

# A Case Report: Role of Human Amniotic Membrane Mesenchymal Stem Cells-Conditioned Medium (hAMMSC-CM) Combine with Vitamin E for Treating Chronic Plantar Pedis Ulcer in Leprosy Patient

Marissa Astari<sup>1</sup>, Afif Nurul Hidayati<sup>1</sup>, Medhi Denisa Alinda<sup>1</sup>, Bagus Haryo Kusumaputra<sup>1</sup>, Linda Astari<sup>1</sup>, M. Yulianto Listiawan<sup>1</sup>, Indropo Agusni<sup>1</sup>, Fedik A Rantam<sup>2,3</sup>, Sunarso Suyoso<sup>1</sup>, Evy Ervianti<sup>1</sup>, Linda Astari<sup>1</sup>, Yuri Widia<sup>1</sup>, Sylvia Anggraeni<sup>1</sup>, Cita Rosita Sigit Prakoeswa<sup>1</sup>

<sup>1</sup> *Departement of Dermatology and Venereology, Dr. Soetomo Teaching Hospital / School of Medicine, Universitas Airlangga, Surabaya, Indonesia*

<sup>2</sup> *Stem Cell Laboratory, Institute of Tropical Disease, Universitas Airlangga, Surabaya, Indonesia*

<sup>3</sup> *Virology and Immunology Laboratory, Department of Microbiology, Faculty of Veterinary Medicine, Universitas Airlangga, Surabaya, Indonesia*

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**Abstract:** Leprosy ulcers are mostly present in plantar pedis especially in areas with bony prominence. Plantar ulcers healing in leprosy is often difficult and time consuming because of the declining of growth factors and cytokines as a result of a prolonged inflammatory condition. A 70-years old man working as pedicab driver had an ulcer at his left feet since 2 years ago, painless and not itchy. On regio caput metatarsal digiti 1 pedis sinistra there were 4 x 4 x 0,4 cm with necrotic tissue around. The patient was suffering from borderline leprosy since 10 years and already finished the treatment without history of drop out. We applied topical human amniotic membrane mesenchymal stem cells-conditioned medium (hAMMSC-CM) combine with vitamin E gel for 5 weeks and the ulcer healed completely.

## 1 INTRODUCTION

Ulcers are loss of continuity of skin tissue up to the dermis or deeper (subcutis). Approximately 30% of patients with Leprosy have peripheral nerve damage, and 10-20% of them have neuropathic ulcers due to peripheral nerve damage. Leprosy ulcers are mostly present in plantar pedis especially in areas with bony prominence. Plantar pedis is a part of the body that works for walking, so the risk for experiencing trauma is greater than other body parts (Diegelmann, 2004). Plantar ulcers healing in leprosy is often difficult and time-consuming because of the declining of growth factors and cytokines as a result of a prolonged inflammatory condition.

## 2 CASE

A 70-years old man working as pedicab driver came with chief complaint ulcer at his left feet since 2 years ago, painless and not itchy. At first the ulcer is small and getting bigger and never healed. On regio caput metatarsal digiti 1 pedis sinistra there were ulcus 4 x 4 x 0,4 cm, with necrotic tissue around.

The patient was suffering from borderline leprosy since 10 years ago. He had already got multibacillary multi-drug therapy for 12 months and had finished the treatment without history of drop out. The result of microbiology Mycobacterium leprosy examination was bacterial index (BI) 0 and morphological index (MI) was negative.

The initial treatment for the ulcer was sterile normal saline and surgical debridement to remove necrotic tissue, callus, and debris. After obtaining a clean ulcer, wound area and wound depth measurements were performed. Then the ulcer was

given framycetin gauze dressing (FGD) and sterile gauze above the FGD. On subsequent visit, the ulcers begin to be given topical hAMMSC + Vitamin E gel and covered with transparent film dressings. Application of gel was done every 3 days, and weekly evaluation included measurement of the

size and the depth of the ulcer was done. Initial measurements of the ulcer was 4x4x0.4 cm. Patient received hAMMSC + vitamin E gel for 5 weeks. After the therapy with hAMMSC + Vit C gel for 5 weeks, the ulcer healed completely.



