

Successful Conservative Management of Delayed Doxorubicin Extravasation during R-CHOP Chemotherapy in the Absence of Dexrazoxane: A Case Report

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ABSTRACT

Doxorubicin extravasation is a rare but serious complication of chemotherapy that may result in progressive soft tissue injury and necrosis. Dexrazoxane is currently the only approved antidotal therapy for anthracycline extravasation; however, its availability may be limited in some healthcare settings.

We report the case of a woman in her 40s with diffuse large B-cell lymphoma who developed peripheral doxorubicin extravasation during the first cycle of R-CHOP chemotherapy administered through a peripheral intravenous cannula. The event was recognized immediately, and standard management, including cessation of the infusion, attempted aspiration of the extravasated drug, limb elevation, and application of intermittent cold compresses, was initiated. Because dexrazoxane was unavailable, the patient was managed with close clinical monitoring and conservative wound care, including topical dimethyl sulfoxide and hydroactive dressings. The lesion progressed to superficial ulceration without evidence of deep tissue necrosis. Serial clinical examinations and Doppler ultrasonography excluded vascular compromise. Complete epithelialization was achieved within approximately 6 weeks without surgical intervention. Although dexrazoxane remains the standard treatment for anthracycline extravasation, this case suggests that favorable outcomes may be achieved in carefully selected patients through structured conservative management and close multidisciplinary follow-up when the antidote is unavailable. Nevertheless, conservative management should not be considered a substitute for guideline-recommended antidotal therapy when dexrazoxane is accessible.

Keywords: Doxorubicin; Extravasation; Anthracycline toxicity; Diffuse large B-cell lymphoma; Wound management

INTRODUCTION

Anthracyclines, including doxorubicin, remain essential components of curative chemotherapy regimens for hematologic malignancies such as diffuse large B-cell lymphoma¹. However,

doxorubicin is a DNA-binding vesicant, and accidental extravasation may cause progressive local

tissue injury ranging from pain and swelling to erythema, blistering, ulceration, and deep necrosis. Although the overall incidence of antineoplastic

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extravasation is low, the clinical consequences may be substantial because anthracycline injury can evolve over several days and may lead to treatment interruption, functional impairment, cosmetic sequelae, or surgical intervention^{2,3}.

Current guidelines recommend prompt recognition and immediate intervention when anthracycline extravasation is suspected. Initial management includes stopping the infusion, attempting aspiration through the existing catheter, elevating the limb, applying appropriate local thermal measures, documenting and demarcating the affected area, and administering dexrazoxane as the preferred antidote when available⁴. Early dexrazoxane administration has been associated with reduced risk of severe tissue necrosis and surgical intervention⁵⁻⁷. Topical dimethyl sulfoxide (DMSO) has also been used historically as an adjunctive or alternative treatment, but the supporting evidence remains limited and heterogeneous⁸.

Despite guideline-based recommendations, dexrazoxane may be inaccessible in some healthcare settings because of regulatory, logistical, or financial barriers. In such situations, clinicians may need to rely on structured conservative management, close monitoring, wound care, and multidisciplinary follow-up. Reports describing successful healing of delayed superficial doxorubicin extravasation without dexrazoxane or surgery remain clinically relevant, particularly in resource-limited settings^{9,10}. Here, we describe a patient with diffuse large B-cell lymphoma who developed delayed superficial ulceration following doxorubicin extravasation despite prompt recognition and guideline-concordant initial management. The case demonstrates that complete healing without surgery may be achieved in carefully selected patients through structured multidisciplinary conservative management when dexrazoxane is unavailable, while reinforcing that dexrazoxane remains the recommended standard of care whenever accessible.

