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Case Report

Management and Outcomes of a Foot Ulcer Caused by Extravasation: A Case Report

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Abstract

Extravasation occurs during an intravenous infusion (IV), and the severity of the tissue damage depended on factors like the volume of leaked solution, infusion site, patient characteristics, and the infused agent's toxicity. We herein present the case of a 52-year-old woman who developed a foot ulcer due to unexpected extravasation and highlight the successful use of Aquavis® an innovative product that, when combined with other treatments, shows promise in promoting wound healing and addressing related challenges.

Keywords: ***ulcer, extravasation, magnetized water, autophagy, wound healing***

Introduction

Extravasation occurs when a solution leaks from a vessel into the surrounding tissues during an intravenous infusion [1]. The severity and extent of tissue damage are influenced by various factors, including the volume of the leaked solution, the site of IV insertion, patient characteristics, and the toxicity of the infused agent [2]. Common sites for extravasation include the forearm, antecubital fossa, dorsum of the hand, and foot, where there is minimal fat to act as a barrier. This condition can result in the full-thickness loss of skin and significant damage to underlying structures [3]. In this case report, we present a 52-year-old woman who experienced unexpected extravasation leading to a foot ulcer, and we discuss the management strategies employed to prevent disability and dysfunction.

Case report

A 52-year-old female patient with a history of hypertension and smoking was admitted on October 19, 2022, after being found unconscious with involuntary movements in her right arm. A brain CT scan revealed a subarachnoid hemorrhage and an aneurysm in the anterior communicating artery. During a medically induced coma due to seizures, she received SOLDESAM® (Dexamethasone), but drug extravasation occurred through a cannula in her foot. In November 2022, she began neuromotor rehabilitation and consulted a plastic surgeon at Papardo Hospital for an eschar on her left foot. Despite treatment with gentamicin and betamethasone, the ulcer worsened by December 2022, as shown in Figure 1a.

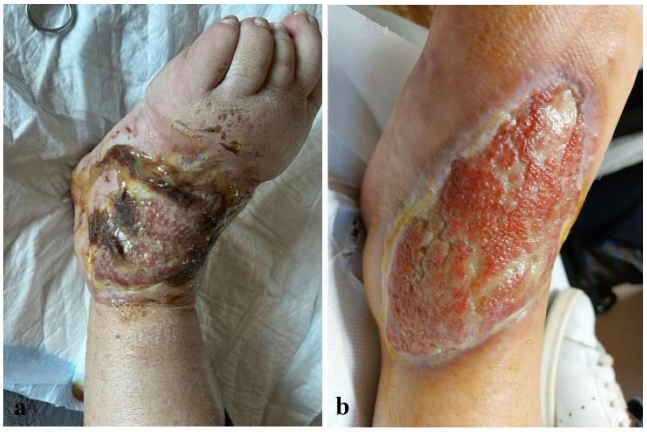

Figure 1: (a) Patient left foot ulcer in December 2022. (b) Infected ulcer on the left foot dorsum in January 2023, when the patient presented to the private plastic surgeon.

At the beginning of January 2023, Plastic Surgery evaluation at Papardo Hospital confirmed a large ulcer on the left dorsum of the foot with a partially necrotic bottom apparently non-secreting. The perilesional skin was normal. While awaiting possible hospitalization for autologous skin grafting, it was recommended to medicate with Noruxol ointment and Connettivina Plus gauze.

The initial rehabilitation plan at Bonino Pulejo Hospital noted that the patient, while alert and cooperative, could not be assessed for standing or walking due to bilateral vitreous haemorrhage. She had an advanced trophic lesion on her left foot but showed improvement in head and trunk control, reduced pain, and increased plantar flexion, despite a slight strength deficit. Visual impairment continued to affect her balance, but cognitive and

cerebral improvements were observed. Vascular surgery confirmed adequate blood flow to the ulcer, while plastic surgery recommended autologous skin grafting, which the patient declined.

On January 30, 2023, the ulcer appeared as shown in Figure 1b. Following a private consultation with a plastic surgeon, in February, after thorough wound cleansing, a culture confirming a Staphylococcus aureus infection, and subsequent antibiotic therapy, the patient began treatment with Aquavis®. This included daily wound care with saline solution and Aquavis® gel compresses.

Aquavis®, kindly provided by AQUAVIS S.R.L. (Brescia, Italy), is a magnetized saline water, processed through electromagnetic treatment, heating, and multiple filtrations. This innovative biophysical ingredient serves as the foundation for a revolutionary product line that promotes skin health by providing analgesic and anti-inflammatory benefits, while enhancing cell regeneration. Formulated with AI-selected active ingredients, Aquavis® effectively treat skin conditions, including acne, urticaria, dermatitis, and inflammatory disorders.