Figure 1: (A) After debridement and first application of hAMMSC + vitamin E (B) After 2 weeks of application (C) After 3 weeks of application (D) After 4 weeks of application (E) After 5 weeks of application and the ulcer completely healed.

### 3 DISCUSSION

We present a case of chronic plantar pedis ulcer in leprosy patient that could completely healed with topical gel combination of hAMMSC-CM and vitamin E. Plantar ulcers in MH are neuropathic ulcers, occurring due to prior nerve damage or sequelae. Chronic ulceration results from one or more extinctions of the wound healing phase. (Diegelmann, 2004) In a chronic wound, one may detect a prolonged inflammatory response, elevated protease activity and decreased growth factors. These findings may account for the delayed wound healing process. The prolonged inflammatory response may be caused by infection or just inflammation. The FGD is an antibiotic wound dressing that works in the inflammatory phase of wound healing by treating the infection and contracting the colonisation. It is not effective in an inflammatory phase of wound healing that is not caused by infection. It is also not effective in the proliferative phase of wound healing. (Ennis et al., 2013; Nuschke, 2014)

Studies on the human amniotic membrane mesenchymal stem cells (hAMMSC) for the repair and regeneration of cells showed good results. The growth factors and cytokines can be found in the tissue medium of stem cells in *in vitro* conditions through its metabolite product so it can be utilized as a useful modality in the process of cell regeneration. (Jayaraman et al., 2013; Maxson et al., 2012)

The previous research has proved that injuries that are difficult to heal in humans have high levels of oxidative stress. Wounds or chronic ulcers often show the increasing levels of reactive oxygen species (ROS) or free radicals that can delay wound healing process, inhibit the formation of granulation tissue and epithelialization. Free radicals are formed in response to tissue damage which then inhibits the recovery process by attacking DNA, membranes, proteins, and lipids from cells. Antioxidants are believed to repair wounds by reducing the damage caused by free radicals released by neutrophils in the inflammatory phase of the wound healing process. (Moro, 1999; Telang, 2013)

The hAMMSCs contains many cytokines and growth factors, which may be effective in the inflammatory and the proliferation phase of the wound healing. In the inflammatory phase of wound healing, the pro-inflammatory cytokines in hAMMSCs may influence the infection and colonisation via its antimicrobial effect and the anti-inflammatory cytokines in hAMMSCs will diminish the inflammation (immunomodulatory effect). In the proliferation phase of the wound healing, the growth factors in hAMMSCs will stimulate proliferation and migration of cells, induce angiogenesis, and stimulate the formation of tissue granulation and epithelialization. (Jayaraman et al., 2013; Maxson et al., 2012)

Vitamin E is a non-enzymatic natural antioxidant and the most important lipid soluble in human tissue which is absorbed by the skin well. Several studies

have shown that vitamin E, especially  $\alpha$ -tocopherol, gives good results in the wound healing process. Alpha tocopherol may serve as an antioxidant, reducing ischemic damage due to reperfusion disorders, may stimulate growth and stabilize the granulation tissue, as well as re-epithelialization.

Prakoeswa et al. (2018), study analytical experimental approach comparing the topical hAMMSC-CM and the framycetin gauze dressing (FGD) applied every 3 days up to 8 weeks on the healing of chronic plantar ulcer of leprosy. Ulcer healing in the hAMMSC-CM group was significantly better than that in the FGD group was significant clinical and statistical differences ( $p < 0.005$  and  $p < 0.005$ ).

#### 4 CONCLUSIONS

In this study we found that hAMMSC-CM combination with Vitamin E may improve healing of chronic plantar ulcer of leprosy.

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