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Case report of the first Caucasian burn patient transplanted with Cutimed Sorbact®-based cultured epithelial autografts technique at Tygerberg Hospital, Cape Town, South Africa: An 8-year follow-up

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Abstract

Cultured epithelial autograft applications are limited by the associated cost and time constraints in resource-limited settings. A modified composite technique using the patients' own tissue and Cutimed Sorbact dressing was employed as a life-saving emergency measure. Since the non-Caucasian population was more commonly treated at the center, it was important to report the first Caucasian patient outcome, as the graft-take outcome for all populations was unknown. A 54-year-old male with extensive flame burns and a low chance of survival was admitted to the Tygerberg Burn Center. He received traditional skin grafts and cultured epithelial cells, after the 2 week-culture period using the current technique. Short- (⩽2 weeks) and long-term graft take (⩽8 years) was inspected. Good graft take and complete epithelialization was observed during short-term inspection with partially healed areas initially attributed to extensive burn depth and dressing removal. Long-term follow-up indicated a near normal tissue appearance and excellent pliability.

Keywords

Cultured epithelial autografts, Cutimed Sorbact dressing, severe burns, Tygerberg Hospital, transplant

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Introduction

Cultured epithelial autograft (CEA) has gained widespread recognition and subsequent application into the clinical treatment of cutaneous burn wounds. Autologous cultured skin substitutes were shown to improve aesthetic outcome and cosmesis, allow earlier wound coverage,[1,2] have minimal infection transmission, immunological responses,[3] and donor site morbidity. It is not without its shortcomings though, especially related to the ease of CEA transferal to wound bed,[4] culturing period necessary for cell confluency and maturation (2 weeks), and the exorbitant cost.[3,5] Although the Western Cape Provincial Adult Tertiary Burn Center (WCPATBC) offers reputable burns care to adult burns victims (>13 years old), it is a public-funded hospital unable to meet the monetary demands that would otherwise enable treatment using the Food and Drug Administration (FDA)-approved CEA. CEA is a treatment modality that is particularly required by the more vulnerable, extensively injured victims.

In 2014, Dr Wayne George Kleintjes employed a composite CEA technique under emergency ethical approval that made use of autologous CEA grown on routinely used

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and readily available Cutimed Sorbact® dressing (Essity AB, BSN Medical (Pty) Ltd., Pinetown, South Africa). The technique proved to be low cost, and the CEA was easy to transfer (direct application of dressing containing CEA to wound bed). Importantly it proved to be life-saving to a patient that had recurring septic shock, prolonged burns intensive care unit (BICU) stay, and a subsequent low chance of survival.[6] The patients admitted to the WCPATBC with thermal injuries are mostly from impoverished, urbanized areas and comprise the non-Caucasian cohort. This was also the most common population that comprised the emergency cases using the Sorbact-CEA method at our Center. We have experienced overall favorable graft take and survival outcome with the non-Caucasian cohort. Therefore, the first Caucasian case was important to ascertain whether graft take using this novel modality would vary with different skin type. This would indicate whether the technique could be utilized in future without having to consider the potential adverse impact that pigment variability may have on graft take. It would ultimately mean that this composite CEA method could essentially eliminate population bias and be a potentially low-cost alternative to the currently approved cell therapy.

Case presentation

A 54-year-old male was admitted to the WCPATBC with 64% total body surface area burns following flame burns. He was intubated prior to admission for the suspicion of inhalation injury. The primary survey revealed that the patient had deep, partial, and full-thickness burns to the entire abdominal region, both forearms (anterior and medial), and both legs (nearly the entire surface). Superficial partial thickness burns on both hands and the face were also observed. The secondary survey indicated the absence of co-morbidities or additional injuries, and he was not on any chronic medication. The calculated abbreviated burn severity index[7] score of 12 denoted the likelihood of less than 10% chance of survival. First aid and fluid resuscitation initially occurred at the referred hospital (Paarl Hospital). On admission to the WCPATBC, general treatment commenced as per standard protocols for wound care and for fluid resuscitation using the modified Parkland™ formula.[8] Skin grafting commenced after satisfactory stabilization on day 4 post-administration.

