Our Dermatology Online

Case Report

Cutaneous necrosis secondary to subcutaneous extravasation of acyclovir

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ABSTRACT

Subcutaneous extravasation of infused vesicant solutions is becoming a common problem in medical practice, and can result in severe and progressive tissue dysfunction, ranging from persistent tissue edema to tissue necrosis. Although Acyclovir is a known vesicant drug, responsible for venous and soft tissue irritation, they are a few reported cases of extravasation of Aciclovir. We report here the 5th case of Subcutaneous extravasation of intravenous (IV) acyclovir in a patient hospitalized for herpes zoster cruris, causing skin necrosis on day 4 of her hospitalization and leaving a residual scar. Early recognition of extravasation and prompt management are essential to prevent additional morbidity and optimize outcomes.

Key words: Skin necrosis; Intravenous extravasation; Acyclovir

INTRODUCTION

Subcutaneous extravasation of drugs into perivascular space or subcutaneous issues is a rare event but a real problem in medical practice especially chemotherapy agents, which can result in severe and progressive tissue dysfunction, ranging from persistent tissue edema and fibrosis to delayed tissue necrosis [1,2].

Based on the type of local damage inducted by extravasation, we can distinguish 3 different classes of compounds: nonvesicants drugs (not including any local irritation), irritants (causing local pain, swelling, and local irritation nut no necrosis), and vesicants (including ulcerations and necrosis). The local damage is correlated to characteristics and amount of drug extravasated. Acyclovir is a known vesicant drug, which appears to irritate venous and soft tissues upon extravasation [3,4]. It has been reported 4 cases of cutaneous extravasation of Acyclovir with different local damages.

Therefore, medical personnel should be aware of the potential dermatologic side effects of intravenously infused acyclovir, even long after infusion, and the possible absence of initial local symptoms and signs. The therapeutic management must be immediate and adapted according to the type and the damage of the extravasated agent.

CASE REPORT

A 70-year-old patient followed for adenocarcinoma of the lower rectum who received concomitant radio-chemotherapy followed by an abdominopelvic amputation with a definitive left colostomy in 2020, hospitalized for management of crural zoster of the S2 territory dating back to 10 days before admission.

The patient was put on aciclovir injection at a dose of 10mg/kg/d. On day 4 of her hospitalization, the patient developed a warm, painful, edematous erythematous placard at the infusion site in the elbow. The course of action was to stop the infusion, remove the peripheral venous line, circumscribe the lesion, elevate the limb and apply cold compresses.

How to cite this article: Couissi I, Douhi Z, El Fid K, Soughi M, El Loudi S, BayBay H, Soughi M, Mernissi FZ. Cutaneous necrosis secondary to subcutaneous extravasation of acyclovir. Our Dermatol Online. 2023;14(e):e20.

Submission: 08.10.2022; **Acceptance:** 23.02.2023

DOI: 10.7241/ourd.2023e.20

The evolution was marked by the installation of a necrotic ulcerated placard surrounded by hot and painful edematous erythematous skin (Figs. 1a and 1b). The patient was put under a hydrocolloid dressing with a detachment of the necrosis leaving ulceration topped by fibrin for which she benefited from a mechanical detersion, associated with cold dressings and a healing cream on the peri-lesional skin (Fig. 2).

An EMG was performed showing a sensitive-motor polyneuropathy of the axonal mechanism, for which she was put on gabapentin with improvement.

The evolution was marked by a healing of the ulceration after one month and the installation of pain-like electric discharge along the forearm (Fig. 3).

DISCUSSION

Extravasation is a devastating complication of intravenous (IV) therapy that develops when a drug infiltrates the interstitial tissue surrounding the vein.

The frequency of extravasation in adults is considered to be between 0.1% and 6% of IV therapies.

Common sites of extravasation injury include the back of the hand, forearm, antecubital fossa, and back of the foot, as these are the areas of the body where the skin and subcutaneous tissue are the thinnest.

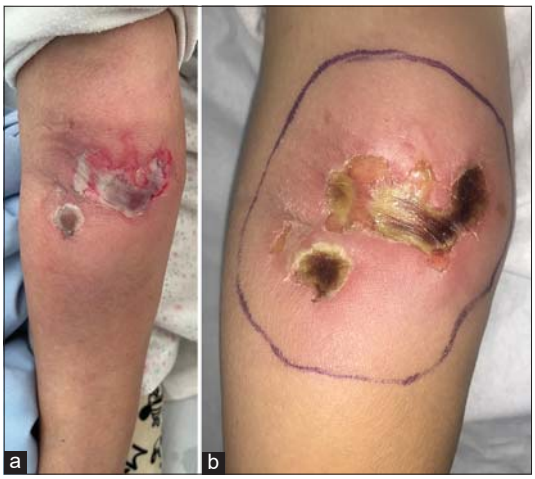

Figure 1: (a) A well-limited rounded erosion of irregular contours surmounted by whitish patches with a peri-lesional erythema located at the level of the elbow crease. (b) A well-limited rounded ulceration with irregular contours and a fibrinous surface surmounted by necrotic plaques with a peri-lesional erythema extending up to 3 cm around the lesion located at the level of the elbow crease.

