



# Management of Epirubicin Extravasation Injuries of the Hand with Debridement and Flap Cover—A Case Series

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## Abstract

Chemotherapy extravasation injury is an iatrogenic injury due to extravasation of the drug from the vessel during infusion therapy. Among various chemotherapeutic drugs, DNA binding vesicants like epirubicin and doxorubicin can lead to extensive tissue necrosis following extravasation. They are commonly used in many chemotherapy regimens including those for carcinoma breast. We present our case series in the management of these wounds with aggressive debridement and regional (pedicled groin)/free flaps (superficial circumflex iliac artery perforator, lateral arm) for cover in five patients. All flaps healed well with patient returning to further treatment in 3 to 4 weeks post-surgery with preservation of hand function. Thus, early recognition of the type of drug that has extravasated is crucial. Regional and free flaps are superior to local flaps because there are no extra incisions and grafts on the limb that has already been injured.

## Keywords

- ▶ chemotherapy extravasation
- ▶ vesicants
- ▶ free flap cover

## Introduction

Chemotherapy extravasation injury is an iatrogenic injury due to extravasation of drug from the vessel during infusion therapy. The kind of drug that has extravasated is one of the major determinants of extent of tissue damage. Chemotherapy drugs can be broadly classified into three types depending on their ability to produce local tissue damage following extravasation.<sup>1</sup>

1. DNA binding vesicants like anthracycline derivatives: epirubicin, doxorubicin, and daunorubicin.

2. Non-DNA binding vesicants like vinca alkaloids: vincristine, vinblastine. Taxane group: docetaxel and paclitaxel.
3. Irritants like alkylating agents: cisplatin, carboplatin, cyclophosphamide, and ifosfamide. Antimetabolites: 5-fluorouracil, methotrexate, and gemcitabine.

Vesicants extravasation can produce blistering and severe local tissue damage. Epirubicin is a type of DNA binding vesicant and its extravasation can lead to severe local tissue necrosis. Once extravasated, it binds to DNA in the local tissue leading to cell death. The dead cells in turn release the drug that is taken up by adjacent healthy cells by endocytosis.

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**Table 1** Case details of patients with epirubicin extravasation injury

Sl. no.	Injury details	Type of flap	Disease details	Flap surgery timing
1	Epirubicin extravasation dorsum of left hand 2 weeks old	Pedicled two stage groin flap	Breast cancer patient post-mastectomy receiving adjuvant chemotherapy with EC regimen 3rd cycle	Patient had interruption of chemotherapy till wounds healed (1 month). Patient succumbed to original disease after 2 years of surgery
2	Epirubicin extravasation dorsum of left hand 6 weeks old	Pedicled two stage groin flap	Breast cancer patient post-mastectomy receiving adjuvant chemotherapy with EC regimen 4th cycle	Patient had finished her course of chemotherapy. Patient succumbed to original disease after 2 years of surgery
3	Epirubicin extravasation dorsum of right hand 10 days old	Pedicled two stage groin flap	Breast cancer patient receiving NACT with EC regimen 1st cycle	Patient had interruption of chemotherapy till wounds healed (1 month)
4	Epirubicin extravasation dorsum of left hand 3 weeks old	SCIP free flap using ulnar artery and its vena comitantes as donor vessels	Breast cancer patient post-BCS receiving adjuvant chemotherapy with EC regimen 1st cycle	Patient had interruption of chemotherapy till wounds healed (3 weeks)
5	Epirubicin extravasation dorsum of left hand 2 weeks old	Lateral arm free flap using superficial radial artery and dorsal vein as donor vessels	Breast cancer patient receiving NACT with EC regimen 4th cycle	Flap cover was done simultaneously with breast surgery

Abbreviations: BCS, breast conserving surgery; EC, epirubicin, cyclophosphamide; NACT, neoadjuvant chemotherapy; SCIP, superficial circumflex iliac artery perforator.

This leads to a continuous cycle of tissue damage and drug is retained locally for a longer period of time. The dorsum of the hand is the most common site for intravenous infusion therapy and hence the plastic surgeons' role is critical in the management of these. We present our case series of management of these injuries with debridement and flap cover.

## Case Series

Between January 2017 and February 2021, a total of five patients presented with epirubicin extravasation injury wounds on the dorsum of the hand (► **Table 1**). All the patients presented in the delayed phase at least 2 weeks after the extravasation injury. Once identified they were planned for immediate debridement and flap cover as the wounds had demarcated. Three patients underwent debridement and regional flap cover with pedicled groin flap (► **Figs. 1a–c**). They settled well apart from slight marginal discoloration in one due to subflap collection that settled with dressings.

