Evaluation of Wound Healing Ability with Human Embryonic Stem Cells in Patients with Non-Healing Wounds: A Case Series

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Abstract

Wound healing occurs by regeneration or repair in which the damaged tissue at the wound site is replaced with fibroblastic mediated scar tissue. However, inadequate cell repair due to poor vascularity at the wound site results in non-healing wounds. This study evaluated the effect of human embryonic stem cell (hESC) therapy in six patients with non-healing wounds. The wound was cleaned and washed with normal saline and cotton gauze. The ready to use form of hESCs was sprayed on the wound and final dressing was done with antibiotics, vaseline gauze and cotton pads. The wounds of all the patients healed after receiving hESC therapy. Reduction in the size of wounds and granulation was observed among all the patients. hESC therapy showed improved and faster wound healing in non-healing wounds of different etiologies.

Keywords: hESC therapy; Stem cell therapy; Non-healing wounds

Background

Wound healing occurs either by regeneration or repair. However, most wounds heal by the process of repair in which the damaged tissue at the wound site is replaced with connective tissue resulting in the formation of scar [1]. Chronic wounds or non-healing wounds result from inadequate cell repair due to poor vascularity at the wound site [2]. Stem cells hasten the wound healing process by secreting growth factors and cytokines essential for wound healing [3]. Previous studies have reported the use of bone marrow derived stem cells, hematopoietic stem cells, endothelial progenitor cells, and extracellular matrix molecules for the treatment of non-healing wounds [4,5].

Of the several types of stem cells, the embryonic stem cells possess the highest potential to differentiate into any cell type. However, difficulty in isolation of these cells has resulted in scarce research in this area [3]. In the present case series, we evaluated the wound healing potential of human embryonic stem cells (hESCs) by using them directly on a cotton mesh at the wound site among six patients with non-healing wounds.

Materials and Methods

The present study evaluated the effect of hESC therapy on non-healing wounds in six patients. The patients who were referred to our facility with non-healing wounds between Jun 2011 and Sep 2014 were included. All the patients had previously received conventional treatment for non-healing wounds but had not recovered. Chronic wound was defined as a wound that failed to proceed through an orderly and timely reparative process to produce anatomic and functional integrity of the injured site. The patients included in the study had non-healing wounds as a result of trauma, infection, metabolic disorders, pressure sores, or radiation burns. Patients were excluded if conventional treatment for non-healing wounds was successful, if pregnant, or if patients had received treatment with other stem cells within one year of the study.

The study protocol was approved by an Independent Ethics Committee (IEC). The institutional committee for stem cell research and therapy of our institute reported all research with respect to embryonic stem cells to the National Apex Body. The study was conducted in accordance to the declaration of Helsinki [6]. A written, on camera informed consent was obtained from the patients prior to treatment.

Cell Culture, Preparation, and Transplantation

hESCs of ectodermal origin were cultured in the year 2000 as per our patented technology (United States Granted Patent No US 8592, 208, 52) in a GMP, GLP, and GTP certified laboratory. A biocompatible flask with media and sterile submerged cotton gauze was used to grow stem cells in a carbon dioxide incubator. This was incubated in a water jacketed carbon dioxide incubator for 24 h and then retrieved. The sample was checked for viability and sterility before administration to the patient. The detailed cell culture technique has been elaborated elsewhere [7,8]. The safety and efficacy of our cell line has been established [9]. The cells grown on a cellulose mesh were frozen. The cotton gauze contained 106 hESCs per inch. Before transplantation, the hESCs were thawed and cellulose membrane with the viable cells was transplanted. Patient’s wound was cleaned and washed with normal saline and the cotton gauze with hESCs was laid out carefully on the wound. In addition, the ready to use form of hESCs (hESCs suspended in normal saline) was sprayed on the wound and the final dressing was done with antibiotics, if required; vaseline gauze, and cotton pads. The entire process of dressing was repeated on daily basis. All the processes were carefully monitored by in house wound experts. Use of hydrogen peroxide, antiseptic solutions, or any form of aggressive agents for debridement was avoided to ensure that the cells transplanted the previous day are not lost. The patients received a daily dose of intramuscular and a weekly dose intravenous hESCs along with the daily dressing. The patients did not receive compression therapy, hyperbaric oxygen therapy and did not undergo surgery while

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on hESC therapy. The patients received antibiotics only in case of infection. Serial photographs of the wounds were taken to evaluate the daily improvements and to assess the presence of possible infections.

