Scientific Research Publishing

Case Reports in Clinical Medicine, 2025, 14(9), 549-558
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

Fat Emulsion Extravasation-Induced Diabetic Foot Ulcers: Case Report and Literature Review

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How to cite this paper: Hao, L., Wang, Y.C., Yu, J.B., Li, L.X., Chen, T.W. and Xu, L.B. (2025) Fat Emulsion Extravasation-Induced Diabetic Foot Ulcers: Case Report and Literature Review. *Case Reports in Clinical Medicine*, **14**, 549-558.
https://doi.org/10.4236/crcm.2025.149070

Received: August 25, 2025
Accepted: September 21, 2025
Published: September 24, 2025

Abstract

A case of Diabetic Foot Ulcer (DFU) induced by fat emulsion extravasation was treated with Electroacupuncture (EA) in combination with basic Fibroblast Growth Factor (bFGF) gel over an 8-week period. The findings demonstrated a significant reduction in local inflammation, acceleration of ulcer healing, notable alleviation of pain, and the absence of any adverse reactions. This case preliminarily suggests the potential effectiveness of EA in the management of DFU resulting from fat emulsion extravasation. However, these results require validation through larger-scale studies. Currently, the treatment of severe extravasation injury remains a subject of controversy. In summary, electroacupuncture, as a safe and straightforward non-drug therapeutic approach, may play a crucial role in the treatment of DFU caused by fat emulsion extravasation. Specifically, it can enhance local microcirculation, mitigate the inflammatory response, promote wound healing, and relieve pain. Future research should delve deeper into the mechanism of action and long-term efficacy to offer patients more treatment alternatives.

Keywords

Fat Emulsion Extravasation, Diabetic Foot Ulcer, Electroacupuncture, Ulcer Healing, Inflammation Relief, Pain Relief, Non-Drug Therapy, Microcirculation Improvement, Clinical Efficacy

1. Introduction

Drug extravasation represents a grave iatrogenic complication associated with in-

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travenous infusion therapy. It is precisely defined as the abnormal leakage of drugs or solutions from the lumen of blood vessels into the surrounding tissues, thereby leading to local tissue damage [1]. The clinical manifestations encompass pain at the injection site (the pain may present as tingling or burning sensations), localized edema, and tissue inflammation. If timely intervention is not implemented, extravasation can progress to tissue necrosis.

Based on the degree of injury, extravasation-related tissue damage can be categorized into mild, superficial reversible skin lesions, and severe full-thickness skin ulcers that involve deep structures such as tendons, muscles, joints, and peripheral nerves. Moreover, the formation of scar tissue subsequent to extravasation may give rise to functional limitations and deformities. Notably, severe extravasation injuries frequently necessitate surgical intervention, including debridement, tissue reconstruction, and, in extreme cases, amputation.

Epidemiological investigations have revealed that children aged ≤ 6 years and elderly patients aged > 65 years are at a heightened risk of experiencing extravasation events. The risk factors primarily include: 1) the underdeveloped vascular wall structure in infants; 2) the hardening and reduced elasticity of blood vessels in elderly patients; 3) age-related pain perception dysfunction. Additionally, patients with neurological and circulatory diseases exhibit a significantly elevated risk [2].

From the pathophysiological point of view, extravasation is closely related to the osmotic pressure and pH value of fluid. Hypertonic or hypotonic solutions, antitumor drugs, and drugs with extreme pH values (pH < 4.1 or >9.0) are the main causes of extravasation. The risk of extravasation of antineoplastic drugs was 10.692 times higher than that of conventional drugs, the study showed.

Of note, Lipid Emulsion Extravasation-related Diabetic Foot (LEE-DF) is a clinically significant complication in a population of diabetic patients receiving Parenteral Nutrition (PN). Epidemiological data show that the incidence of this complication is approximately 0.1% - 1.0% [3]. Diabetic patients have increased susceptibility to microangiopathies and peripheral neuropathy, resulting in significantly reduced tissue integrity, thereby increasing the risk level for extravasation events. These events can lead to severe tissue damage and secondary infection. In addition, the inherent high osmolarity and potential chemical irritability of fat emulsions further aggravate the degree of tissue damage. Clinically, LEE-DF is characterized by local sensory abnormalities, tissue necrosis, and a significantly increased risk of infection.