Case presentation

After diagnosis of diffuse large B-cell lymphoma, a woman in her 40s was scheduled to receive first-line R-CHOP chemotherapy. She had no diabetes

mellitus, peripheral vascular disease, connective tissue disease, smoking history, or other known risk factors for impaired wound healing. Doxorubicin was administered through a peripheral intravenous cannula placed in a forearm vein and diluted in normal saline according to institutional protocol. The exact volume of extravasated doxorubicin could not be reliably quantified because the infusion was discontinued immediately after symptom onset. Approximately 2 minutes after initiation of doxorubicin, the patient reported sudden burning pain at the infusion site. Clinical examination revealed localized swelling measuring approximately 5 × 5 cm in diameter, without erythema, blistering, ulceration, or skin breakdown at that time. The affected area was demarcated for serial assessment, and the initial appearance is shown in Figure 1A. The infusion was immediately discontinued. Aspiration of residual drug through the intravenous cannula was attempted, the affected limb was elevated, and intermittent cold compresses were applied in accordance with the institutional extravasation management protocol. The patient was observed closely and educated regarding warning signs of progression, including increasing pain, erythema, blister formation, ulceration, discharge, fever, sensory change, or functional impairment.

Over the following 48 hours, mild erythema developed within the affected area. By day 4, a small central blister formed and subsequently enlarged before rupturing, resulting in a superficial ulcer. This chronological evolution is shown in Figure 1B–E, with arrows indicating the initial blister and the area of superficial ulceration. Despite these changes, the patient had no fever, purulent discharge, progressive severe pain, neurovascular deficit, functional limitation, or clinical evidence of deep tissue necrosis.

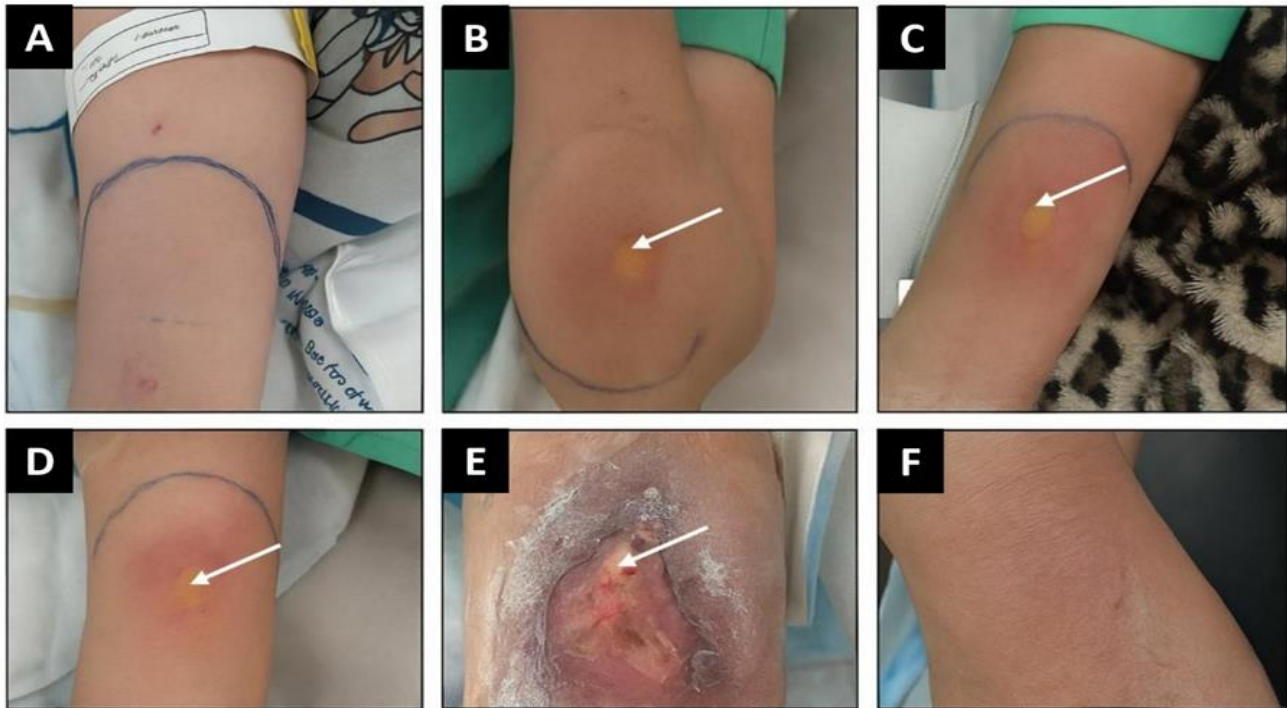


Figure 1. Clinical evolution of doxorubicin extravasation in the right forearm during and after R-CHOP chemotherapy. Panel A shows localized swelling shortly after infusion without skin breakdown. Panels B–D show development and enlargement of a central blister, indicated by arrows. Panel E shows superficial ulceration after blister rupture, indicated by an arrow, without evidence of deep tissue necrosis. Panel F shows complete re-epithelialization with mild residual hyperpigmentation. This figure was created by the authors and is original work.

