Open Access Library Journal
2023, Volume 10, e10361
ISSN Online: 2333-9721
ISSN Print: 2333-9705

Effective Treatment of Epirubicin Extravasation with Dexrazoxane: A Case Report of Positive Clinical Outcomes

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How to cite this paper: Sbaiti, Y., Ghozali, N., Meliani, M., Ruck, S., Darif, K., Amzerin, M. and El M'rabet, F.Z. (2023) Effective Treatment of Epirubicin Extravasation with Dexrazoxane: A Case Report of Positive Clinical Outcomes. *Open Access Library Journal*, **10**: e10361.
https://doi.org/10.4236/oalib.1110361

Received: June 8, 2023
Accepted: June 18, 2023
Published: June 21, 2023

Abstract

Accidental extravasation of anthracyclines is a rare incident but if ever it happens, it can lead to serious complications, which could go as far as tissue necrosis with the need for surgery in most of the cases. In accordance with current recommendations, intravenous administration of Dexrazoxane within 6 hours of extravasation is recommended to reduce the risk of skin necrosis. We report the case of a 63-year-old patient, diagnosed with breast cancer, who presented with extravasation of Epirubicin, during her first cycle of adjuvant chemotherapy, with a favorable evolution after being treated with Dexrazoxane.

Subject Areas

Clinical Medicine

Keywords

Chemotherapy, Extravasation, Epirubicin, Dexrazoxane

1. Introduction

Chemotherapy extravasation, an infrequent event with an approximated incidence of 0.1% - 6%, may result in substantial morbidity, delay in oncological treatment, and potential mortality [1] [2].

Epirubicin, an anthracycline agent, is commonly utilized in the treatment of various cancers including breast cancer, lymphomas, and leukemias. Its primary mechanism of action involves acting as a topoisomerase II inhibitor, thus inter-

fering with DNA replication and transcription, and impeding the growth and proliferation of cancer cells. These agents are classified as DNA-binding vesicants. In the event of extravasation, which involves the leakage of these cytotoxic agents into the surrounding tissue, it can result in severe blistering and tissue damage, ultimately leading to necrosis and ulceration [3].

Dexrazoxane, an iron chelating agent, is the sole approved antidote for treating anthracycline extravasation. It is believed to prevent tissue damage by inhibiting topoisomerase II and removing free iron, thereby limiting the oxidative damage caused by anthracyclines. However, its cost is prohibitively high, making it inaccessible to the vast majority of healthcare centers.

In this case report, we present the successful treatment and favorable evolution with the use of Dexrazoxane after accidental Epirubicin extravasation, further demonstrating the pivotal role of Dexrazoxane in the management of anthracycline extravasation.

2. Case Report

A 63-year-old patient, diagnosed with luminal HER2 negative nonspecific carcinoma of the right-side breast in January 2021, has been under medical supervision for this condition since her diagnosis. Her past medical history is otherwise unremarkable. After the diagnosis, the patient underwent a partial mastectomy and axillary dissection in February 2021. Following surgery, a multidisciplinary consultation meeting in March 2021 retained the indication of adjuvant treatment. The treatment plan included chemotherapy with 3 cycles of EC (Epirubicin + Cyclophosphamide) and 12 weekly administrations of Paclitaxel, which began in April 2021. This was to be followed by radiotherapy and hormonal therapy. In preparation for the chemotherapy, a port-a-cath was placed via the left internal jugular route in April 2021, with no immediate complications observed. Positioning was verified by chest X-ray and was interpreted as normal (**Figure 1**). During the first cycle of chemotherapy, the port-a-cath was functional, with good flow and venous return. The premedication regimen of Ondansetron and Methylprednisolone was administered without complications. In May 2021, during the second cycle of EC treatment, the patient complained of a burning sensation in the area around the port-a-cath after administration of 50 ml of Epirubicin, the patient complained of a burning sensation in the area around the port-a-cath.

The infusion was stopped immediately. The patient was hospitalized urgently for monitoring and the catheter was opacified within 30 minutes of the incident. The opacification revealed a rupture of the catheter in the supraclavicular region with passage of a part of the contrast product subcutaneously (**Figure 2**).

Immediately, the needle was removed. The extravasation procedure was implemented in accordance with the establishment's recommendations. There was no observation of fluid collection requiring aspiration at the site of extravasation. There was an erythematous aspect measuring 12 × 7 cm without associated trophic disorders or loss of substances (**Figure 3**).

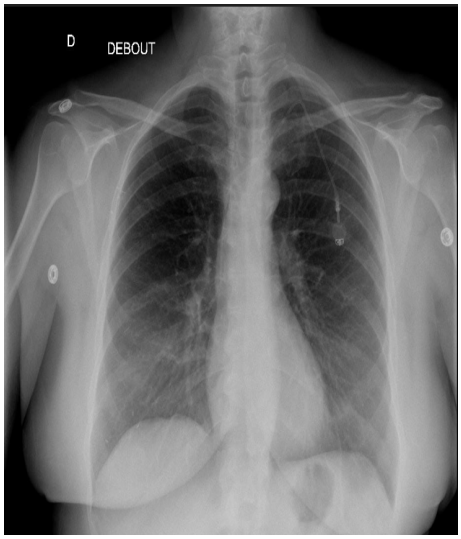


Figure 1. Chest radioraphy post placement of the left port-a-cath with the tip overlying the superior vena cava and the line appearing intact.