**Case 1**

A man in his mid-twenties presented with chronic non-healing ulcer on the left tibial shin on 11 Nov 2011. The patient had an accidental fall from a height of 15-20 feet about 8 months back in his village resulting in a small abrasion on the left shin. The wound was not treated resulting in swelling and pus formation around it a week after the fall.

The patient then received treatment for the wound from a local medical practitioner for 2 to 3 months. No improvement was observed and the patient developed a sinus opening at the lower end of the wound. On consulting another physician, the wound was debrided and dressed appropriately. The wound also had signs of infection. In the absence of recovery for 8 months, the patient was referred to our facility. The patient was treated with hESC infiltration at the ulcer site along with daily hESC dressing. Prior to treatment with hESC therapy, the wound was of 10 cm × 5 cm × 4 mm dimension.

The patient received a total of 28 dressings over a period of 2 months (Figure 1). On receiving hESC dressing, the wound size decreased gradually (22 Nov 2011: 8.5 cm × 4.5 cm × 3 mm, 06 Dec 2011: 8 cm × 4 cm × 2 mm, 13 Dec 2011: 7 cm × 3 cm × 2 mm, 21 Dec 2011: 5 cm × 3 cm × 1 mm, 31 Dec 2011: 4 cm × 1 cm × 1 mm, and 04 Jan 2012: 3.5 cm × 1 cm × 1 mm). The wound size had reduced to 3 cm × 0.5 cm × 1 mm (Table 1). At the time of last visit, the wound had healed.

**Case 2**

A child aged < 10 yr presented with a crush injury on the left leg and foot. The patient had injury on the left leg, talus, calcaneum, and second metatarsal. A cemented pole had fallen on the patient’s left leg and foot while he was playing on 11 Nov 2013. The patient underwent a surgery in a tertiary hospital on 17 Nov 2013 with external fixator, decreased CSE for left talus, left calcaneum, and second metatarsal. However; the patient had fever and observed persistent discharge from the wound along with a non-healing wound and exposure of the metatarsal. A culture and sensitivity test of the sample obtained from the wound revealed growth of Pseudomonas. The patient was treated with antibiotics (Monocel® and Augmentin®), short debridement, and amputation up to demarcation line on left foot on 08 Dec 2013. The patient was administered antibiotics systemically as he was diabetic.

The patient still showed impaired wound healing and was thus referred to our facility where he started to receive hESC therapy on 04 Jan 2014. On presentation, the wound dimensions were: 6 cm × 11 cm (fasiotomy wound-upper one third of left leg) and 4 cm × 8 cm (lacerated wound-dorsum of foot and lower one third of foot). The metatarsals were sticking out of the wound and osteomyelitis had set in. The wound culture showed infection with Staphylococcus aureus.

The patient was treated with hESC therapy along with antibiotics. On receiving hESC therapy, reduction in wound size was observed with good granulation and the wound completely healed as on 15 Feb 2014 (Figure 2). The patient had a total of 38 dressing applications (Table 1).

**Case 3**

A man in his early eighties presented with a non-healing ulcer on the left ankle and back on 19 Nov 2013. The patient had a small non-healing ulcer on his back near the left scapula for more than a year due to removal of a skin cancer patch. The patient developed another deep ulcer on his left foot 5 months ago which had increased in size and depth requiring a flap surgery. The wound culture and sensitivity test revealed Staphylococcus growth. The relevant medical history included diabetes mellitus for which he was taking insulin, hypertension, Coronary Artery Disease (CAD), Coronary Artery Bypass Grafting (CABG) with pacemaker implant 23 years ago, and depression since an unknown duration.

The patient was treated with antibiotics (Monocel®, 2 gm two times a day intravenously and Metrogyl®, 800 mg three times a day) along with regular dressings of hESCs.