Extravasation injury arises from several mechanisms, including vasoconstriction-induced ischemia, direct cytotoxicity, osmotic gradients across the cell membrane, abnormal pH and buffering capacity, and mechanical compression. For lipid emulsions, the predominant contributors are osmotic disequilibrium, pH imbalance, and sustained mechanical pressure. Concomitant medications may further exacerbate injury by inducing vasoconstriction, increasing cytotoxicity, or compromising vascular integrity.

Hyperosmolar stress not only disrupts cell homeostasis but also triggers protein and DNA damage, reactive oxygen species generation, and apoptosis. Although central venous administration is recommended to prevent phlebitis from hyperosmolar infusates, extravasation inevitably results in transmembrane water shifts, membrane dysfunction, and dysregulated cell volume, leading to extensive and persistent skin injury. Tissue damage due to pH alterations is considered chemical in nature. Most lipid emulsions are near neutral (pH 6.5 - 7.5), with some slightly alkaline (pH 7.5 - 8.5). Exposure to alkaline solutions permits hydroxide ion penetration into deeper tissues, causing protein denaturation, collagen disruption, vasoconstriction, and apoptosis, although a direct correlation between solution pH and extravasation severity has not been conclusively demonstrated. Electrolytes such as calcium, potassium, sodium, and magnesium, when extravasated with lipid emulsions, may further potentiate chemical and osmotic injury, producing severe and persistent tissue damage. Moreover, due to their large infusion volume and limited capacity for tissue dispersion and absorption, lipid emulsions often persist in the extravasated space, where mechanical compression impairs microcirculation, resulting in tissue ischemia and necrosis [4].

To date, no standardized clinical guidelines have been established for the treatment of tissue damage caused by fat emulsion extravasation. Current treatment strategies are primarily based on general principles of integrated diabetic foot management and extravasation injury management, including but not limited to local wound care, anti-infective therapy, nutritional support, and timely surgical debridement [5]. However, the clinical efficacy of these interventions is significantly limited by delayed wound healing and high recurrence rates prevalent in diabetic patients. Commonly used treatments such as 50% magnesium sulfate wet compress, hydrocolloid dressing, and sodium malonate gel have limited effectiveness as monotherapy in severe extravasation cases.

The purpose of this study was to explore the clinical value of Electroacupuncture (EA) combined with Betoxin gel in the treatment of Lipid Emulsion Extravasation-induced Diabetic Foot (LEE-DF). We report the efficacy of this combination therapy in a LEE-DF patient with severe extravasation injury due to intravenous infusion. This may be a new way to treat fat emulsion extravasation injury.

Although there are no large-scale clinical trials supporting the use of EA in LEE-DF treatment, studies have shown that EA, as a non-pharmacological intervention, has significant therapeutic potential in the management of diabetic foot ulcers and chronic wounds.

Electroacupuncture (EA) appears to benefit patients with LEE-DF through integrated neurovascular, immunomodulatory, and tissue-repair mechanisms. By activating neurovascular reflex pathways and promoting peripheral nerve regeneration, EA enhances local microcirculation and tissue perfusion, thereby mitigating ischemia. Concurrently, EA modulates inflammatory signaling—downregulating proinflammatory mediators—which may reduce secondary infection risk and limit tissue injury. These effects collectively accelerate wound healing, alleviate neuropathic pain, and improve health-related quality of life. Beyond local actions, EA may also support systemic homeostasis, including improved glycemic control and immune function, which could further facilitate recovery from diabetic foot pathology [6]. In the acupuncture treatment of diabetic foot, commonly selected acupoints include Zusanli (ST36), Sanyinjiao (SP6), Yinlingquan (SP9), Taixi (KI3), Taichong (LR3), and Xuehai (SP10). According to traditional meridian theory and supported by contemporary clinical studies, stimulation of these acupoints has been shown to enhance microcirculatory perfusion and improve peripheral nerve function [7].