Investigations

Because persistent swelling and delayed wound evolution raised concern for possible vascular compromise, arterial and venous Doppler ultrasonography of the affected limb was performed. The examination demonstrated patent arterial flow in the evaluated upper-limb arteries, preserved venous compressibility and flow, and no evidence of arterial stenosis, venous thrombosis, vascular occlusion, or hematoma. These findings supported continued conservative management and made vascular obstruction or thrombophlebitis unlikely. Laboratory testing was performed to evaluate for systemic infection, inflammatory response,

cytopenia-related complications, renal impairment, hepatic dysfunction, metabolic abnormalities, and other factors that could affect wound healing or suggest an alternative diagnosis. The laboratory results are summarized in Table 1. Although mild leukocytosis and elevated C-reactive protein were noted, there was no fever, purulent discharge, hemodynamic instability, progressive cellulitis, or other clinical evidence of systemic infection. Renal and hepatic parameters were interpreted in the context of the patient's overall oncologic condition and clinical course.

Table 1: Laboratory evaluation during follow-up after doxorubicin extravasation

Laboratory parameter	Patient value	Unit	Suggested adult reference range	Clinical relevance
White blood cell count	12.8	×10 ⁹ /L	4.0–11.0	Evaluates leukocytosis/infection or leukopenia
Hemoglobin	7.9	g/dL	Female: 12.0–16.0	Baseline hematologic status
Platelet count	430	×10 ⁹ /L	150–450	Evaluates bleeding risk and marrow status
C-reactive protein	20	mg/L	<5	Screens for systemic inflammation/infection
Erythrocyte sedimentation rate	21	mm/h	Female <50 years: 0–20	Supports assessment of inflammation
Serum creatinine	1.3	mg/dL	0.5–1.2	Assesses renal function
Blood urea nitrogen	16	mg/dL	7–20	Assesses renal/metabolic status
Blood glucose	99	mg/dL	Fasting: 70–99	Screens for impaired glycemic control affecting wound healing
Aspartate aminotransferase	17	U/L	10–40	Assesses hepatic function
Alanine aminotransferase	22	U/L	7–56	Assesses hepatic function
Alkaline phosphatase	120	U/L	44–147	Assesses hepatobiliary status
Total bilirubin	0.9	mg/dL	0.1–1.2	Assesses hepatic/biliary function
Albumin	3.4	g/dL	3.5–5.0	Nutritional/wound-healing status

Differential Diagnosis

The initial clinical differential diagnosis included irritant contact reaction, early cellulitis, thrombophlebitis, and chemotherapy-related vesicant injury. The subsequent evolution of the lesion, including blister formation and superficial ulceration following confirmed exposure to doxorubicin, together with the clinical course and exclusion of vascular pathology, supported the diagnosis of anthracycline extravasation injury.

Treatment

Initial management was performed immediately following recognition of extravasation and included cessation of chemotherapy infusion, attempted aspiration of residual drug via the intravenous cannula, limb elevation, intermittent application of cold compresses, and demarcation of the affected area for ongoing monitoring.

As the lesion evolved over the subsequent days, conservative wound care was initiated. Sterile hydroactive dressings were used to maintain a moist wound environment and promote epithelialization. Following disruption of the epidermal barrier, topical mupirocin was applied to reduce the risk of secondary bacterial infection. Topical DMSO was subsequently introduced as adjunctive therapy and

applied every 8 hours to the intact surrounding skin for approximately 14 days because dexrazoxane was unavailable. Additional topical agents, including zinc oxide cream for protection of the peri-lesional skin, a Centella asiatica-containing preparation during the healing phase, and a short course of 0.1% mometasone cream for localized inflammation at the wound margins, were used according to local wound-care practice to support skin protection and symptom control rather than as specific treatments for anthracycline toxicity.

