

Painless skin erythema in a patient with a chemoport: Anthracycline therapy extravasation presenting with skin necrosis

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Figure 1.



Figure 2.



CASE

A 67-year-old Hispanic woman was admitted to the hospital with newly diagnosed diffuse large B cell lymphoma. The patient underwent right internal

jugular port placement and was started on R-CHOP therapy (rituximab, cyclophosphamide, doxorubicin hydrochloride, oncovin, prednisone). Her nurse reported that the port was flushing nicely but not drawing blood. She was asked to start chemotherapy as long as the port was flushing. The patient was discharged home next day after finishing her first cycle of chemotherapy. On the day of discharge patient had some redness around the port site possibly second-

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ary to the surgical incision but didn't complain of any pain or discomfort in that area.

She presented to the ER three days after discharge with redness, swelling, and desquamation of the skin on her right chest and breast along with pain (Figure 1). A CT of the chest showed marked inflammation of the right chest wall and probable mastitis and abscess formation in the right breast. There were no inflammatory changes around the port. She was diagnosed with chemical burn secondary to extravasation of chemotherapy (doxorubicin hydrochloride) and was taken to the OR for extensive debridement, right mastectomy, and port removal (Figure 2). Post operatively she received wound care and antibiotics and was discharged to a LTAC with a wound-vac and plans for a possible skin graft at a later date. She was readmitted twice within the next two months for the surgical site abscess and persistent infection with *Pseudomonas aeruginosa*.

DISCUSSION

Extravasation is leakage of any liquid (fluid or drug) into the perivascular or subcutaneous space. It is one of the most dreaded complications of chemotherapy due to the potential for severe tissue destruction, long term complications, and morbidity¹. Extravasation injuries accounts for 0.5% - 6% of adverse effects related to chemotherapy² with an annual incidence is of 0.1% - 0.7%³. In 2012 the European Society for Medical Oncology released clinical guidelines for management of chemotherapy extravasation using a simplified scheme for management, prevention, and classification. Chemotherapy medications can be classified according to their ability to cause local damage after extravasation as blistering agents, as non-blistering agents, and as irritants (Table 1). Vesicants are defined as chemicals causing blister formation of the skin and/or mucous membranes; irritants are drugs, not associated with blistering, that

Table 1 Classification of chemotherapeutic drugs according to their potential for damage.

Blistering	Irritants	Non-Blistering
DNA-Binding Compounds	Alkylating agents • Ifosfamide	Arsenic trioxide
Alkylating agents • Mechlorethamine	Anthracyclines • Liposomal class	Asparaginase
Anthracyclines • Doxorubicin • Danorubicin	Topoisomerase II	inh. Bleomycin
Dactinomycin	5-FU	Fludarabine
Non-DNA-Binding	Platin salts	Interferons
Vinka Alkaloids	Topoisomerase I inh.	Monoclonal antibodies
Taxanes		Cyclophosphamide

Adapted from: Management of chemotherapy extravasation: ESMO-EONS clinical practice guidelines. Perez Fidalgo J A, Garcia Fabregat L, Cervantes A, et al. Ann Oncol 2012; 23 Suppl 7:viii167-73.

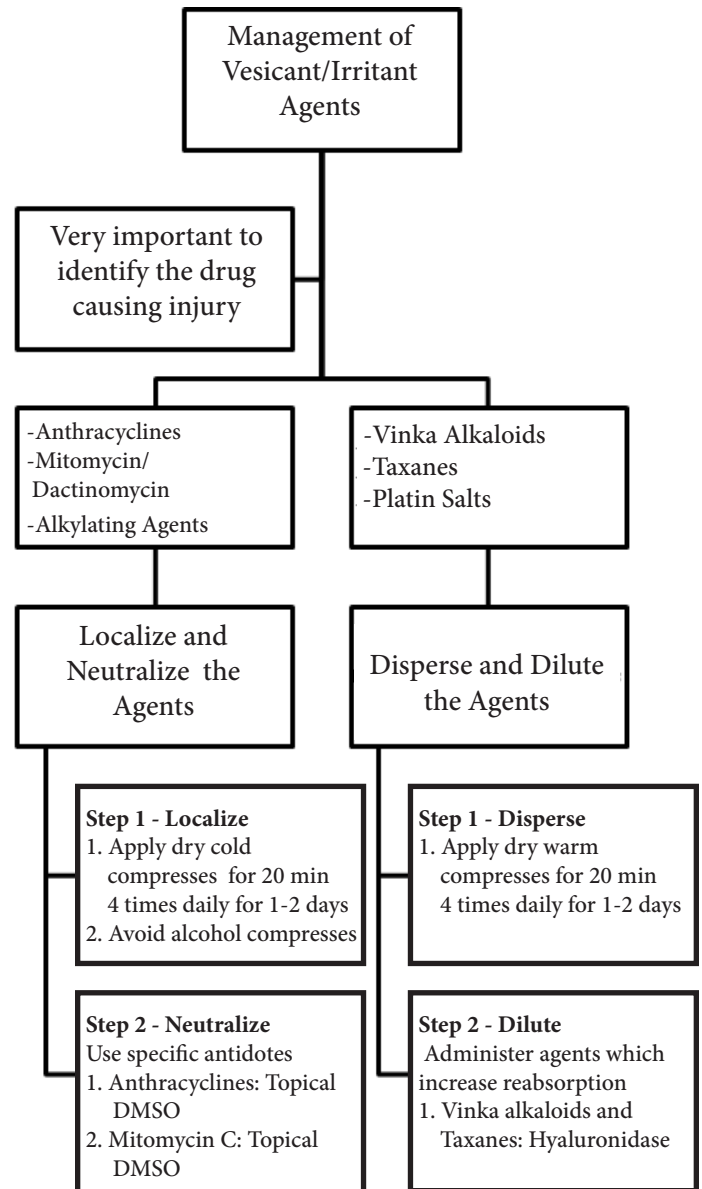
cause local inflammation or irritation. There are two mechanisms proposed for vesicant tissue damage. One involves damage to DNA with polymerase activation and depletion of NAD+ that lead to inhibition of glycolysis and cleavage of the fibrils which connect the basal epidermal cells to the basement membrane by the cellular proteases. The other mechanism involves direct damage to the tissues due to local depletion of glutathione and subsequent damage from free radicals⁴.