During the first operation, traditional meshed skin grafts were harvested from the patient's back and transplanted onto the deep partial thickness and full-thickness burns regions after wound bed preparation (debridement/tangential excisions): right anterior forearm and posterior thigh, and nearly the entire anterior portion of the left leg. However, due to the extensive nature of the burns, the need for CEA use was evident, and a skin biopsy was taken. Xenografts (EZ Derm®, Molnlycke Health Care, UC LLC, Norcross, GA, USA) were used as temporary coverage on the open burn wounds due to insufficient skin graft availability. A 3×2 cm full-thickness skin section was biopsied from the right inguinal region and prepared as previously described.[6] A scalpel (15/0 blade) was used to separate the epidermis from the dermis on a sterile surface and the epithelial fragments further segmented. These fragments were then immersed in trypsin for separation of the remaining dermal elements. The trypsin was rinsed off, and the remaining epidermal keratinocytes were transferred with forceps to the central areas of 20×10 cm of the Sorbact dressing pad. The cells were supplemented daily with fresh autogenous platelet-rich plasma for growth stimulation. Progressive growth and confluence was macroscopically observed. Keratinocytes' appearance changed from an initial pale white-grey on day 1 after seeding to a light brown tint by day 10, indicating possible pigmentation. On day 14 (final culture assessment day), the CEA displayed abundant cell growth and shrinking of the gauze which indicated possible fibroblast activity (Figure 1). Mechanical debridement with the VersajetTM hydro-debridement system (VersajetTM, Smith+Nephew, Inc., Fort Worth, TX, USA) was employed to remove the superficial layers of the xenograft in preparation for CEA application.[6,9] The Sorbact-containing CEA dressing was then directly transferred onto the following regions: abdomen, right anterior forearm, anterior-medial region of the entire left leg, anterior patella region, and posterior lower right leg (Figure 1). Graft-take percentage was calculated as a surface area percentage of skin graft to CEA and assessed on days 7 and 14. The long-term follow-up using the Vancouver Scar Scale[10] for visual assessments took place 15 months, 3 years, 6 years, and 8 years (the 8-year checkpoint was done verbally).

Discussion

The CEA technique proved effective especially when the donor site locations could not meet the extensive coverage requirements. After 1 week posttransplant (Figure 2), very good healing on the forearm and abdomen was observed based on good graft take and complete epithelialization. Only small sections showed signs of partial healing which was related to dressing removal. Both legs displayed areas of good and partial CEA take, as well as sloughing. The latter indicated nonviable tissue possibly due to the blood supply in the distal extremities being poorer and the burn depth more severe. Two weeks posttransplant (Figure 2), the grafts showed excellent results owing to 100% CEA graft take with some crusting of dried exudate. One of the benefits of the applied CEA is that both dermis and epidermis were grown and transplanted which could have increased graft take and skin quality outcomes. The patient was discharged from BICU after 6 weeks; and after a prolonged rehabilitation period, from the ward. Follow-up after 8 years posttransplant (Figure 3) displayed almost normal skin quality with CEA in addition to excellent pliability and cosmetic outcome on the abdomen. The right forearm (CEA transplanted) had a better cosmetic result with a smoother surface, less pigmentation

