CASE REPORT

The Amazing Wound Healing Accelerator; Topical Bioactive Solution: A Case Report

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ABSTRACT

Managing chronic wound requires multimodality approach for excellent healing result. This report concentrates on tissue proliferation phase of wound healing, observing the effect of topical bioactive solution onto chronic ulcers with poor healing potential. We report a case of 36-year-old male with underlying multiple chronic co-morbidities, presented with infected chronic right diabetic foot ulcer with osteomyelitis in sepsis. He underwent multiple wound debridements and ray amputation of right fifth toe. As tissue culture grew Pseudomonas aeruginosa, IV Ceftazidime was commenced along with daily wound dressing. His poor diabetic skin condition hindered autologous skin graft harvest, thus topical liquid bioactive factors solution (CelltiSS®) was applied onto exposed tendon and bone to expedite wound healing process. Granulation tissues rapidly grew covering these bare areas and deep pocket reduced within a week. This new modern dressing technology advancement is very beneficial in treating chronic ulcers with poor healing potential as it expedites the tissue proliferation phase.

Keywords: CelltiSS® topical liquid bioactive solution, Chronic wound healing, Diabetic foot, Growth hormone, Tissue proliferation

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INTRODUCTION

Over the centuries, many studies had been carried out to improve wound healing potential. Chronic wound management requires multimodality approach in order to heal well. This is due to the multifactorial influence onto a wound especially in chronic diabetic wounds which are complicated to heal. Initiated by utilizing natural substances like honey, tumeric, curcumin, and aloe vera for wound healing, further advancement had lead to the emergence of modern dressing techniques such as negative wound pressure therapy, hydrocolloid, and incorporation of antimicrobials agent. On top of that, hyperbaric oxygen therapy and usage of human skin equivalent (HSE) had produced a favourable outcome in facilitating healing process.

The current wound management framework includes tissue management, inflammation and infection control, moisture balance and epithelial edge advancement (T.I.M.E.) (1). Recently, technology has delved into the molecular level of tissue repair to accelerate wound healing process in tissue proliferation phase. Growth hormone (GH) and cytokines are found to be interesting pleiotropic factors that are able to promote angiogenesis, cell proliferation, and extracellular matrix synthesis (ECM) (1-4). This excellent discovery certainly delivers a great news in tackling difficult and chronic wound during our daily routine care.

We report a challenging case of an infected chronic diabetic foot ulcer in a patient with multiple chronic co-morbidities which has low healing potential according to current management. It is interesting to discover how a topical liquid bioactive solution accelerates tissue proliferation phase in such case.

CASE REPORT

A 36-year-old married young Malay gentleman had multiple co-morbidities which succumb him to loose his job as a breadwinner. He currently has to depend on his wife in order to help him support his family until his wound is properly healed. His underlying co-morbidities are hypertension, diabetes mellitus, end stage renal failure on regular haemodialysis and right eye rubeotic glaucoma. He presented to casualty with infected chronic right diabetic foot ulcer with osteomyelitis changes in sepsis. He already had five days history of fever associated with poor oral intake and lethargy after an ulcer surrounded by callous on his right foot worsened over a period of three months.

The pale, sloughy and foul-smelling ulcer measuring 3cm by 4cm had pus discharge. The foot was swollen and erythematous but had no crepitus. Both dorsalis pedis (DPA) and posterior tibial (PTA) arteries were not palpable, yet capillary refill time (CRT) of all toes remained less than two seconds. Right foot radiograph showed osteomyelitis changes. He had risks of poor wound healing due to his uncontrolled diabetes mellitus with dextrose of 17 mmol/L, peripheral vascular disease with ankle-brachial systolic index of 0.77, hypoalbuminemia (23 g/L) and severe infection with total white cell of 25.1x109/L, C-reactive protein of 45.41 mg/dL and growth of Pseudomonas aeruginosa on tissue culture. On contrary, his haemoglobin level is good (12.4 g/dL). The wound was debrided multiple times and ray amputation of right fifth toe was done resulting in exposed tendons and bone (Fig. 1).