In TCM, diabetes mellitus (xiaoke) is primarily attributed to Qi and Yin deficiency; as the disease progresses, internal dryness may intensify into dryness-heat. Diabetic Foot Ulcers (DFUs), a representative chronic complication of diabetes, are understood to involve intertwined pathogenic factors—dryness-heat, blood stasis, and phlegm turbidity—resulting in impaired lower-limb perfusion. Progressive Qi deficiency and blood stasis can generate heat that transforms into fire or toxin-heat, damaging muscle and soft tissue and predisposing to ulceration. Accordingly, acupoints were chosen to tonify Qi, nourish Yin, clear heat, and invigorate blood circulation. Evidence from TCM literature and clinical reports suggests that ST36 replenishes Qi and supports meridian function, while SP6, SP9, and KI3 are key points for enriching Yin. SP6, the confluent point of the spleen, kidney, and liver meridians, also supports spleen function and blood nourishment. As liver Qi stagnation may contribute to heat, LR3 is commonly used to soothe the liver, regulate Qi, and disperse heat. SP10 is frequently employed to activate blood circulation and resolve stasis, thereby facilitating nutrient delivery to muscles and vessels [8].

To further verify the clinical efficacy of electroacupuncture combined with Betoxin gel in LEE-DF treatment, we designed and conducted a preliminary clinical study. The study protocol has been reviewed and approved by the Ethics Committee of the Third Affiliated Hospital of Zhejiang University of Traditional Chinese Medicine, aiming to provide a scientific basis for this new treatment strategy with potential application value.

2. Patient History

An 84-year-old female patient was admitted to the hospital on 18 June 2024 for “unconsciousness with impaired limb movement for more than 2 years”. The patient needed parenteral nutrition support due to poor limb mobility, long-term bed rest, and malnutrition (ALB: 24.4 g/L). Deep vein infection occurred 3 months after administration by deep vein puncture during hospitalization. After removal of the deep vein catheter, peripheral venous access was established in the left dorsal venous network. When fat emulsion was injected through this peripheral vein, an event of drug extravasation occurred, resulting in localized subcutaneous tissue damage and eventual ulceration on the dorsolateral side of the left foot. The patient has a history of diabetes, hypertension, lung infection, and low immunity.

3. Clinical Manifestation

Fasting blood glucose 7.8 mmol/L, local assessment: location: left dorsum of foot, left lateral malleolus, and left anterior leg. Size and shape: irregularly shaped ulcer of 16 cm × 6 cm. Color staging: red wound, basal whitish wound (suspected deep necrosis), grayish black wound. Infection: ++, Exudate: none, peculiar smell: none, surrounding skin: swelling, skin temperature is high (**Figure 1**). Laboratory tests revealed elevated white blood cell counts and marked increases in C-Reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR), suggesting infection and systemic inflammatory response.

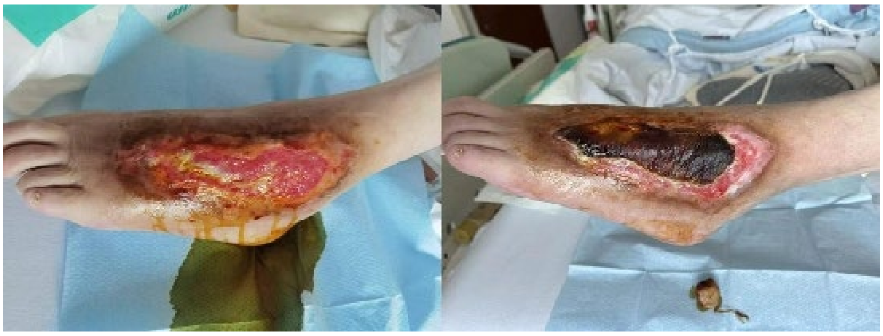

Figure 1. Diabetic foot ulcer wound. a: The wound before treatment. b: The wound after treatment.

Based on the patient's medical history, clinical manifestations, and laboratory results, the diagnosis of Diabetic Foot Ulcer (DFU) with infection was made. The occurrence of the ulcer is closely related to the local tissue damage caused by fat emulsion extravasation, and the patient's inherent diabetic microcirculation dysfunction further aggravates the disease. Together, these factors contribute to poor wound healing and an increased risk of infection.

4. Treatment Course

4.1. Local Debridement

4.1.1. Wound Management

1) Disinfect the area around the wound with iodophor, clean the wound with 0.9% sodium chloride solution, remove necrotic tissue, and reduce the bacterial load.

