth factors, thereby hindering and consequently delaying wound healing².

Macrophages can be broadly classified into the M1 and M2 subtypes. Balance between these two subtypes is essential for wound healing. The proinflammatory M1 subtype predominates during the inflammatory phase of wound healing, whereas the anti-inflammatory M2 subtype (or the proremodeling subtype) predominates during the proliferation and remodeling phases^{3,4}. After a burn injury, the proportion of M1 macrophages increases; these macrophages prevail until the proliferation phase of wound healing, during which M2 macrophages predominate. Disruption of the balance between the M1 and M2 subtypes can delay wound healing.

ON101, a topical cream, is an effective and safe

treatment option for various wounds, including diabetic wounds⁵. ON101 cream is the first-in-class macrophage modulator to promote healing by regulating the balance of M1 and M2 macrophages in wound environment. Herein, we report the case of a flame burn victim whose chronic wound, located at her post-auricular area, was successfully treated using ON101 cream.

Case Report

A 26-year-old woman presented to our plastic surgery clinic with a chronic burn wound behind her left ear. She had no previous chronic disease, long-term medication use, or food or drug allergy.

The patient was a chemistry teacher who sustained a 13% TBSA (Total Body Surface Area), second- or third-degree flame burn injury on the face, bilateral upper limbs, and anterior chest during an accident in her practical class. She was admitted to a burn center, where she received first-aid care for a month.

Her facial wounds, including a post auricular burn wound, were treated with silver dressings. No surgical intervention regarding the wound was arranged. She diligently applied silver dressing to the postauricular wound for approximately 3 months but noted no improvements. This prompted her to visit our facility. Physical examination revealed a 2nd degree, deep burn wound of size 5.5 cm × 7.5 cm behind her left ear; the wound had redness and discharge (Fig. 1). The wound was treated with moisturizer and silicone-based dressing (ALCARE SI-AID®). The patient was closely monitored at our outpatient department. Despite receiving long-term care for 3 weeks, the patient's wound healing was slow with limited improvements (Fig. 2).

The advantages and disadvantages of ON101 were thoroughly explained to the patient before initiation of the treatment. Informed consent was obtained from the patient for the use of her data and photographs in the current report.

ON101 was applied twice a day after wound sterilization. First, the wound was cleaned using

normal saline solution. After, a thin layer of ON101 was applied, with as much of the wound as possible being covered with the cream. The patient independently applied the wound dressing at home for 3 consecutive weeks. The treatment progress was documented through photographs. Healing started with a reduction in serous secretion (Fig. 3), followed by granulation tissue formation and wound epithelialization (Fig. 4). The wound was treated within 1 tube of ON101 and healed uneventfully by end of the treatment period, with acceptable aesthetic outcomes (Fig. 5). No recurrence or infection was noted at the 6-month outpatient follow-up (Fig. 6). The patient reported no topical side effect such as allergy or itching.

Discussion

Flame burns represent a key medical concern, regardless of wound depth or extent. Burn victims not only experience systemic complications, such as burn shock or systemic infection, but also are required to cope with local wounds that affect them both physically and mentally.⁶ Burn wounds are typically associated with problems such as acute pain or infection. Chronic burn wounds also compromise patients' quality of life, imposing a substantial burden on both patients and their caregivers⁶.

Under normal circumstances, wound healing typically concludes within 6 weeks. Wounds persisting beyond this period are labelled chronic wounds. The exact reason for delayed wound healing remains unclear; however, various hypotheses have been proposed. Alterations in the expression levels of M1 and M2 subtype markers during burn injury are closely associated with delayed wound healing. Unlike the M2 subtype, the M1 subtype predominates during inflammation^{3,4}. Multiple cytokines, such as interferon- γ , tumor necrosis factor, interleukin-6, and interleukin-8, are released during the inflammatory phase⁷. These cytokines facilitate the adhesion of proinflammatory monocytes to the endothelium and their subsequent translocation to wound tissues. Consequently, the

proportion of M1 macrophages in wound tissues increases⁸, prolonging the inflammatory phase and delaying wound healing. Metalloproteinase (MMPs) play a key role other in addition to that of regulating macrophage proliferation. Release of appropriate levels of MMPs is crucial for preparing the wound matrix for cell proliferation and migration. However, sustained release of high levels of MMPs can lead to wound failure through various mechanisms. MMPs, being proteases, disrupt the wound matrix and injure the tissue scaffold². Elevated levels of MMPs create a highly proteolytic environment within the wound, promoting the degradation of growth factors and reducing the responsiveness of cells to these factors². These mechanisms collectively contribute to the stagnation of wound healing, thereby delaying the process.

ON101 cream contains *Plectranthus amboinicus* and *Centella asiatica*. ON101 cream has been identified as having various clinical applications. This cream functions through multifold mechanisms^{9,10}.