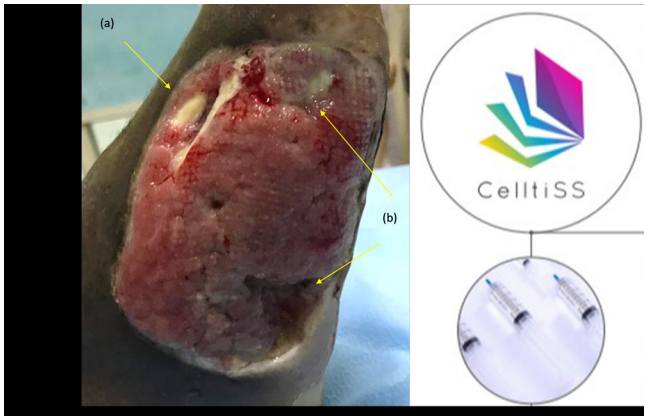

Fig. 1 : Initial wound (9cm x 4.5cm) after multiple debridements and ray amputation of right fifth toe with exposed bone, tendons (a) and deep lateral pockets (b). It is treated with CelltiSS® topical liquid bioactive factors solution in a 5mm syringe preparation.

IV Ceftazidime 1g daily was commenced for two weeks along with daily acetic acid and Bactigras® dressing for five days. Subsequent swab cultures were negative.

In view of his co-morbidities, patient was anticipated to have a poor wound healing process. He was also planned for split-thickness skin grafting to facilitate wound closure, however was not a good candidate for skin autograft in view of poor diabetic skin condition on areas to be harvested. Therefore, he was deemed to be a suitable candidate for a trial of a new topical liquid bioactive factors solution (CelltiSS® – Allogenic human skin derived secretome). Patient consented himself for this study. This conditioned media contains multiple bioactive factors (cytokines and growth factors) produced by fibroblasts responsible for wound healing process. After a single drop of CelltiSS® application onto bare areas, which are the exposed bone, tendons and deep wound pocket respectively, the granulation tissue rapidly grew to cover these areas within one week (Fig. 2). Subsequently, patient was advised for daily Hydrocyn® solution with Bactigras® application. The wound was monitored weekly for a month, then followed by a monthly basis follow up. Finally, the wound healed well after four months (Fig. 3).

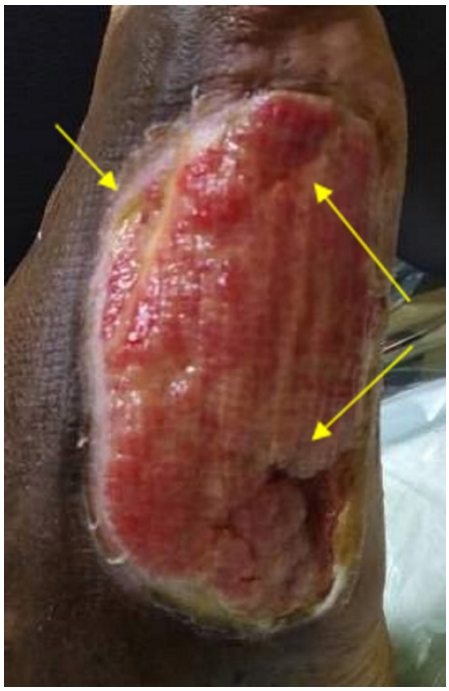

Fig. 2 : After one week of a single drop of CelltiSS® application onto exposed bone, tendons, and deep pocket, these areas are covered and lateral pockets shrunken in size.

Fig. 3 : Subsequently, the wound healed well after 4 months of contact dressing.

