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Case Report

Vesicant extravasation due to doxorubicin administration in a patient with primary unknown peritonitis carcinomatosa

Askin Dogan[1,*], Ulas Solmaz[1], Emre Mat[1], Gokhan Tosun[1], Mehmet Adiyeke[1], Yusuf Yildirim[1], Yasemin Yildirim[2],

[1] Tepecik Education and Research Hospital, Department of Obstetrics and Gynecology, Izmir, Turkey
[2] Internal Medicine Nursing, Ege University Nursing School, Izmir, Turkey

Abstract

Anthracyclines are the major anti-neoplastic drugs used in gynecological cancer chemotherapy. The overall incidence of extravasation due to vesicant anti-neoplastic agents such as anthracyclines is low. This type of extravasation may cause severe tissue damage. A 58-year-old woman with a prediagnosis of peritonitis carcinomatosa of unknown origin was referred to our center. After the initial work-up, our multidisciplinary gynecologic oncology council decided to perform a treatment strategy consisting of neoadjuvant chemotherapy and interval debulking surgery. Initially she received 3 cycles of Cyclophosphamide (600 mg/m2) and Carboplatin (6 AUC) combination. Because of obtaining suboptimal response to the initial treatment, the chemotherapy regimen was replaced by Cisplatin (75mg/m2) and Doxorubicin (25 mg/m2). During the 2nd course of Doxorubicin, an extravasation occured at the catheter site in the back of the patient's left wrist. In the acute stage of this extravasation, local cold compression therapy was performed and affected extremity was elevated. Due to unavailability of specific antidotes, we could not apply any topical drug such as dimethyl sulfoxide (DMSO) and dextrazoxane. Three weeks later, necrosis and ulceration developed in the area of injury. After a wide debridement of necrotic tissues, full-thickness skin graft was applied to close the wound properly. The wound healed completely, but about one year later the patient died from the progression of the cancer. Oncology specialists and nurses should be aware of vesicant extravasation and keep specific antidotes available for certain vesicant chemotherapeutic agents. Also it should be kept in mind that aggressive surgical interventions and skin grafts could be required for the appropriate treatment of this condition.

Key words:

Chemotherapy extravasation, doxorubicin, treatment

Introduction

The extravasation of cancer chemotherapeutic agents is an undesirable situation that can easily occur and may cause severe and irreversible local injuries. Drug extravasation is one of the most devastating complications, as many drugs can cause varying degrees of local tissue injury when extravasated [1]. The overall incidence of extravasation injuries from chemotherapy administration has been reported to be as high as 1 to 7 percent [2]. Cytotoxic drugs are classified as irritants or vesicants based upon their potential for local toxicity [1]. Vesicant extravasation may result in loss of the full thickness of the skin and if severe, underlying structures. An irritant drug causes an inflammatory reaction with clinical signs include warmth, erythema, and tenderness in the extravasated area without tissue sloughing or necrosis. Although local symptoms (i.e., pain, erythema, swelling) are usual, a change in the rate of drug infusion or the absence of blood return from the vascular catheter may be the initial indicator that extravasation has occurred. Medical treatment of extravasation is based on proper maintenance of the intravenous line and application of cold or warm compresses, plus the use of antidotes when available. Antidotes for extravasation that have been shown to be useful are sodium thiosulfate, dimethylsulfoxide, and hyaluronidase. New treatments include dexrazoxane, sargramostim, and hyperbaric oxygen for doxorubicin extravasations [3]. Non-healing ulcers resulting from an extravasation injury often require debridement and skin grafting. However, the optimal timing of surgical intervention is controversial. Failure of initial conservative management with continued erythema, swelling and pain, or the presence of large areas of tissue necrosis or skin ulceration is indication for surgery [4]. In about 11% of cases, if the harmful action of the drug is not blocked, it results in necrosis of the tissue and then tissue necrosis develops into a chronic ulcer [5,6]. The type of drug and the concentration used are also important factors in assessing the severity of the lesion, as some drugs, such as doxorubicin, remain in the tissues for months and continue to exert their harmful action [6,7]. Some authors suggest early intervention during the initial phase of extravasation that includes the excision of the affected zone and the insertion of cutaneous grafts to substitude lost tissue [8]. Other

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***Correspondence:** Askin DOGAN, M.D.
Tepecik Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Bölümü, Yenişerhir, İzmir, Türkiye:
Tlf:+90 232 4494949 | Fax: +90 232 4579651 | E-mail: kindoganmd@gmail.com

authors think that surgical treatment should only be reserved for cases when conservative treatment has failed and necrosis has already present [9].