A multidisciplinary review including plastic surgery consultation confirmed appropriate healing progression and supported continued conservative management without indication for surgical intervention. The structured conservative management and monitoring strategy used in this patient, including criteria supporting continued conservative care and criteria for surgical escalation, is summarized in Table 2

Table 2: Structured conservative management and monitoring strategy for doxorubicin extravasation in this case

Management domain	Intervention/ Assessment	Clinical rationale
Immediate management	Immediate cessation of doxorubicin infusion; attempted aspiration of residual drug via the intravenous cannula; limb elevation; intermittent cold compresses; demarcation of the affected area	To minimize further tissue exposure to the vesicant agent, reduce local drug diffusion, and facilitate serial assessment of lesion progression
Patient education and monitoring	Education regarding warning signs, including increasing pain, erythema, blistering, ulceration, discharge, fever, sensory change, functional limitation, or necrosis; reinforcement of limb elevation and cold compresses; close outpatient follow-up	To facilitate early recognition of lesion progression, infection, neurovascular compromise, or functional impairment requiring escalation of care
Adjunctive pharmacological therapy	Topical DMSO applied every 8 hours to the intact surrounding skin for approximately 14 days because dexrazoxane was unavailable; topical mupirocin after epidermal disruption	DMSO was used as adjunctive therapy in the absence of dexrazoxane; mupirocin was used to reduce the risk of secondary bacterial infection following skin barrier disruption
Wound care	Hydroactive dressings to maintain a moist wound environment; zinc oxide barrier cream for peri-lesional skin protection; adjunctive topical Centella asiatica preparation during the healing phase; short course of 0.1% mometasone cream for localized inflammation	To maintain an optimal wound-healing environment, protect surrounding skin, support tissue repair, and control local inflammation
Diagnostic assessment	Arterial and venous Doppler ultrasonography of the affected limb	To exclude vascular compromise, thrombosis, stenosis, occlusion, or hematoma as contributors to swelling or delayed wound evolution
Multidisciplinary follow-up	Serial clinical assessment and plastic surgery consultation	To confirm suitability for conservative management, monitor wound evolution, and identify early indications for surgical escalation
Criteria supporting continued conservative management	Preserved distal perfusion; no neurovascular deficit; no progressive deep necrosis; no purulent discharge or systemic infection; controlled pain; no functional impairment; progressive granulation and epithelialization on follow-up	To avoid unnecessary surgical intervention while ensuring timely escalation if the lesion progressed
Criteria for surgical escalation	Serial assessment for findings that would warrant surgical escalation, including progressive necrosis, suspected tendon or deep soft-tissue involvement, uncontrolled pain, worsening infection, vascular compromise, functional limitation, or failure of wound healing to progress. None of these findings developed during follow-up in the present case.	To identify patients who may require debridement, reconstruction, or other surgical intervention

Outcome and Follow-Up

Over 40 days following the extravasation event, the lesion demonstrated progressive healing, with gradual resolution of inflammation, formation of healthy granulation tissue, and complete epithelialization. At final follow-up, the wound had fully healed with no residual ulceration, infection, or functional impairment.

Only mild post-inflammatory hyperpigmentation and residual erythema remained at the affected site. The patient reported no pain and had returned to normal daily activities without limitation.

The clinical evolution of the lesion and response to conservative management is shown in Figure 1.

This case report was prepared in accordance with the CARE (Case Report) guidelines.

DISCUSSION

Chemotherapy extravasation remains a rare but potentially severe complication of systemic cancer therapy, particularly when vesicant agents such as anthracyclines are involved. Doxorubicin is well recognized for its potential to induce progressive tissue injury even after relatively small-volume extravasation events¹¹. This case demonstrates that delayed superficial ulceration after doxorubicin extravasation may heal completely with structured conservative management when dexrazoxane is unavailable, provided that careful monitoring excludes progressive deep tissue injury, infection, vascular compromise, and functional impairment. The extravasation was recognized within minutes, and immediate standard measures were initiated; nevertheless, the lesion evolved over several days from localized swelling to blister formation and superficial ulceration. This clinical course is consistent with the delayed nature of anthracycline-induced tissue injury and emphasizes that initial findings may underestimate subsequent tissue damage¹².

