

Combination Therapy Revives Hope for Patients with Diabetic Foot Ulcer: A Case Report

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Case report

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Abstract

Background

Diabetic foot ulcers, as one of the most debilitating complications of diabetes, can lead to amputation. Treatment and management of diabetic foot ulcers are among the most critical challenges for the patients and their families.

Case presentation

The present case report is of a 63-year-old man with a 5-year history of uncontrolled type 2 diabetes who has had diabetic foot ulcers for the past three years on three sites of the left external ankle in the form of two deep circular ulcers with sizes of 6×4 cm and 6×8 cm, the sole as a superficial ulcer with a size of 6×3 cm, and the left heel as a deep skin groove. Moreover, the left hallux was completely gangrenous. The patient's ulcers were infected with *Staphylococcus aureus* and multidrug-resistant *Pseudomonas aeruginosa*. Despite antibiotic therapy and routine dressing changes, the patient showed no improvement during the hospital stay. Accordingly, the patient was transferred to our service after consulting with the wound management team. Diabetic foot ulcers were treated and managed using a combination of maggot therapy, the Negative Pressure Wound Therapy (NPWT), and silver foam dressing. After three months and ten days, the patient's ulcers completely healed, and he was discharged from our service with the excellent and stable condition.

Conclusions

Based on the present case report study's clinical results, wound-care teams can use the combination therapy applied in this study to treat refractory diabetic foot ulcers.

1. Background

Diabetic Foot Ulcer (DFU) is one of the most important and debilitating complications of diabetes (1). More than 25% of people with diabetes develop DFU during their lifetime (2), and about 20% of moderate to severe DFUs lead to amputation (3). The mortality risk in a diabetic patient with DFU due to the ulcer complications (such as infection and sepsis) is twice as high in 10 years as in a diabetic patient without DFU (1).

Current methods for managing DFU include necrotic tissue debridement, wound care and exudate management, Negative Pressure Wound Therapy (NPWT), vascular health assessment, combating diabetic wound infection through topical antibiotic therapy, silver foam dressing, and glycemic control (4–5). In this regard, newer treatment strategies include Maggot Therapy (MT), NPWT, Hyperbaric Oxygen Therapy (HBOT), stem cell-based therapy, growth factor therapy, and therapeutic application of extracellular matrix proteins (6). The MT, also known as larval therapy, is the intentional application of medical-grade fly larvae (such as *St. Lucilia sericata*) grown under controlled laboratory conditions for

therapeutic purposes, especially for the treatment of DFUs (7). The main therapeutic mechanisms of MT are the ability to reduce wound bacteria through their digestion, production of antibacterial secretions and destruction of bacterial biofilms (8). MT has been shown to be effective for a variety of wounds with necrotic and gangrenous tissue (5). The NPWT is used as another modern treatment method for complex wounds, especially DFUs, which involves applying a foam dressing attached to a negative pressure vacuum pump through which wound exudate is collected in a capsule (9). The NPWT also increases local blood flow, inhibits pathogenic bacteria's growth and minimizes tissue edema (10). Another common and cost-effective treatment method for DFUs is silver foam dressing. Silver ions bind to bacterial DNA, interfere with bacterial electron transfer, and disrupt bacterial growth (11).

Regarding that DFU does not respond to standard drug therapies, combination therapies are recommended for treating and managing DFUs (12). This study describes a patient with DFU who completely recovered using combination therapy (MT, NPWT, and silver foam dressing).

2. Case Presentation

The patient is a 63-year-old man with a 5-year history of type 2 diabetes who has had left DFUs for three years. He is also a retired employee of the education department with a middle level of socioeconomic status. So far, he has been hospitalized three times for the routine treatment of DFU (normal saline wound dressing and antibiotic therapy). He shows poor glycemic control and has a history of hypertension and iron deficiency anemia. The patient also has a family history of diabetes and high blood pressure. He is not a smoker and denies a history of drug and alcohol abuse.