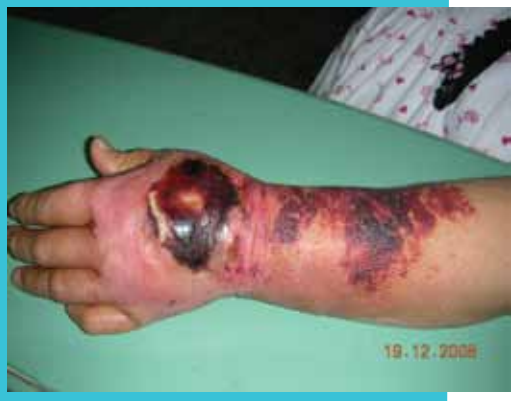
Case presentation

A 58-year-old woman with massive ascites and multiple solid tumors varying in size from 2 cm to 6 cm of the abdominal wall in the abdominal CT scan, prediagnosed with peritonitis carcinomatosa of unknown origin was referred to our center in April 28, 2008. She has complaints of abdominal discomfort and distension caused by severe ascites. After the initial work-up, our multidisciplinary gynecologic oncology council decided to perform a treatment strategy consisting of neoadjuvant chemotherapy and interval debulking surgery because of her unfavorable medical conditions. Initially, she received 3 cycles of Cyclophosphamide (600 mg/m2) and Carboplatin (6 AUC) combination. Because of inadequate response to the initial treatment, the chemotherapy regimen was replaced by Cisplatin (75 mg/m2) and Doxorubicin (25 mg/m2). During the 2nd course of Doxorubicin, an extravasation was occured at the catheter site in left vena dorsal venous arch. At acute phase of extravasation the infusion was immediately stopped, cold local compresses applied and affected extremity was elevated. We could not apply any topical drug such as dimethyl sulfoxide and dextrazoxane due to the unavailability of specific antidotes. Three weeks later, necrosis and ulceration developed in the area of the injury (Figure 1). As a result of plastic and reconstructive surgery consultation, a wide debridement of the necrotic tissue should be performed. Usually if an open ulcer develops, the area of excision may need to be quite large and may involve deep structures, i.e. nerves and tendons. Although there were necrosis and ulceration in the area of the injury, full-thickness skin graft was applied to close the wound properly by plastic and reconstructive surgeons. As seen in the Figure 2, the wound healed completely, but the patient died from progression of her disease in March 2009.

Discussion

IOncology specialists and nurses should be aware of vesicant extravasation and keep specific antidotes available for certain vesicant chemotherapeutic agents. First of all, prevention of extravasation should be the main objective. Irritant agents generally do not cause permanent damage, but may cause pain and inflammation of the vein at an intravenous catheter site. Vesicants have the potential to cause blistering and ulceration when they extravasate from the vein or are inadvertently administered into the tissue. Varying degrees of tissue damage, from mild skin reactions to severe necrosis, usually occur if vesicant chemotherapy extravasations are left untreated. So many foundations initiated projects to develop guidelines to help medical employers especially nurses to understand and recognize extravasations and improve the prevention and management of vesicant extravasations. The specific aims were to increase the medical knowledge of specific elements of extravasation including causes, risk factors, prevention, signs and symptoms, potential consequences. There are too many guidelines which have been developed for administration of vesicant drugs have been published in the nursing literature and in oncology reviews.

Figure 1.



Wound due to doxorubicin extravasation

According to these guidelines precautionary steps that should be taken to prevent extravasation include standardized procedures for administering chemothreapeutic agents and managing extravasations. Ideal vein selection for intravenous medication administration is important. Therefore, all vesicant chemotherapy, especially if it requires continuous infusion, should be administered through a central line whenever possible for improved safety. If a chemotherapeutic agent has to be given through a peripheral vein, one should keep in mind their potential toxicity and complications when extravasated. Antidotes for vesicant and irritant agents as dexrazoxane [10] must be kept available in chemotherapy units. A peripheral intravenous (i.v.) catheter must be tested with i.v. fluids first at a high flow rate to determine the patency of the vessel to be used and to exclude extravasation prior to the administration of chemotherapy drugs. The dorsum of the hand and volar aspect of the wrist are not recommended for this purpose. Veins that are small and fragile, veins in areas of flexion, and veins in arms with lymphoedema or neurologic impairment should not be used for cannulation. Large veins in the forearm are recommended for peripheral vesicant administration. If there is any

doubt about the patency of the vessel, the infusion should not be attempted at all.

Figure 2.

Wound healed after reconstructive surgery

The intravenous line should be flushed prior to chemotherapy administration, between each chemotherapeutic agent infusion given consequtively, and after the chemotherapy is finished. When extravasation occurs or is suspected, the first course of action is to stop the infusion and check the list below (Table 1) [11]. These guidelines also must be kept available in chemotherapy units. Moreover, oncology specialists and nurses should keep in their mind that aggressive surgical interventions and skin grafts could be required for the appropriate treatment of this condition.

Conflict of interest statement

The authors declare no conflict of interest.

Table 1 Management of extravasation [11]

Initial management of vesicant chemotherapy extravasation
Stop administering the vesicant.
Leave the cannula or port needle in place and attempt to aspirate the vesicant.
Mark and measure the extravasation area.
Photograph the extravasation area and include the date in the photograph.
Remove the cannula or port needle.
Apply topical heat or cooling.
Notify the physician.
Administer analgesics as needed.
Complete required documentation.
Disperse and dilute
Apply a cold pack to the affected area for 20 minutes 4 times daily for 1—2 days.
Neutralise the drug by using the specific antidote (if available).The antidote should be given as per the specific directions provided by the manufacturer.
Remove the cannula (delivering the antidote) after confirming no more antidote will be prescribed or given.
Elevate the limb
Document the incident using extravasation documentation sheet.
Arrange follow up for the patient as appropriate.
Treatment for non vesicants
Elevate the limb.
Consider applying a cold pack if local symptoms occur.
Document the incident using extravasation documentation sheet.
Arrange follow up for the patient as appropriate.

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