2) After local application of recombinant bovine basic Fibroblast Growth Factor gel (bFGF), MEBO should be applied to cover the wound surface to keep the wound moist, so as to promote granulation tissue formation and accelerate tissue healing.

4.1.2. Infection Control

Based on wound and systemic assessment, intravenous broad-spectrum antibiotics (Latamoxef sodium) were administered to control infection and prevent systemic complications.

4.2. Electroacupuncture Therapy

To improve local blood circulation of the lower limbs and accelerate wound healing, Electroacupuncture (EA) was administered for 8 weeks. The following 6 acupoints were selected: Zusanli (ST36), Sanyinjiao (SP6), Yinlingquan (SP9), Taixi (KI3), Taichong (LR3), and Xuehai (SP 10). After disinfection of the skin, sterile stainless steel needles were inserted at appropriate angles. The treatment was conducted with a constant direct current of 1 - 2 mA and a frequency of 20 Hz for 30 minutes each time until the patient felt a sensation of "getting qi" (*i.e.*, soreness, numbness, fever, heaviness, or swelling around the acupoints). Electroacupuncture was performed 4 times a week for 8 weeks. The treatment was performed by an acupuncturist registered in China with 5 years of clinical experience. No adverse events were observed during treatment. (**Figure 2**)

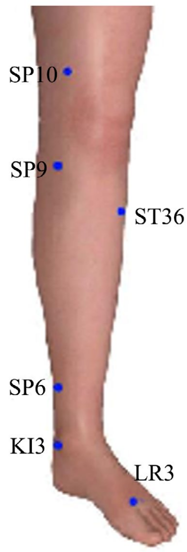

Figure 2. Illustration of electroacupuncture points.

4.3. Blood Sugar Management

Adjust insulin dosage, strictly control blood glucose level, target fasting blood glucose below 7.0 mmol/L, and postprandial blood glucose below 10.0 mmol/L.

4.4. Prevent Complications

Because patients are in bed for a long time, their biochemical indicators should be closely monitored, their skin should be kept clean and dry, and adequate nutritional support should be provided.

5. Results

This study reports on an elderly patient with a history of diabetes mellitus and malnutrition who experienced an event of extravasation during the infusion of lipid emulsion in the dorsal venous network of the foot after a complicated deep vein infection, resulting in localized subcutaneous tissue damage and secondary ulcer formation. In the clinical diagnosis and treatment process, the attending physician accurately diagnosed the patient's foot swelling symptoms as caused by extravasation of fat emulsion hypertonic solution through timely identification and evaluation, and immediately took measures to remove the indwelling needle, effectively preventing possible serious complications.

During the treatment of this case, the objective clinical indices of the patient showed significant improvement after EA combined with PFX gel intervention. Specifically, this is manifested as follows: Transcutaneous oxygen pressure ($TcPO_2$) was significantly increased by 15 mmHg compared with that before treatment, indicating that local microcirculation was effectively improved; the Visual Analogue Scale (VAS) of pain was reduced by 3 points, indicating that pain symptoms were significantly relieved; Wagner classification of diabetic foot was reduced from grade 3 to grade 2, reflecting that the severity of the wound was significantly reduced (**Table 1**). However, limited improvement in symptoms such as foot deformity and dry skin suggests that longer treatment cycles may be needed to achieve further clinical benefit.

Table 1. Clinical results before and after electroacupuncture treatment.

Parameter	Prior treatment	After treatment	3-month follow-up
$TcPO_2$ (mmHg)	25	40	38
VAS score	7	4	4
CRP (mg/L)	12.5	5.2	6.0
Wagner classification	3	2	2
Dorsal artery blood flow (cm/s)	15	25	24

6. Discussion

No standardized clinical practice guidelines have been established for the treatment of tissue damage caused by fat emulsion extravasation. At present, clinical treatment strategies mainly rely on drug intervention, in which improving microcirculation is regarded as one of the key links to promote tissue repair. In clinical practice, drugs used to improve blood circulation mainly include vasodilators and antiplatelet drugs. However, the widespread use of these drugs is significantly limited by their potential adverse effects, including hypotension, bleeding risk, and effects on liver and kidney function. Therefore, exploring safer and more effective treatment strategies has become the focus of current research. Electroacupuncture (EA), as a non-drug therapy combining traditional Chinese medicine theory with modern electrostimulation technology, is safe and simple to operate.