The patient’s wound decreased in size and depth showing healthy margins with granulation tissues. Although the patient was advised to undergo skin grafting, he refused due to old age and other associated medical complications. The dimension of the wound had decreased from 6 cm × 11 cm at the time of first presentation to 3 cm × 7 cm at the time of last visit on 24 Jun 2014 (Figure 3). The patient received a total of 100 dressing applications over a period of 6 months (Table 1). The wound healed completely.

**Case 4**

A child aged < 10 yr presented with a crush injury on the left leg and foot. The patient had injury on the left leg, talus, calcaneum, and second metatarsal. A cemented pole had fallen on the patient’s left leg and foot while he was playing on 11 Nov 2013. The patient underwent a surgery in a tertiary hospital on 17 Nov 2013 with external fixator, decreased CSE for left talus, left calcaneum, and second metatarsal. However; the patient had fever and observed persistent discharge from the wound along with a non-healing wound and exposure of the metatarsal. A culture and sensitivity test of the sample obtained from the wound revealed growth of Pseudomonas. The patient was treated with antibiotics (Monocel® and Augmentin®), short debridement, and amputation up to demarcation line on left foot on 08 Dec 2013. The patient was administered antibiotics systemically as he was diabetic.

The patient still showed impaired wound healing and was thus referred to our facility where he started to receive hESC therapy on 04 Jan 2014. On presentation, the wound dimensions were: 6 cm × 11 cm (fasiotomy wound-upper one third of left leg) and 4 cm × 8 cm (lacerated wound-dorsum of foot and lower one third of foot). The metatarsals were sticking out of the wound and osteomyelitis had set in. The wound culture showed infection with Staphylococcus aureus.

The patient was treated with hESC therapy along with antibiotics. On receiving hESC therapy, reduction in wound size was observed with good granulation and the wound completely healed as on 15 Feb 2014 (Figure 2). The patient had a total of 38 dressing applications (Table 1).

**Case 5**

A man in his early eighties presented with a non-healing ulcer on the left ankle and back on 19 Nov 2013. The patient had a small non-healing ulcer on his back near the left scapula for more than a year due to removal of a skin cancer patch. The patient developed another deep ulcer on his left foot 5 months ago which had increased in size and depth requiring a flap surgery. The wound culture and sensitivity test revealed Staphylococcus growth. The relevant medical history included diabetes mellitus for which he was taking insulin, hypertension, Coronary Artery Disease (CAD), Coronary Artery Bypass Grafting (CABG) with pacemaker implant 23 years ago, and depression since an unknown duration.

The patient was treated with antibiotics (Monocel®, 2 gm two times a day intravenously and Metrogyl®, 800 mg three times a day) along with regular dressings of hESCs.

The patient’s wound decreased in size and depth showing healthy margins with granulation tissues. Although the patient was advised to undergo skin grafting, he refused due to old age and other associated medical complications. The dimension of the wound had decreased from 6 cm × 11 cm at the time of first presentation to 3 cm × 7 cm at the time of last visit on 24 Jun 2014 (Figure 3). The patient received a total of 100 dressing applications over a period of 6 months (Table 1). The wound healed completely.

**Case 6**

A child aged < 10 yr presented with a crush injury on the left leg and foot. The patient had injury on the left leg, talus, calcaneum, and second metatarsal. A cemented pole had fallen on the patient’s left leg and foot while he was playing on 11 Nov 2013. The patient underwent a surgery in a tertiary hospital on 17 Nov 2013 with external fixator, decreased CSE for left talus, left calcaneum, and second metatarsal. However; the patient had fever and observed persistent discharge from the wound along with a non-healing wound and exposure of the metatarsal. A culture and sensitivity test of the sample obtained from the wound revealed growth of Pseudomonas. The patient was treated with antibiotics (Monocel® and Augmentin®), short debridement, and amputation up to demarcation line on left foot on 08 Dec 2013. The patient was administered antibiotics systemically as he was diabetic.