An in vitro proteomic analysis using liquid chromatography-tandem mass spectrometry revealed significant differences in protein expression in normal human dermal fibroblasts exposed to Aquavis® for 48 hours compared to controls. 27 proteins were differentially expressed, with 16 up-regulated and 11 down-regulated. These proteins were involved in various biological processes, including metabolism [4,5], autophagy [6-9], cell motility [10,11], extracellular matrix [12], inflammation [13], cell proliferation [14,15], DNA replication [16].

Aquavis® was found to stimulate the expression of several extracellular matrix key molecules, including Collagen alpha-1(V) chain, Collagen alpha-1(VII) chain, Extracellular Matrix Protein 1, Filamin-A and Lumican. Notably, the upregulation of Collagen alpha-1(VII) chain (COL7A1) is of particular interest, as this molecule plays a crucial role in the physiological wound healing process.

Aquavis® promotes skin autophagy through a non-pharmacological approach, enhancing the degradation and recycling of damaged components to maintain youthful skin. It activates autophagy by upregulating key activators (ATG5, BECN1, DAPK1, DMXL2, NFE2L2) and downregulating the inhibitor RHEB. By activating autophagy, Aquavis® can: reduce skin pigmentation by promoting melanosome degradation [6]; combat inflammation by regulating the inflammatory response and fighting infections [7]; promote wound healing by stimulating angiogenesis and re-epithelialization [8]; potentially inhibit hypertrophic scar formation due to its ability to downregulate RHEB [9].

Complementing in vitro proteomics studies on supernatants of human dermal fibroblasts exposed to magnetized saline water, in vivo research was also carried out. A pioneering study explored magnetized saline water in a topical serum formulation for the first time. After 12 weeks of application on human skin, the treatment was safe, well-tolerated, and led to significant changes in two key autophagy-related molecules: an increase in Beclin-1 (+38%) and a concurrent decrease in mTOR (mechanistic target of rapamycin) expression (-24%) [17]. Beclin-1 is a protein playing a crucial role in regulating autophagy by inducing the maturation of autophagosomes and phagosomes and the regulation of endosome recycling. mTOR is a kinase that regulates cell growth, metabolism, and autophagy, functioning as the catalytic core of two complexes: mTORC1 and mTORC2. The activation of mTORC1 increases the demand for energy by blocking autophagy. The cell compensates by enhancing nutrient uptake and synthesis, and by using proteasomal degradation to remove unwanted materials and increase the availability of free amino acids for protein synthesis. Similarly, an increase in autophagic flux and the recycling of cellular macromolecules during prolonged inhibition of mTORC1 can partially restore intracellular or intra-lysosomal amino acid reserves and reactivate mTORC1 [18].

Recent studies have shown that a topical gel containing 95% magnetized saline water effectively treats hard-to-heal wounds, such as pressure and venous ulcers, in elderly patients unresponsive to standard therapies. The autophagy-stimulating gel promoted healing by reducing fibrous and necrotic tissue, enhancing granulation, improving re-epithelialization, and achieving partial or complete wound closure [19].

Results

Following the treatment with Aquavis®, it is possible to observe the progression of the patient left foot ulcer recovery (**Figure 2**).

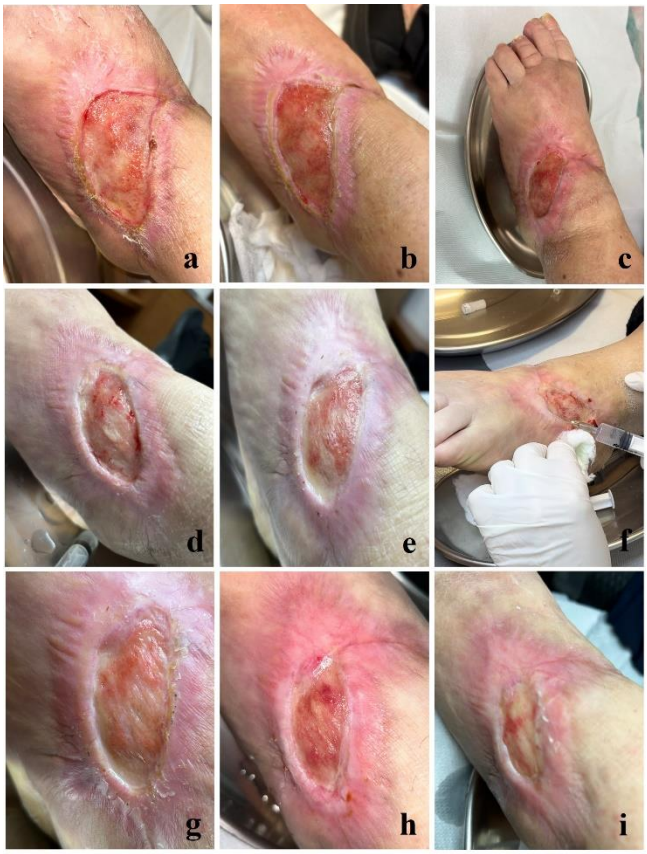

Figure 2: Progression of the patient left foot ulcer recovery. (a) August 2023. (b) September 2023. (c) December 2023. (d-e-f) January 2024. (g) February 2024. (h) March 2024. (i) June 2024.