A key clinical issue in this case was determining whether the evolving lesion required surgical intervention. Delayed blistering and superficial ulceration alone do not necessarily mandate surgery if serial examinations demonstrate preserved perfusion, stable or improving superficial involvement, absence of infection, controlled pain, and no functional compromise. In this patient, Doppler ultrasonography excluded arterial or venous compromise, laboratory and clinical monitoring did not support systemic infection, and plastic surgery consultation confirmed that continued conservative management was appropriate. These findings supported avoidance of premature surgical debridement.

Conservative management in this setting should be active and structured rather than passive observation. Important components include serial clinical examination, photographic documentation, demarcation of the affected area, patient education regarding warning signs, wound protection, infection prevention, maintenance of a moist wound environment, and timely multidisciplinary reassessment^{3,4,7}. Surgical consultation remains

essential when necrosis progresses, deeper soft-tissue or tendon involvement is suspected, pain becomes uncontrolled, infection develops, or wound healing fails to progress¹³.

Dexrazoxane remains the preferred specific antidote for anthracycline extravasation and should be administered as early as possible, ideally within 6 hours, when available¹⁴. Although the precise mechanism by which dexrazoxane limits local tissue injury following anthracycline extravasation remains incompletely defined, two principal protective mechanisms have been proposed. Dexrazoxane is a bisdioxopiperazine that undergoes intracellular hydrolysis to metal-chelating metabolites capable of reducing iron-dependent anthracycline-mediated reactive oxygen species formation. In addition, dexrazoxane acts as a catalytic inhibitor of topoisomerase II and may thereby limit anthracycline-mediated topoisomerase II–DNA injury^{2,7}. These complementary actions may attenuate the progressive cellular and tissue damage characteristic of anthracycline extravasation. Prospective multicenter data have shown that dexrazoxane markedly reduces tissue necrosis and the need for surgical intervention⁶. Therefore, the favorable outcome in this patient should not be interpreted as evidence against dexrazoxane. Rather, this case supports conservative management only as a pragmatic approach for carefully selected patients when dexrazoxane is unavailable and the injury remains superficial.

Topical DMSO has long been used in the management of anthracycline extravasation. Proposed mechanisms include free-radical scavenging, anti-inflammatory effects, and increased skin permeability that may facilitate local dispersion and absorption of the extravasated drug^{8,15,16}. In the present case, DMSO was selected because dexrazoxane was unavailable and topical DMSO represented an accessible, noninvasive alternative supported by historical prospective clinical studies and contemporary guidance for anthracycline extravasation when dexrazoxane cannot be used. Nevertheless, the available evidence for DMSO remains limited and heterogeneous, and it should not be regarded as equivalent to dexrazoxane, which remains the preferred specific antidote. Because

DMSO was incorporated as one component of a multimodal conservative management strategy, its independent contribution to the favorable clinical outcome cannot be determined.

The wound management strategy applied in this patient was based on established principles of moist wound healing and infection prevention. Topical antimicrobials were used selectively when barrier disruption occurred. Adjunctive agents, including zinc oxide and Centella asiatica extract, were used to support skin integrity and tissue repair, while short-term topical corticosteroids were applied to control local inflammatory response^{17,18}. Overall, the wound-care strategy followed established principles of maintaining a moist wound environment, protecting the surrounding skin, preventing secondary infection, and supporting spontaneous tissue repair while carefully monitoring for signs of progression requiring surgical intervention^{19,20}.

This report has several limitations. The volume of extravasated doxorubicin could not be accurately quantified, and the independent effects of the individual topical therapies cannot be determined because multiple conservative interventions were applied concurrently. Furthermore, observations from a single case cannot establish the efficacy of conservative management or replace guideline-recommended treatment with dexrazoxane when it is available.

CONCLUSION

Anthracycline extravasation remains a potentially serious complication of chemotherapy that may continue to evolve despite prompt initial management. This case demonstrates that, in carefully selected patients with superficial tissue injury, structured conservative management and close multidisciplinary follow-up may result in complete healing without surgical intervention when dexrazoxane is unavailable. Nevertheless, dexrazoxane remains the recommended standard of care for anthracycline extravasation and should be administered whenever available. This case emphasizes the importance of early recognition, serial clinical reassessment, and timely multidisciplinary wound management, while

highlighting the need to improve global access to dexrazoxane.

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Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

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