The patient had referred to Imam Reza Hospital in Urmia on 8 June 2019 with a chief complaint of ulceration on the left foot. In history-taking and physical examination, it was found that the patient had antibiotic-resistant DFUs (the organisms of *Staphylococcus aureus* and *Pseudomonas aeruginosa* has been reported responsible for the infection in patient culture-antibiogram) on three sites of the left external ankle in the form of two deep, circular ulcers with sizes of 6×4 cm and 6×8 cm, the sole as a superficial ulcer with a size of 6×3 cm, and the left heel as a deep skin groove (Fig. 1). Moreover, the left hallux was completely gangrenous (Fig. 1). Some of the patient's laboratory data on admission were as follows:

- Hemoglobin A1C = 7/5%
- Blood Sugar = 550 mg/dl
- High-density lipoprotein 38 mg/dl
- Low-density lipoprotein 75 mg/dl
- Cholesterol 182 mg/dl
- Triglycerides 79 mg/dl
- Blood urea = 19.1 mg/dl
- Blood creatinine = 0.83 mg/dl

- Hemoglobin = 8/9 g/dl
- Hematocrit = 32%

During the hospital stay, the patient first received Amp Ciprofloxacin 400 mg Intravenous (IV) q12h (BID) and Amp Clindamycin 900 mg IV q8h (TDS) for four days, and then he received Amp Meropenem 1 g IV TDS and Amp Vancomycin 1 g IV BID for two weeks. In addition, to control blood sugar, he was on Novorapid insulin six units TDS and Lantus Insulin 25 units at night before bedtime. To control blood pressure, he was taking Tab Captopril 25mg BID.

The patient underwent an initial examination, Color Flow Doppler, and Magnetic Resonance Imaging (MRI). The findings did not show any abnormalities in the left foot's circulatory system, although the results of the MRI confirmed the diagnosis of osteomyelitis of the left hallux. Moreover, due to a low hemoglobin level on admission, a single unit of packed red blood cells was injected into the patient. The patient's DFU also had an annoying odor, so that other patients complained of an unpleasant odor. The severity of diabetic foot infection was such that the patient suffered from sepsis symptoms (fever, chills, tachycardia, and hypotension). The patient's vital signs on admission were as follows: Temperature: 38.3°C, Respiration Rate: 19 bpm, Pulse Rate: 103 bpm, Blood Pressure: 150/85 mmHg. During the hospital stay, the patient received the routine DFU care (normal saline dressing twice a day and intravenous antibiotic therapy). However, she did not recover from DFU using routine wound care, so she was referred to our wound management team.

2.1. Management

First, *St. Lucilia Sericata* (L1 larvae) medicinal maggots were provided from the laboratory of medical entomology of the School of Public Health, Tehran University of Medical Sciences, Iran. Then on 11 June 2019, the MT was begun to conduct debridement and bacterial disinfection. For this case, the MT included preparing the wound, putting the larvae on DFUs, and finally dressing and removing the larvae after 48 hours (Fig. 2). After beginning the MT, the odor of the infection completely ended, and the MT continued for four weeks [see Additional file 1].

Furthermore, after the completion of MT, the patient's DFUs were stimulated by mechanical debridement and saline irrigation so that the whole necrotic tissue was completely removed and granulation tissue formed on the surface of the DFUs (Fig. 3). After completing the MT on 12 July 2019, the patient was discharged from the hospital with good general condition, and the treatment process was continued as home care by the wound management team. After completing the MT, to accelerate the treatment process and speed up recovery, the NPWT (applying a pressure of 125 mmHg intermittently) was used for five four-day sessions. After each session, foam dressings of the DFUs were changed until the next session (Fig. 4). All deep parts of the DFUs, especially the deep heel ulcer, were recovered due to the rapid granulation tissue growth.

Moreover, after completing the MT, silver dressing was used once every three days for two months to completely heal the DFUs (Fig. 5). The patient was finally able to walk on his left foot. Another essential part of the DFU treatment was offloading, in which the patients were instructed to avoid excessive pressure on the granulation tissue throughout the treatment period. They were also educated to use the crutch and wheelchair to transfer until the completion of the treatment. The patient's DFUs were completely healed after three months and ten days, and the patient was discharged from our service with a good and stable general condition (Fig. 5).