In the previous clinical practice, we observed that patients with Wagner grade 3 ulcers treated solely with standard modalities—such as glycemic control, anti-infective therapy, wound care, and vasodilator administration—often experienced poor outcomes. Extensive necrotic tissue, abscess formation, and severe lower-limb ischemia frequently facilitated progressive infection, leading to osteolytic destruction and, in severe cases, the need for amputation. In contrast, the present case demonstrated a favorable response to Electroacupuncture (EA) treatment, and no adverse reactions were observed. As a typical example of the multifactorial nature of diabetic foot ulcers, this case highlights the critical role of preventive measures in high-risk patients and confirms the significant efficacy of EA in improving subjective symptoms and objective indicators in DF patients. Transcutaneous Oxygen Pressure ($TcPO_2$) monitoring technology significantly improves the objectivity of diagnosis and efficacy evaluation. It is worth noting that there is no literature report on the specific application of EA in the treatment of DFU caused by fat emulsion extravasation. This study demonstrates that EA combined with Belvesine Gel is safe and effective for DFU caused by fat emulsion leakage.

Despite the significant treatment response achieved in this case, Wagner classification and inflammatory marker levels remained above clinical cut-offs, suggesting that continued EA therapy may be required to maintain efficacy and further improve prognosis. Moreover, this case represents a single instance of clinical improvement and therefore carries the inherent limitations of a case report. Owing to variations in patient adherence, the therapeutic regimen has not yet been widely implemented. The absence of control cases further limits the ability to account for confounding factors such as glycemic status, antibiotic administration, vasodilator use, lower-limb rehabilitation, and alternative surgical interventions, thus introducing potential bias.

Fat emulsion extravasation, as a rare but serious iatrogenic factor, needs to be given close attention. EA may provide a new therapeutic strategy for DFU by improving microcirculation, promoting nerve regeneration, and regulating inflammatory response. It is necessary to conduct large-scale, multicenter clinical studies in the future to optimize treatment regimens and evaluate long-term efficacy, providing evidence-based support for comprehensive management of DFU.

Through this clinical case, this study systematically discussed the clinical problems of chronic wound formation caused by extravasation of high-risk drugs, and provided an important reference for improving the clinical diagnosis and treatment level. In view of the extensive clinical application of fat emulsion as a parenteral nutrition support program, medical institutions urgently need to strengthen the capacity building of drug extravasation prevention and management of medical care teams, and significantly reduce the incidence of such adverse events by improving relevant clinical operation standards and norms.

Facing the current clinical challenges, it is important for future research to establish a comprehensive management model based on multidisciplinary collaboration, including systematic strategies for prevention, early identification, and effective intervention of extravasation events. In addition, the establishment of a perfect extravasation event registration system and a standardized database has important clinical significance for revealing its epidemiological characteristics and providing a scientific basis for evidence-based medicine to guide the formulation of prevention and treatment strategies.

Based on the findings of the study, the following key links should be focused on in clinical practice: 1) priority should be given to establishing central venous access for high-risk patients; 2) a sound infusion monitoring system and early warning mechanism should be established; 3) standardized extravasation event handling protocols should be formulated and implemented; 4) informed consent procedures should be strictly implemented before clinical operations. In view of the limitations of current research, future research directions should focus on the following aspects: 1) optimizing extravasation prevention strategies, including developing evidence-based risk assessment models and preventive interventions; 2) improving early diagnosis methods, integrating imaging techniques and the application of biomarkers; 3) developing specific targeted therapeutic drugs for the pathological mechanisms of extravasation-related tissue damage; 4) establishing a multi-center clinical research database to provide data support for the generation of high-quality evidence-based medical evidence. Through the coordinated promotion of the above systematic research and practice, it is expected to significantly improve the prevention and management efficiency of extravasation events, thereby improving the clinical prognosis of patients and promoting the standardization and optimization of clinical practice standards in this field.

Funding

This work was supported by Zhejiang Province Traditional Chinese Medicine Science and Technology Project (No.2023ZL073).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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