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Case report

Second-degree burns with six etiologies treated with autologous noncultured cell-spray grafting

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ABSTRACT

Partial and deep partial-thickness burn wounds present a difficult diagnosis and prognosis that makes the planning for a conservative treatment versus mesh grafting problematic. A non-invasive treatment strategy avoiding mesh grafting is often chosen by practitioners based on their clinical and empirical evidence. However, a delayed re-epithelialization after conservative treatment may extend the patient's hospitalization period, increase the risk of infection, and lead to poor functional and aesthetic outcome. Early spray grafting, using non-cultured autologous cells, is under discussion for partial and deep partial-thickness wounds to accelerate the re-epithelialization process, reducing the healing time in the hospital, and minimizing complications. To address planning for future clinical studies on this technology, suitable indications will be interesting. We present case information on severe second-degree injuries after gas, chemical, electrical, gasoline, hot water, and tar scalding burns showing one patient per indication. The treatment results with autologous non-cultured cells, support rapid, uncomplicated re-epithelialization with aesthetically and functionally satisfying outcomes. Hospital stays averaged 7.6 ± 1.6 days. Early autologous cell-spray grafting does not preclude or prevent simultaneous or subsequent traditional mesh autografting when indicated on defined areas of full-thickness injury.

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Abbreviations: ABSI, abbreviated burn severity risk index; BMI, body mass index; HD, hospital day; POD, post-operative day; LOS, length of stay; TBSA, total body surface area; IRB, Institutional Review Board; FDA, Federal Drug Administration USA; UPMC, University of Pittsburgh Medical Center PA USA.

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1. Introduction

The initial clinical diagnosis of a burn wound depth usually determines the treatment, however, intermediate partial thickness burns can be difficult to classify accurately with an early evaluation [1]. Deeper partial-thickness injuries may need to undergo surgical treatment, including excision and optional split-skin mesh grafting [1–3]. Conservative treatment of extensive, deep partial-thickness wounds avoids early mesh grafting at the risk of a delay in wound closure, which may result in infection and poor aesthetic and functional outcomes. Possible complications of this therapeutic approach include hypertrophic scarring, contracture, and poor functional and aesthetic outcomes that could result in a reduced range of motion and unsatisfactory psychosocial adjustment [4]. Thus, in this borderline indication, an early autologous cell-spray grafting of extensive, deep partial-thickness wounds could be an interesting therapeutic option [5]. In addition, an enlargement of the donor-to-graft-area ratio from a routine 3:1 has its typical clinical limitation at 6:1, while using cell-spray grafting the ratio is between 20:1 and 80:1 [6,7].

Skin regeneration is a dynamic process that involves different cell lineages and cell signaling, which leads progenitors cells to restore the tissue structure and function [8]. Epidermal burn-wound regeneration starts from the edge of the wound where the epidermal structures remain. The adjacent epidermis contains all different functional structures including the hair follicle (HF), inter follicular epidermis (IFE), and the sebaceous glands that are involved in the healing process [9–11]. Epidermal homeostasis and regeneration are enabled by quiescent epidermal stem cells (Fig. 1A), some of which can be activated and proliferate as transient amplified keratinocytes in the *Stratum basale* [12,13]. Through post-mitotic differentiation and migration, cells from the basal layer can regenerate the entirely stratified epidermis [10,14–17]. In deep partial-thickness burn wounds, mesh and cell-spray grafting aim to distribute these cells over the center of the wound and speed up central re-epithelialization.

Various cell-spray grafting methods have been introduced and are thought to provide a fast re-epithelialization and then reduce the healing time and minimize complications [5,18,19]. This innovative technique is still under clinical evaluation and to address planned future clinical studies, suitable indications are of interest. Since 2008, skin-cell-spray grafting, using isolated non-cultured autologous keratinocytes (Fig. 1B), has been used at our center as a treatment option for 45 partial-thickness burn patients. Our chosen regulatory Innovative Practice Institutional Review Board (IRB) approach precludes a study with controls. At times, the procedure has been used in combination with mesh grafting for patients with combined second- and third-degree burn wounds. Here, we present six second-degree burn patients and their treatments, showing different burn etiologies: gas, chemical, electrical, gasoline, hot water, and tar (Table 1). In all indications, the results, after early autologous cell-spray grafting shows a fast re-epithelialization and an aesthetic and functionally satisfying outcome with no major complications. We suggest considering these indications for future clinical studies in this new field.

2. Material and methods

2.1. *Patient criteria for study inclusion*

The Institutional Review Board (IRB) from UPMC Mercy Hospital, through its Technology and Innovative Practice Assessment Committee, approved the cell-based grafting procedures under an innovative practice approach. Therefore, performing a clinical study with controls was not possible. Patient data collection for this retrospective analysis was performed under an authorization from the Institutional Review Board (IRB# PRO14010023, 23-01). Exclusion criteria for the treatment consisted of age <18 years, pre-existing local and systemic infections, hypersensitivity to trypsin or other enzymatic wound treatments, and the risks associated with anesthesia. For inclusion, the team of surgeons at UPMC Mercy Trauma and Burn Centers (Pittsburgh, PA) decided that the treatments should be limited to deep, relatively extensive partial-thickness burn wound patients. The decision to offer a patient treatment was based on clinical judgment of the surgeon in charge, and consultation with the burn service as a whole. Consideration typically involved the wound appearance after the first debridement, and at 24 and 48 h. Before cell-spray therapy, a consent form was obtained from each patient after the alternative conservative or invasive treatment was explained in detail. The physicians explained to the patient

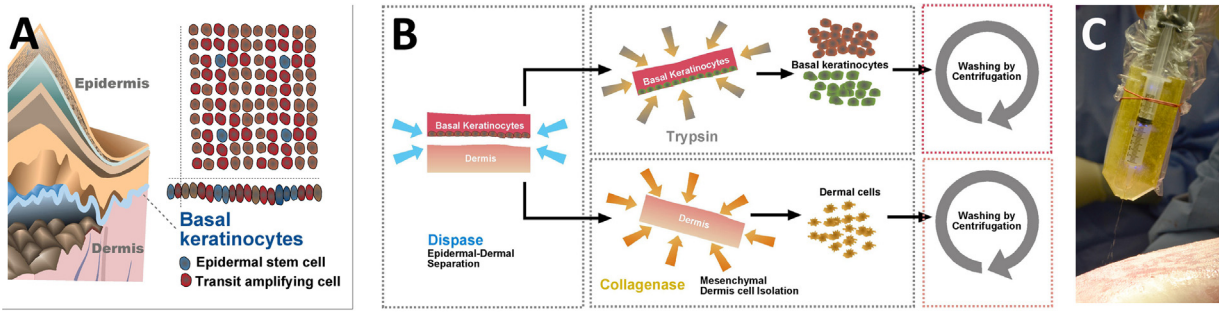

Fig. 1 – Single cell-spray therapy proof of concept. (A) The basal layer contains epidermal stem cells and transient amplifying proliferative keratinocytes that we included for spray-grafting on the wound. (B) Three-enzymatic step isolation process. Epidermal–dermal separation is performed by dispase and followed by trypsin digestion of the epidermis and, a collagenase digestion on the dermis. (C) Isolated cells are combined and seeded onto wound through cell-spray deposition.

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