The risks for chemotherapy extravasation can be either patient or infusion related^{1,2,5,6}. For example, a small, frail vein with an unfavorable cannulation site which is running a bolus injection in a morbidly obese patient will have a high risk for extravasation. In the event of an extravasation, the general consensus for treatment is a step by step approach to diminish acute injury and to prevent further morbidity. No randomized trials on the treatment of extravasation have been carried due to ethical reasons. But regardless of the chemotherapy drug, early initiation of treatment is considered mandatory, and infusion personnel need training to manage these adverse events^{1,2,6,7}.

First, it is important to stop the infusion and try to aspirate as much drug as possible. It is mandatory to identify the leaked agent. Second, remove the cannula but avoid exerting any manual pressure over the extravasated area⁶. After the chemotherapeutic agent is identified and classified as either non-blistering or blistering/irritant, the next steps are clear. If it is a non-vesicant (non-blistering agent) local management, such as dry cold compresses, should be adequate. But if the extravasated agent is identified as a vesicant, the management will be drug specific and more difficult^{1,2,6,8}(Figure 3). Finally, the use of corticosteroids is uncertain. A single-arm clinical study in 53 patients with extravasations due to different drugs showed that multiple subcutaneous injections of hydrocortisone followed by topical betamethasone prevented tissue necrosis or sloughing necessitating surgical treatment. However, in a retrospective series of 175 cases of extravasation, up to 46% patients receiving intralesion corticosteroids needed surgical

debridement. In contrast only 13% of those without corticosteroid treatment needed surgery, suggesting a deleterious effect of these agents. Therefore, subcutaneous corticosteroids are not recommended⁶.

Figure 3 Recommended Management for Irritants and Blistering Agents.



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References

1. Harrold K, Gould D, Drey N. The efficacy of saline washout technique in the management of exfoliant and vesicant chemotherapy extravasation: a historical case series report. *Eur J Cancer Care (Engl)* 2013; 22(2):169-78.
2. Goolsby TV, Lombardo FA. Extravasation of chemotherapeutic agents: prevention and treatment. *Semin Oncol* 2006; 33(1):139-43.
3. Hahn JC, Shafritz AB. Chemotherapy extravasation injuries. *J Hand Surg Am* 2012; 37(2):360-2.
4. Barbee MS, Owonikoko TK, Harvey RD. Taxanes: vesicants, irritants, or just irritating? *Ther Adv Med Oncol* 2014; 6: 16–20, DOI: 10.1177/1758834013510546.
5. Langer SW. Extravasation of chemotherapy. *Curr Onc Rep* 2010 Jul; 12(4):242-6.
6. Perez Fidalgo JA, Garcia Fabregat L, Cervantes A, et al. Management of chemotherapy extravasation: ESMO-EONS clinical practice guidelines. *Ann Oncol* 2012; 23 Suppl 7:vii167-73.
7. Perez-Fidalgo JA, Cervante A. Reply to “comment on: management of chemotherapy extravasation: ESMO-EONS clinical practice guidelines”. *Ann Oncol* 2013; 24(4):1129-30.
8. Schulmeister L, Pollack CV Jr. Images in emergency medicine. Swollen hand. Anthracycline chemotherapy extravasation. *Ann Emerg Med*. 2011; 57(4): 417,422.

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