3. Discussion

Diabetic foot infections are associated with considerable significant mortality and morbidity, affecting the quality of life. It can also be life-threatening and cause complications such as infection, sepsis, and amputation. Common standard treatments for DFU include the following: (a) reduction of pressure on the area, (b) necrotic tissue debridement, (c) infection control, and (d) revascularization (13). However, with standard treatment methods of DFU, only 30% of DFUs heal within 20 weeks (14). Since DFUs are caused by various pathological mechanisms, the monotherapy strategy would lead to a very low level of recovery. Therefore, DFU management requires multimodal care and interdisciplinary treatment (13).

In our study, the patient had poor glycemic control for 2 years after diagnosing type 2 diabetes, which led to microcirculatory changes and eventually DFU (2). The patient's DFU has spread due to poor glycemic control over 3 years and antibiotic resistance.

In this regard, the basic and essential conditions for treatment success are adequate tissue perfusion and the absence of osteomyelitis, as osteomyelitis can negatively affect wound healing (12). However, due to the lack of underlying and chronic disease in the case of the present study, he was an appropriate case for treatment.

In this case report study, after obtaining the patient's written informed consent to the treatment, we used a combination therapy (MT, NPWT, and silver foam dressing) to treat the patient's DFUs. After one month of hospitalization, the patient was discharged from the hospital, and the physician prescribed him post-discharge oral antibiotics. To continue the treatment process, the wound management team went to the patient's home and performed five sessions of NPWT with debridement and silver foam dressing. After completing the treatment process on 19 September 2019, the patient's DFUs recovered significantly (Fig. 5), and the patient could walk.

In line with the results of the present case report study, Zhang et al. (2014) (10) and Liu et al. (2018) (9) showed that NPWT, along with maggot debridement therapy and silver foam dressing, is an appropriate treatment method for DFU. Hajimohammadi et al. (2019) showed that NPWT with silver foam dressing effectively treats DFU (15). In line with the present case report study results, Malekian et al. (2019) conducted a clinical trial on the effect of maggot therapy on DFU indicated that MT is a safe and effective method for the treatment of DFU (8). In addition, Siavash et al. (2020) concluded that MT is an effective and new treatment for complex DFUs which are resistant to conventional and routine therapies

(16). However, due to limited studies in this area, the effectiveness of NPWT on the prevention of diabetic foot amputation remains clinically unclear (12).

4. Conclusion

Despite current standard treatments, DFUs are a major cause of mortality and morbidity in patients with diabetes. DFUs are complex wounds due to multiple pathological mechanisms. Therefore, instead of a single treatment approach, new and innovative treatment methods, especially the combined use of MT, NPWT, and silver foam dressing, should be used to prevent the spread of the wound and control diabetic foot infection. Since the treatment of complex wounds (such as DFU) is a time-consuming and costly process, it is recommended to use innovative methods to reduce costs and accelerate the wound healing process.

Abbreviations

NPWT: Negative Pressure Wound Therapy, DFU: Diabetic Foot Ulcer, MT: Maggot Therapy, HBOT: Hyperbaric Oxygen Therapy, MRI: Magnetic Resonance Imaging,

Declarations

Ethics approval and consent to participate

All ethical principles were considered in conducting this case report. The patient signed the consent form and all patient information kept confidential.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing Interest

The authors declare that they have no conflict of interest

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Authors' contributions

NP, RG, KH: Conceptualization, Methodology. NP, RG, KH: Data curation, Writing- Original draft preparation. NP, RG, KH: Visualization, Investigation NP: Supervision: NP, RG, KH: Writing- Reviewing and Editing, all authors read and approved the final manuscript before submission.

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Figures



Figure 1

Diabetic foot ulcer before starting the combination therapy



Figure 2

Maggots of *Lucilia sericata* in diabetic foot ulcer



Figure 3

Diabetic foot ulcer after maggot therapy



Figure 4

NPWT applied following maggot therapy



Figure 5

Diabetic foot ulcer of the patient after combination therapy

Supplementary Files

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