DISCUSSION

In this case report, CelltiSS® solution (an allogenic skin derived secretome) is a conditioned media being used to treat the chronic wound. It is harvested from a cell culture collected at 80-90% confluency during cells mitotic phase which contains maximum production of multiple bioactive factors produced by fibroblasts and remain viable for 7 days. These include interleukin-6 (IL-6), vascular endothelial growth factor receptor-1 (VEGFR-1), interleukin-1 receptor type-1 (IL1R1), TGF-beta receptor type-2 (TGFBR2), fibroblast growth factor-1 (FGF1), interferon gamma (IFNG), fibroblast growth factor receptor-2 (FGFR2), granulocyte-macrophage-colony-stimulating factor receptor subunit alpha (CSF2RA), platelet-derived growth factor receptor beta (PDGFRB), transforming growth factor beta-1 (TGFB1), and tumour necrosis factor (TNF). A cold chain transport maintained a temperature in between 4 to 8 degrees Celcius to preserve this media. These pleiotropic factors stimulate extracellular matrix (ECM) synthesis, collagen deposition, cell proliferation, angiogenesis, thus promoting granulation tissue formation and facilitates epithelialization (1-3). Ultimately, with a single application of CelltiSS® solution, the granulation tissue proliferates rapidly compared to carrying out routine dressing onto other wounds in the ward.

On top of that, Hydrocyn® solution and Bactigras® dressing are being used to further minimise risk of infection and enhance wound healing process for this patient. It was observed that no new slough or signs of infection developed subsequently throughout follow up after the application of this topical bioactive solution and daily dressing.

Chronic wound management requires multimodality approach in order to heal well. Looking at the molecular level, the role of fibroblasts in wound healing is to synthesize collagen fibres for added strength and to form a basal lamina by producing fibronectin, integrins, thrombospondin and vitronectin (1). These extracellular matrix (ECM) components provide the template and scaffold for angiogenesis, endothelial cell and keratinocyte migration and also epithelialization in which its level is modulated by fibroblast by mediating the expression of proteases and cytokines (i.e elastase and matrix metalloproteinases) (1-3).

The previous theory that the main mediator of GH actions which is circulating insulin-like growth factor 1 (IGF-1), aids in wound healing is proven inaccurate. This is because the locally produced IGF-1 by macrophages, fibroblasts, and endothelial cells are the one which that expedites wound healing through enhancing protein production, cell proliferation, and migration (2,3). In vivo studies showed that concentration of IGF-1 mRNA in the granulation tissue increased upon topically applied GH onto the wound (2,3,5). Nevertheless, systemic side effects produced by administration of systemic GH such as hypoglycaemia, fatigue, headache, oedema and mental disturbances can be reduced (2,3). Hence, the idea of applying topical bioactive solution comes into the place. The local GH administration to increase IGF-1 production is preferable than the administration of IGF-1 itself, in view of its higher production cost for keeping and transportation of the solution (2,3).

Chronic diabetic wound heals poorly as the remaining fibroblast is dysfunction and fibronectin degradation is rapid due to high proteases and low or absent tissue inhibitor of metalloproteinases (TIMPs) level (1,2,5). The premature, undifferentiated or senescent fibroblast is unable to respond efficiently to mitogenic stimulation by growth factors for instance platelet-derived growth factor (PDGF)-Я and transforming growth factor (TGF)-Я thus producing less growth factors and collagen (1). As a result, the wound healing process stunted and yield poor granulation tissue quality. Therefore, a new proposal emerged where bioactives are produced to tackle this issue.

This case report proves that the topical bioactive factors solution does able to reconcile the above-mentioned distressing issues in a rapid manner.

Since this case report yields a favourable outcome, further study with more samples under controlled environment in encouraged to exclude bias from this case report.

CONCLUSION

Topical bioactive factor solution is a promising new technology in the modern dressing era as it expedites wound healing process in tissue proliferation phase, based on T.I.M.E. management framework. This is a great advancement of technology and is very beneficial especially in treating patients who has chronic ulcers with poor healing potential. From this study, our patient is very satisfied with the wound healing outcome just by dressing, as he anticipated multiple surgical procedures to cover the previously exposed bone and tendon on the wound. The use of this topical bioactive factor solution should be encouraged in order to facilitate patient's recovery, and finally return his function to the society.

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