On January 18, 2024 (Figure 2e), the patient began treatment with two consecutive compresses of equine catalase, an enzyme used in preparations for treating skin wounds. Subsequently, on January 25, 2024 (Figure 2f), two intralesional and perilesional infiltrations, spaced 7 days apart, with PDRN (Placentex FL Mastelli) were initiated due to a slowdown in healing. Placentex contains polydeoxyribonucleotide (PDRN), derived from DNA fragments of salmon trout (Oncorhynchus mykiss) or chum salmon (Oncorhynchus keta), with a molecular weight ranging from 50 to 1500 kDa [20]. PDRN is used for tissue repair, as it accelerates the healing of wounds, ulcers, and burns, and promotes reparative activity for damaged organs or tissues.

In June 2024, after over a year of treatment, the patient's foot ulcer had significantly improved (**Figure 3**). Necrotic tissue was nearly eliminated, the ulcer size was reduced by approximately 80%, and dermal tissue reconstruction was evident.

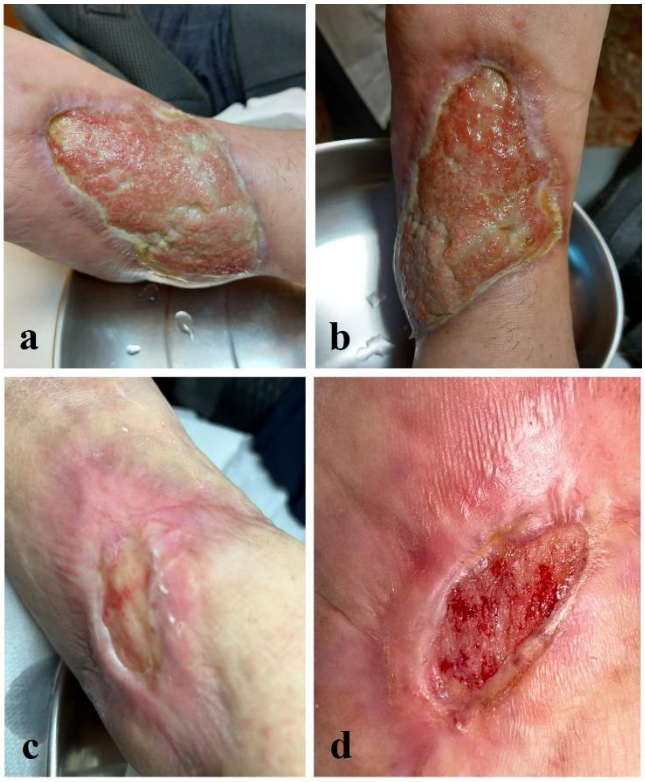

Figure 3: Patient foot ulcer at the beginning (a-b) and after over a year of treatment (c-d).

Discussion

Since the treatment had been prolonged, it was decided to discontinue it. However, given that an 80% improvement had been achieved, the patient was advised to consult with plastic surgery for a minor flap procedure. Despite a partial loss of sensitivity, mainly due to the surgical interventions, the treatment is considered a success for saving the limb. Careful management of the surrounding tissues also effectively reduced the risk of necrosis.

Conclusions

This case report emphasizes the severe tissue damage caused by extravasation, especially in the foot. Vigilant IV infusion monitoring is crucial for prevention. Aquavis® therapy, in conjunction with other treatments, shows promise in promoting wound healing and addressing extravasation-related challenges. Future research should focus on optimizing treatment strategies and investigating the potential of Aquavis® in preventing extravasation-induced ulcers and other types of ulcers resistant or prone to chronic complications.

List of abbreviations

IV: intravenous infusion
COL7A1: Collagen alpha-1(VII) chain
ATG5: Autophagy protein 5
BECN1: Beclin-1
DAPK1: Death-associated protein kinase 1
DMXL2: DmX-like protein 2
NFE2L2: Nuclear factor erythroid 2-related factor 2
RHEB: GTP-binding protein Rheb
mTOR: mechanistic target of rapamycin
mTORC1: mechanistic target of rapamycin complex 1
mTORC2: mechanistic target of rapamycin complex 2
PDRN: polydeoxyribonucleotide

Declarations

Ethics approval and consent to participate

The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with Committee on Publication Ethics (COPE) guidance.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Authors' contributions

IPP collected the patient data; IPP and PF analyzed and interpreted the patient data; MG wrote the manuscript; IPP revised the manuscript and provided final approval. All authors read and approved the final manuscript.

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