The patient still showed impaired wound healing and was thus referred to our facility where he started to receive hESC therapy on 04 Jan 2014. On presentation, the wound dimensions were: 6 cm × 11 cm (fasiotomy wound-upper one third of left leg) and 4 cm × 8 cm (lacerated wound-dorsum of foot and lower one third of foot). The metatarsals were sticking out of the wound and osteomyelitis had set in. The wound culture showed infection with Staphylococcus aureus.

The patient was treated with hESC therapy along with antibiotics. On receiving hESC therapy, reduction in wound size was observed with good granulation and the wound completely healed as on 15 Feb 2014 (Figure 2). The patient had a total of 38 dressing applications (Table 1).

**Table 1:** Dimensions of non-healing wounds before and after receiving hESC therapy.

<table>
<thead>
<tr>
<th>Case</th>
<th>Wound site</th>
<th>Duration of therapy</th>
<th>Dimensions of the wound before treatment</th>
<th>Dimensions of the wound after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>left tibial shin</td>
<td>2 months</td>
<td>10 cm × 5 cm × 4 mm</td>
<td>Healed</td>
</tr>
<tr>
<td>Case 2</td>
<td>left leg and foot</td>
<td></td>
<td>Left leg: 6 cm × 11 cm</td>
<td>Left leg: Healed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Left foot: 4 cm × 8 cm</td>
<td>Left foot: Healed</td>
</tr>
<tr>
<td>Case 3</td>
<td>left ankle and back</td>
<td>6 months</td>
<td>6 cm × 11 cm with exposed tibial artery</td>
<td>Healed</td>
</tr>
<tr>
<td>Case 4</td>
<td>Deep radiation burn</td>
<td>4 weeks</td>
<td>20 cm × 20 cm</td>
<td>Healed</td>
</tr>
<tr>
<td>Case 5</td>
<td>left foot (lateral and dorsal aspect)</td>
<td>6 months</td>
<td>Dorsum Left: 16 cm × 12 cm × 5 mm</td>
<td>Dorsum Left: Healed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dorsum Right: 12 cm × 8 cm × 3 mm</td>
<td>Dorsum Right: Healed</td>
</tr>
<tr>
<td>Case 6</td>
<td>deep bed sore with traumatic paraplegia</td>
<td>first session-3 mo</td>
<td>10 cm × 12 cm with sacral bone exposed</td>
<td>Healed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>second session-4 weeks</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1:** Before and after picture of the wound (Case 1).
A woman in her mid-forties was undergoing radiation as a part of the treatment protocol for rhabdomyosarcoma which had already been operated. She suffered a massive, full thickness radiation burn on her abdomen covering the iliac crest up to the umbilical area on the right side. The wound was approximately 20 cm × 20 cm prior to receiving hESC therapy and was infected (Figure 4). After receiving hESC therapy for 14 days, the dimensions of the wound reduced to 1 cm × 1 cm. The wound healed completely after 30 days of treatment. The patient received a total of 15 dressings.

Case 5

A man in his early sixties presented with non-healing ulcer on the left foot (lateral and dorsal aspect), atherosclerotic plaques in bilateral lower limbs, and decreased hearing in the right ear on 29 Nov 2011. The patient had fallen on the footpath in 2008 which resulted in multiple abrasions on the lateral aspect of left foot, dorsal aspect of the right foot and left hip fracture. The patient experienced severe pain in both legs and noticed swelling with redness and pus formation. On consulting a physician, it was observed that the wounds had gangrenous changes for which he was advised incision and drainage procedure. Medical history of the patient included hypertension since 6 years, rheumatoid arthritis since 22 years, decreased hearing since an unknown duration, and atherosclerotic plaques in bilateral lower left foot with monophasic flow in anterior tibial (ATA)/posterior tibial (PTA)/dorsalis pedis arteries (DPA) since Mar 2011. The patient was a cigarette smoker since 4 years and consumed alcohol since the past 20 years. Although the patient underwent incision and drainage without any complications, there was no improvement in wound healing. The infection in the wound still persisted. The patient was referred to a plastic surgeon for flap surgeries bilaterally and no improvement was observed after 4 surgeries. Later, the patient was referred to Nutech Mediworld for hESC therapy. On presentation, the wound in left foot dorsum was 16 cm × 12 cm × 5 mm and that of right foot dorsum was 12 cm × 8 cm × 3 mm with redness, foul smell, and pus formation.