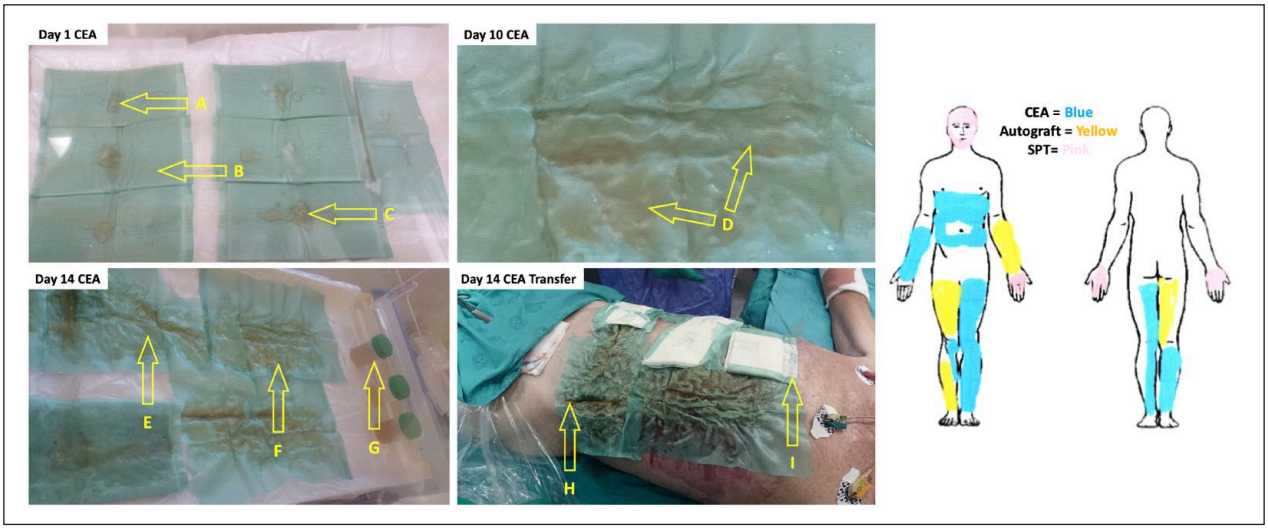

Figure 1. Preparation and transplant of Cutimed Sorbact® dressing containing CEA transplant areas on the transplant diagram (right) are indicated in blue, and yellow indicates skin grafts (A—central placement of keratinocytes (white color)), B—Sorbact dressing, C—autogenous platelet-rich plasma, D—keratinocytes appearance (light brown and grey color), E—abundant cell growth, F—shrinkage indicating fibroblast activity, G—cells in suspension, H—Sorbact dressing gauze with CEA, I—Sorbact dressing pad).
CEA: cultured epithelial autografts; SPT: superficial partial thickness.

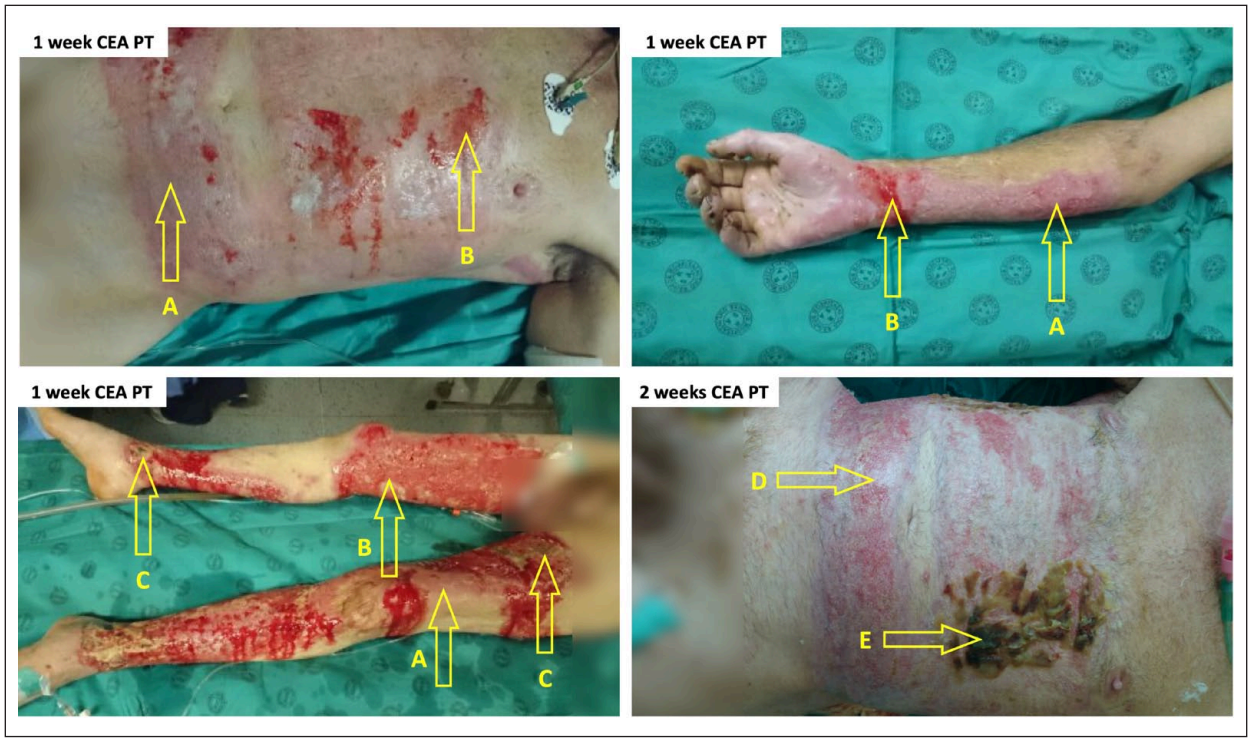

Figure 2. CEA graft take and healing 1 and 2 weeks PT (A—very good graft take, healing, and epithelialization (pink color), B—partially healed (red color), C—slough, D—100% ± graft take, E—dried exudate crusting).
CEA: cultured epithelial autografts; PT: posttransplant.

discrepancy, and more hair growth return compared to the left forearm (traditional mesh allograft transplanted) which displayed the typical irregular mesh pattern hyperpigmentation and slightly rough/uneven surface. Healing on the right leg was visible with meshed grafts and on the left leg, mostly with CEA. The patient was confined to a wheelchair