The thinness of the tissue makes these sites attractive targets for IV access but also the most susceptible to injury from extravasation [1].

The severity of the injury depends on a number of factors, including drug and patient characteristics.

Drugs are classified as vesicants, irritants, and non-vesicants [2].

Vesicant drugs, such as cytostatics, cause tissue destruction that can lead to tissue ulceration.

Non-vesicant drugs, such as saline, rarely produce acute reactions or tissue necrosis.

The initial management of intravenous drug extravasation remains controversial due to the lack

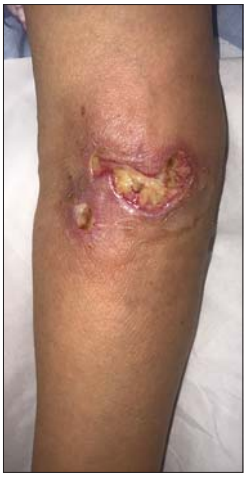

Figure 2: A well-limited oval ulceration with irregular contours and a fibrinous surface with regression of the peri-lesional erythema located in the elbow crease.

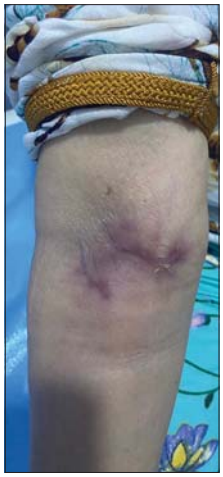

Figure 3: Complete healing of the ulceration one month after.

of evidence in the literature and the wide variety of extravasated solutions [3].

Common recommendations include immediate discontinuation of the infusion, removal of the intravenous catheter to aspirate any remaining fluid, avoidance of pressure on the site, the elevation of the affected limb for 24 hours, and application of cold or warm compresses [3].

The specific drug should be identified to determine its vesicant or non-vesicant property and to ascertain whether an antidote is available.

If an antidote is available, a decision should be made as to whether the amount of fluid and the clinical appearance of the extremity warrant administration of an antidote to prevent tissue necrosis.

The patient should be informed that immediate surgical intervention may be required [4].

The risk of extravasation injury depends on the amount of extravasated drug and the amount of subcutaneous tissue that absorbs it. The accumulated fluid exerts mechanical pressure that obstructs capillary blood flow and compromises oxygenation [4].

The amount of fluid that can lead to compartment syndrome depends on the individual characteristics of the patient, including the elasticity of the subcutaneous tissue, the fragility of the vessels (e.g., children or the elderly), and the osmotic properties of the drug.

The mechanism of tissue damage by extravasating vesicant drugs depends on their osmolarity, pH, and mechanism of action [5].

Studies suggest that hyperosmolality (>600 mOsm; normal range 285-310), extremely acidic or basic pH (<5 or >9), and cytotoxic and vasoconstrictive drugs are associated with a higher risk of subsequent leakage and tissue damage.

A readily available institutional protocol for the management of IV extravasation of high-risk solutions is suggested.

Acyclovir is an acyclic nucleoside purine analog that is a potent inhibitor of herpes simplex virus DNA replication [5].

It is considered a vesicant and has a pH of 11 and an osmolality of 278 mOsm/kg.

Its reported dermatologic adverse events, including injection-site erythema, inflammation, and phlebitis, occur in ≤16% of patients.

In the literature, only four cases of IV acyclovir extravasation have been reported to date [6]. De Souza and Shibu reported a 51-year-old insulin-dependent diabetic man who presented with cellulitis and lymphatic edema at the anterior site of extravasation three months after the infusion.

Meanwhile, Sarica reported the case of a 14-year-old girl with acute lymphoblastic leukemia who was given IV acyclovir for varicella. On day 33 of remission induction, the infusion extravasated and a local bullous rash appeared approximately 10 cm distal to the site of the venipuncture. The bullous rash subsided within 8 hours and completely disappeared, with residual scarring, within 24 hours.

Lau and Lee reported the case of a 55-year-old man with suspected herpes simplex encephalitis and HIV who was treated with IV acyclovir. Diffuse, firm but compressible swelling of the right hand was noted on the second day of hospitalization following extravasation of 150 ml of acyclovir IV [7].

In these case reports, treatment was nonoperative with compression garments and physical therapy, cold compresses, and elevation of the arm in a hook or observation [7].

In addition, no apparent skin breakdown or skin necrosis was noted.

Charalambos Neocleous et al reported the first case of IV acyclovir extravasation in an immunocompetent adolescent girl, resulting in tissue necrosis and leaving a residual scar.

Our case was the second to cause skin necrosis.

This skin necrosis was secondary to the alkalinity of the extravasated solution, resulting in local chemical inflammation and tissue damage associated with sensitive-motor polyneuropathy.

CONCLUSION

Subcutaneous extravasation of vesicant drugs, a common incident in medical practice, can cause severe tissue dysfunction.

Medical personnel should be aware of the potential dermatologic side effects of IV acyclovir (even long after infusion) and the possible absence of initial local symptoms after extravasation.

Prompt management is essential to prevent further morbidity and optimize outcomes.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Source of Support: This article has no funding source.

Conflict of Interest: The authors have no conflict of interest to declare.