On undergoing hESC therapy, the patient showed improvement in granulation and reduction in wound size (Figure 5). On receiving hESC dressing, the wound size decreased gradually (Table 2).

On culture and sensitivity test of samples obtained from both left and right foot ulcers, growth of Klebsiella and Pseudomonas was observed. The patient was started on local antibiotics along with hESC therapy. Eventually, the patient showed healing of the ulcers on both left and right foot dorsum. The patient received a total of 200 dressing applications over a period of 6 months followed by dressing three times a week till Dec 2012 (Table 2). The right foot healed completely and the wound on the left foot had reduced in size.

Case 6

A man in his mid-twenties presented with a deep bedsore with traumatic paraplegia and loss of sensation below the nipple line post trauma, no bowel or bladder sensation, and no mobilization on 21 Jul 2011. The patient had a history of a car accident 3 years ago which resulted in a spinal cord injury at D3 and D4 level followed by loss of sensation below the injury. One year after the injury, the patient
developed a bedsore in the lower back/pelvic region which increased in size. The patient had started to observe discharge from the wound site.

The patient underwent hESC therapy for traumatic paraplegia. This wound did not heal despite medical intervention for 2 yr and hESC dressings for the bedsore. Swab samples taken from the sacral lesion for culture on 10 Sep 2011 revealed growth of *E. Coli*. The febrile patient received antibiotics (Monocef®, 1 gm two times a day) along with local application of hESC and showed improvement in the granulation tissue, and reduction in the depth of bedsore after receiving the first session of hESC therapy. The patient showed improvement of 70% at the end of second session with healthy margins and granulation tissue and decreased depth of wound. The patient received a total of 104 dressing applications during the first session which lasted for 3 months and 80 dressing applications in the second treatment session. The patient showed improvement of 70% at the end of second session with healthy margins and granulation tissue and reduction in the depth of bedsore after receiving the first application of hESC and showed improvement in the granulation tissue, and reduction in the depth of bedsore after receiving the first session of hESC therapy. The patient showed improvement of 70% at the end of second session with healthy margins and granulation tissue and decreased depth of wound. The patient received a total of 104 dressing applications during the first session which lasted for 3 months and received 80 dressing applications in the second treatment session which lasted for 4 weeks (Figure 6). The wound had healed completely at the time of last visit on 15 Jun 2012 (Table 1).

Discussion

The results of the present study demonstrated decreased wound size and complete healing of the skin with good granulation among patients who received hESC therapy for non-healing wounds. Although most patients had been receiving other conventional treatments for non-healing wounds prior to being referred to our facility, they observed no improvement in the wound. All the patients included in the study had not previously responded to conventional therapy and antibiotics treatment.

Impaired wound healing may result from incomplete or postponed healing process due to ischemia, diabetes mellitus, or venous stasis disease. In addition, there are several local and systemic factors that may influence the process of wound healing [10]. Treatment of non-healing wounds involves creating an ideal environment for optimal healing process. hESC therapy is of high importance for the treatment of non-healing wounds due to the ability of hESCs to differentiate into various cell types. Stem cells derived from bone marrow, peripheral blood, umbilical cord blood, adipose tissue, and skin/hair follicles have been used for the treatment of non-healing wounds [11].

Embryonic stem cells have shown promising results in wound healing however; there are fewer studies which have used embryonic stem cells [12,13]. The hESCs transform into keratocytes which have the potential to heal. Accelerated wound healing was observed in diabetic rats on topical application of undifferentiated embryonic stem cells [12]. hESCs are gaining more importance in regenerative medicine because they can be stored in an undifferentiated form unlike stem cells from other origins [14]. Lee et al. demonstrated the potential of hESC derived endothelial precursor cells in accelerating wound healing and tensile strength of the wounds with topical treatment and subcutaneous injection. Treatment with hESC resulted in faster formation of granulation tissue and re-epithelialization of wounds [15].