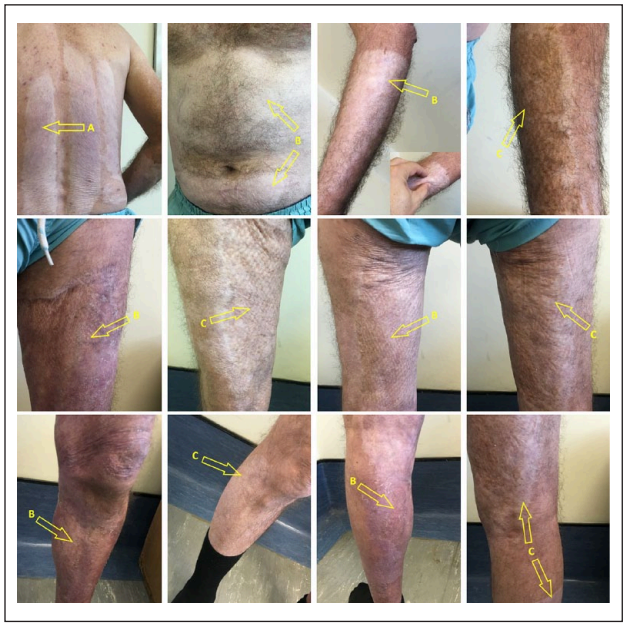

Figure 3. CEA and skin graft healing 6 years PT (A—donor sites, B—CEA, C—skin graft)
CEA: cultured epithelial autografts; PT: posttransplant.

throughout the treatment and check-up period due to the extent of the burns on the legs, but started walking independently without assistance just over a year after the injury. The verbal follow-up at 8 years posttransplant with CEA indicated that the patient was doing well overall with no complaints related to the burn wounds. He was happy with the results. Regarding the case at hand, the CEA not only acts as a protective wound coverage means but also stimulates reepithelialization, the return of pigmentation, and hair growth. Another noticeable benefit was that the applied composite technique was cheaper than if the FDA-approved CEA, EpicelTM (EpicelTM, Genzyme Corporation, Cambridge, MA, USA), were to be used. Epicel was estimated to be as much as $13,000 per 1% total body surface area treated.[11] In 1999, it was reported that the price of a 50 cm^2 Epicel piece was US$790[12] and by 2014, a portion of Epicel (7 × 10 cm) cost approximately US$5000. This far exceeded the cost for Sorbact dressing (10 × 20 cm) at US$6.[6] Treating large burns in the current clinical and socioeconomic setting would therefore not be feasible with Epicel and the Sorbact-composite technique was alternatively low cost. Thus, not only could it offer inclusivity of all socioeconomic backgrounds, but it could also provide a more cost-effective skin therapy option for under-resourced burn centers. More objective investigations are required to definitively attribute the patient's survival solely to CEA. However, the likelihood for complications and subsequent mortality would have been higher in its absence considering the exhausted donor sites for traditional skin grafts and the resultant vulnerable immunosuppressive state. While the composite technique of the CEA has been validated previously[9] and is incorporated into standard treatment protocol for extensive burns, the current case using the novel CEA technique showed promise for future use in the general population irrespective of varying pigmentation as well as age. Although the CEA graft-take outcome for this patient was excellent and similar to those observed in the non-Caucasian CEA-treated burn population, additional cases are required before definitive comparative conclusions can be made.

Conclusion

Good CEA graft take was observed throughout the assessment period with only a small initial setback in the lower extremities due to delayed healing. Since the outcome of the novel CEA technique in the Caucasian population was unknown, the first case results were very satisfactory. The novel CEA technique enabled engraftment and acceptable scar pigmentation in a Caucasian adult in a resource-constrained burn center. The current case therefore showed promise for future use in the general population.

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Author contributions

Both authors have contributed equally to the preparation of the draft and final article. Additionally, WK was responsible for the conceptualization and collection of figures, while TKP contributed by preparing the figures and the required literature.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The skin culture technique is patented and owned by Stellenbosch University (Stellenbosch, Cape Town, South Africa). The first author, Dr Wayne George Kleintjes, is the founder of the modified technique. Beyond this, the authors declare no potential conflicts of interest with the respect to research authorship and/or pulication of the article.

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Ethics approval

Ethical approval to report this case was obtained from Health Research Ethics Committee of the Faculty of Medicine and Health Sciences, Stellenbosch University (REF: C15/01/001).

Informed consent

Written informed consent was obtained for the operation from the patient and for the use of clinical figures for publishing or academic purposes.

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