ON101 was first introduced as a macrophage-regulating agent that promotes wound healing. Through various experiments, Lin et al. demonstrated the macrophage-regulating ability of ON101, offering several explanations for the ability⁵. This cream exerts dual effects on M1 and M2 macrophages. It directly inhibits M1 polarization and restores M2 macrophages by reversing M1-mediated M2 suppression, thus alleviating M1-associated inflammation and creating an environment favoring M1-to-M2 transition. This indicates that ON101 can reshape macrophage subtypes, mitigating the delay in burn wound healing.

Plectranthus amboinicus, one of the two ingredients of ON101 cream, is a perennial herb. Natural compounds extracted from *Plectranthus amboinicus* have multiple pharmacological properties, including anti-inflammatory properties. The NLRP3 inflammasome, an intracellular multimeric protein complex, has been implicated in the pathogenesis of many inflammatory diseases. Leu et al. demonstrated that PA-F4, a *Plectranthus amboinicus* extract, inhibits the activation

of the NLRP3 inflammasome through various pathways¹¹. In the treatment of burn wounds, the inflammasome inhibitory and anti-inflammatory effects of *Plectranthus amboinicus* lead to the creation of an environment that facilitates the transition from the inflammatory phase to the proliferation and remodeling phases, thereby expediting the wound healing process.

The role of *Centella asiatica*, the other ingredient of ON101 cream, in accelerating wound healing has been validated through both in vitro and animal studies. In their animal studies, Liu et al. and Brinkhaus et al. demonstrated that *Centella asiatica* can promote the synthesis of wound collagen and the proliferation and migration of fibroblasts, thus accelerating wound re-epithelialization and contraction^{12,13}. *Centella asiatica* possesses anti-inflammatory and antioxidative properties. In their in vitro studies conducted using human dermal fibroblasts, Hashim et al. and Lu et al. demonstrated that *Centella asiatica* strongly influenced extracellular matrix protein deposition, stimulated fibroblast proliferation, increased collagen synthesis, and reduced MMP levels, thereby promoting wound healing^{14,15}. The aforementioned evidence positions *Centella asiatica* as a promising therapeutic agent for chronic wounds.

In our case, ON101 cream gradually healed the patient's chronic burn wound, ensuring favorable outcomes. Further clinical studies should be conducted to evaluate the healing effects of ON101 cream on chronic burn wounds. The present case, together with the findings presented in our review of the literature, suggests that ON101 cream is an effective alternative treatment option for chronic burn wounds. This is one of the first case reports to reveal the benefits of ON101 cream for patients with burn injury. Our findings suggest that ON101 cream holds promise as a topical agent for the treatment of chronic burn wounds.



Fig. 1. Initial wound condition of a 26-year-old female upon our clinic arrival. A 2nd degree deep burn wound with redness, discharge and chronic inflammation with poor healing for 3 months was noted behind her left ear.



Fig. 2. Despite long-term care for weeks, the wound healing progress was slow with very limited improvement.



Fig. 3. Six days after ON101 cream initiation, showing decreased serous secretion with no sign of severity progression.



Fig. 4. Ten days after ON101 cream usage showing formation of granulation tissue and epithelialization of the wound.



Fig. 5. Wound healed uneventfully with acceptable aesthetic outcome at 18 days of ON101 cream use.



Fig. 6. No sign of recurrence and infection at 6 months OPD follow up.

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速必一乳膏用於燒傷慢性傷口之 —— 個案報告

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背 景：

燒燙傷病人需要面對長期的併發症。延遲的傷口癒合不僅會影響患者的身體，還會影響病人心理狀況。現在有多種治療慢性傷口的方法，但最佳治療方案仍在爭論中。速必一乳膏是一種含有左手香和積雪草成分的外用製劑，通過調節巨噬細胞的型態和改善發炎反應，達到治療慢性傷口的方法。大量研究報導速必一乳膏對糖尿病傷口有良好的治療效果，但目前尚無研究報導其對燒燙傷傷口的效果。

目的及目標：

我們描述一名 26 歲的女性，主訴為左側耳後區域有一慢性燒燙傷傷口。儘管傷口治療了半年多，但癒合狀況仍不佳。本病例報告以速必一乳膏來治療一名 26 歲女性的慢性燒燙傷傷口，達到很好的治療效果。

材料及方法：

這名 26 歲女性接受速必一乳膏治療其左耳後區域之慢性傷口。

結 果：

使用速必一乳膏三週後，傷口順利癒合，沒有明顯的副作用。

結 論：

速必一乳膏可調節巨噬細胞亞型並降低發炎反應。其功效可有效治療慢性燒燙傷傷口。對於患有慢性燒燙傷傷口的患者，速必一乳膏可以達到治療的效果。