One patient underwent debridement and superficial circumflex iliac artery perforator (SCIP) free flap cover (► **Figs. 2a,b**). Microvascular anastomosis was performed to the ulnar artery and vena comitantes at the wrist level after verifying that the recipient vessels were healthy.

The last patient had a smaller defect after debridement and hence lateral arm free flap harvested from the same limb

was used to cover the defect. Anastomosis was done to superficial radial artery and deep vein in the anatomical snuff box. In this patient, simultaneous breast surgery and axillary dissection were performed to reduce the number of surgical procedures. The viable extensor tendons were preserved during debridement in all the cases. For digits where the extensor tendons were lost, the distal cut end was lateralized to the adjacent in continuity tendon. Per op flap thinning of margins was done in all the patients to achieve a thinner flap and facilitate inset. None of the flaps required re-exploration. All the donor sites were closed primarily and healed well, except the SCIP flap donor site that developed a seroma requiring drain insertion. Follow-up period was 2 years. Two of these patients succumbed to the original disease (lung metastasis) 24 months later.

On presentation, patients had stiffness of the metacarpophalangeal and interphalangeal joints due to the injury. After wound healing, they were able to achieve adequate finger flexion. Active finger extension was not possible beyond neutral. None underwent secondary extensor tendon reconstruction. Activity of daily living was not affected but detailed evaluation of hand function was not performed. All patients underwent postoperative physiotherapy

## Discussion

Chemotherapeutic agent extravasation in peripheral line is an iatrogenic complication during treatment, especially DNA



**Fig. 1a** Epirubicin extravasation dorsum of right hand 10 days old.



**Fig. 1b** After debridement.



**Fig. 1c** Pedicled groin flap inset.



**Fig. 2a** Harvested and thinned superficial circumflex iliac artery perforator free flap for epirubicin extravasation injury dorsum of hand.

binding vesicants like epirubicin and doxorubicin as they cause severe skin necrosis and blister formation. Early recognition and referral of extravasation to a plastic surgeon and can minimize complications.<sup>2,3</sup> Identifying the type of drug that has extravasated is crucial because vesicants produce much greater injury requiring operative intervention<sup>4</sup> than nonvesicants where conservative management



**Fig. 2b** One year follow-up with well-settled flap and hand.

can be tried. Immediate identification and instillation of saline or antidotes have been described; however, delayed presentation with skin necrosis and eschars always requires debridement into normal skin and early flap cover. Flap cover ensures good wound healing and subsequent preservation of function of underlying extensor tendons (► **Supplementary Video S1**).

#### Supplementary Video S1

Good hand function. Online content including video sequences viewable at: <https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0043-1774787>.

All the five patients we operated were undergoing chemotherapy for carcinoma breast either in the neoadjuvant or adjuvant setting. They were obese patients with thin veins. Epirubicin is an integral part of chemotherapy regime for breast cancer; hence, those requiring multiple cycles may be benefitted with a more definitive venous access like chemo port or central line early in their treatment to prevent the disabling side effects of extravasation in peripheral intravenous lines. The overall incidence varies from 0.1 to 6.5%.<sup>2</sup> Around 7,000 chemotherapy sessions are

administered in our center every month. Extravasation can be limb devastating; hence, prompt debridement and flap cover need to be considered even in the palliative chemotherapy setting where life span may be short but flap cover reduces suffering and restores hand function.

Skin flaps were opted as the choice for cover in all these patients. Flap thinning was necessary intraoperative and later to give good contour. Free flaps made the reconstruction straight forward by avoiding multiple surgeries as these patients were already burdened by the prolonged duration of treatment. Flap thinning was performed under local anesthesia after the patient completed cancer treatment.

Local flaps like a distally based radial forearm flap<sup>5</sup> and perforator propellor flaps are also an option for cover but we preferred regional and free flaps as the donor site morbidity is much less. These patients already had wounds on the dorsum of hand and surrounding skin changes due to the extravasation. Doing a local flap further reduces the aesthetic result because of visible scars on forearm due to incisions and skin grafts.

## Conclusion

Early recognition of chemotherapeutic agent extravasation is important, particularly in regard to DNA binding vesicants like epirubicin/doxorubicin. Delayed presentation of epirubicin extravasation with skin necrosis always requires immediate radical debridement into normal skin and flap cover. Regional and free flaps where donor sites can be closed primarily are superior to local flaps, which produce additional scars in the forearm and have a need for skin grafts. Prompt flap cover not only ensures wound healing but also restores the function of the hand thus reducing morbidity in the management of these iatrogenic complications.

#### Conflict of Interest

None declared.

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