Other studies have shown that mesenchymal stem cells (MSCs) are effective in accelerating wound closure. Most studies investigated the use of MSC with a concentrated MSC-conditioned medium which was directly applied at the wound site. MSCs secrete cytokines and growth factors which are responsible for faster wound healing [16]. Enhanced regenerative potential of MSCs may be attributed to several trophic mechanisms that are activated when these cells are exposed to an injury environment [16]. Stem cells show their action by homing in the site of injury after being transplanted. The stem cells migrate to the site of injury through chemokines, cytokines, and growth factors released from the site of injury [17,18]. We assume that the hESCs administered in our study also worked in the similar manner. We also applied hESCs directly at the wound site which led to a faster wound healing in all our patients. In conclusion, results of the present study suggest that hESC therapy is effective in the treatment of non-healing wounds. Use of hESC therapy in patients who had previously received other forms of treatment for non-healing wounds resulted in accelerated wound healing and granulation. The application of hESCs grown on a cotton mesh directly on the wound allowed the skin cells to start regeneration and behave akin to a skin transplant at the cellular level. We also used systemically administered antibiotics for our patients to control the infection that was still persisting in the wounds. The use of systemic administered antibiotics is helpful for post-surgical wounds [19]. The use of antibiotics through IV route also gives the earliest and most sustained levels of antibiotic in wound tissue fluid [20]. All our patients had chronic wounds and had taken antibiotic treatment prior to starting the hESC therapy. All these patients had not benefitted from their previous antibiotics treatment. Thus, it is highly unlikely that antibiotics were solely responsible for the improvement that was observed after hESC therapy. The hESCs were isolated and preserved using a patented technology. The evidence for the use of hESCs at our facility has been gathered over a number of years and was accepted as written evidence to House of Lords, Regenerative Medicine, Science and Technology Committee report (Presented at Wound Care Conference conducted at RML Hospital in Nov 2011) [19]. This is the first study reporting the role of hESCs in the treatment of non-healing wounds. We observed remarkable improvement in our patients. However, studies with larger number of patients and with controls may provide better evidence for the use of hESC more efficiently.

Acknowledgements

![BEFORE](image1)  ![AFTER](image2)

Figure 6: Before and after picture of the wound (Case 6).

<table>
<thead>
<tr>
<th>Date</th>
<th>Wound site</th>
<th>Length (cms)</th>
<th>Breath (cms)</th>
<th>Depth (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>29 Nov 2011</td>
<td>Left Dorsum</td>
<td>16</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Right Dorsum</td>
<td>12</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>28 Dec 2011</td>
<td>Left Dorsum</td>
<td>15</td>
<td>11</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>Right Dorsum</td>
<td>11</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>28 Jan 2012</td>
<td>Left Dorsum</td>
<td>12.5-13</td>
<td>9-9.5</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Right Dorsum</td>
<td>6.5-7</td>
<td>5-5.5</td>
<td>1-2</td>
</tr>
<tr>
<td>14 Feb 2012</td>
<td>Left Dorsum</td>
<td>11-11.5</td>
<td>8-8.5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Right Dorsum</td>
<td>6-6.5</td>
<td>4.5-5</td>
<td>1</td>
</tr>
<tr>
<td>28 Mar 2012</td>
<td>Left Dorsum</td>
<td>11</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Right Dorsum</td>
<td>3.5</td>
<td>3.5</td>
<td>1</td>
</tr>
<tr>
<td>30 Apr 2012</td>
<td>Left Dorsum</td>
<td>9</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Right Dorsum</td>
<td>1.5</td>
<td>1.5</td>
<td>1</td>
</tr>
<tr>
<td>24 May 2012</td>
<td>Left Dorsum</td>
<td>7.5</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Right Dorsum</td>
<td>0.5</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>20 Jun 2012</td>
<td>Left Dorsum</td>
<td>6</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Right Dorsum</td>
<td>healed</td>
<td>healed</td>
<td>healed</td>
</tr>
</tbody>
</table>

Table 2: Improvement in wound healing after receiving hESC therapy for Case 5.
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