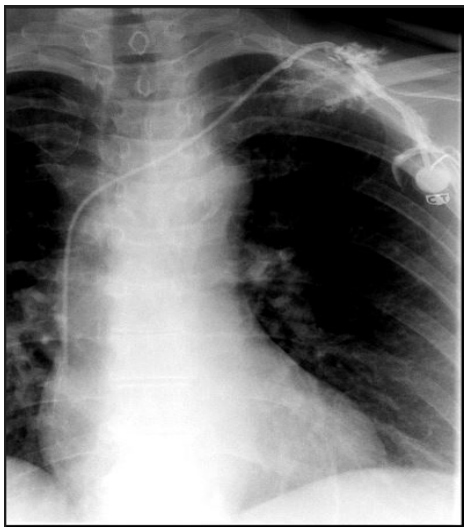
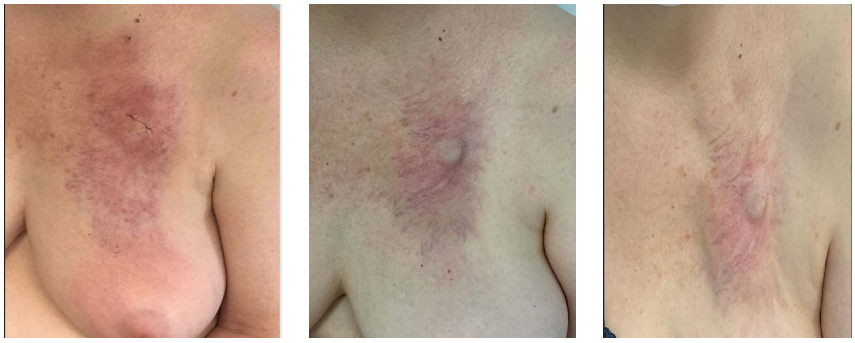


Figure 2. Intensifier image of the right port-a-cath demonstrating a rupture of the catheter located above the clavicle.



(a) (b) (c)

Figure 3. Clinical photographs: (a) Day 1 of extravasation; (b) 6 months after extravasation; (c) 11 months after extravasation.

Ice packs were put in place, a delimitation of the concerned area was carried out and a photo was taken (**Figure 3**). Information was given to the patient and the in-call surgeon was informed of the incident. With the agreement of the surgeon, there was no indication of an emergency surgical intervention.

An injection of Dexrazoxane was performed according to the following schedule: the total dose of 4200 mg intravenously for 3 days (day 1: 1500 mg, day 2: 1800 mg, day 3: 900 mg).

On day 3, the site of extravasation as well as the clinical conditions remained stable without pain or abnormal symptoms.

Regular clinical evaluations were carried out in consultation with her surgeon. Evolution over time was favorable with the persistence of only a simple induration without trophic disorders (**Figure 3**).

3. Discussion

Anthracyclines, including epirubicin, are effective agents for the treatment of solid tumors [4]. Being vesicants, anthracyclines can cause significant and persistent tissue damage and blister development when extravasated. Schulmeister outlines four primary ways in which extravasation injuries may happen: perforation, catheter fracture, incorrect needle placement and thrombus formation [5] [6].

Commonly observed symptoms associated with extravasation involve sensations of tingling, burning, pain/discomfort, inflammation, and erythema at the site of injection [7]. Delayed symptoms can include blister formation, tissue necrosis and ulceration.

Signs that may indicate the potential for extravasation include the absence of blood return, resistance felt while administering a bolus medication, or an interruption in the normal flow of an infusion [8].

Several studies have reported successful outcomes with Dexrazoxane when administered within a few hours after extravasation, and even up to 72 hours in some cases [4] [6] [9] [10] [11]. For instance, a UK study summarized 12 cases of anthracycline extravasation treated with Dexrazoxane, none of which required surgical intervention, and 92% of these cases were able to continue chemotherapy according to the schedule [12]. However, there have also been unsuccessful cases, where delayed treatment led to surgical interventions and significant morbidity. As presented by Hale O, *et al.*, indicate that damage from an extravasation injury can be severe, causing progressive skin ulceration and, in some instances, destruction of joints and nerves [13]. This suggests that the consequences of delayed detection of extravasation may be extensive, including pain, physical defect, psychological distress, cost of hospitalization, and more extensive tissue damage [13].

The European Society of Medical Oncologists has developed the most cohesive guidelines for handling extravasation management [3]. These suggest that the appropriate treatment hinges on the category of the chemotherapy agent in-

volved. In the case of vesicants, early detection and intervention are critical, with the use of cold compresses every 20 minutes, four times a day for 24 to 48 hours, and administration of intravenous Dexrazoxane and topical dimethyl sulfoxide within six hours of extravasation [14].

Moreover, the pharmacological mechanism of the bisdioxopiperazine Dexrazoxane remains incompletely comprehended [10] [11]. Several authors have posited that, as a result of its metal ion chelating property and the creation of chelates, it might, in the first place, impede the formation of free radicals, and in the second place, reversibly inhibit topoisomerase II, thereby serving as a protective agent [4].

The recommended dosage of Dexrazoxane is 1000 mg/m^2 on days 1 and 2 and 500 mg/m^2 on day 3. Several multicenter studies have shown that surgical intervention should be considered as a last resort, as timely treatment with intravenous Dexrazoxane infusion within 6 hours of extravasation occurrence can prevent the need for surgery in a significant number of patients [15].

The cost of a therapeutic dose of Dexrazoxane constitutes the principal negative aspect of the treatment itself.

In this case, we report a favorable evolution after using Dexrazoxane without resorting to surgery.

4. Conclusion

The case presented in this paper shows the importance of using Dexrazoxane to avoid early and extensive surgical intervention in case of extravasation.

Conflicts of Interest

The authors declare no conflicts of interest.

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