Managing Vesicant Extravasations

LISA SCHULMEISTER

Oncology Nursing Consultant, River Ridge, Louisiana, USA

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LEARNING OBJECTIVES

After completing this course, the reader will be able to:

1. Describe how vesicant chemotherapy drugs can extravasate from implanted ports.
2. Recommend procedures to obtain a blood return from central venous access devices.
3. Evaluate the signs and symptoms of a vesicant extravasation.
4. Administer the FDA-approved vesicant extravasation treatments and antidotes.

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ABSTRACT

Extravasation is an unusual but potentially severe complication of vesicant chemotherapy administration. Some extravasation injuries prompt litigation and the oncologist’s actions, or lack of action, are scrutinized in the courtroom. This article presents advice and recommendations for treating patients who receive vesicants and includes a discussion of FDA-approved vesicant extravasation treatments and antidotes. The Oncologist 2008;13:284–288

INTRODUCTION

Vesicant extravasation injuries can occur in patients receiving chemotherapy despite best efforts to prevent them. There are several things oncologists can do to mitigate against both the risk of legal action and the extent of tissue damage.

BEST PRACTICES IN THE CLINIC FOR THE ONCOLOGIST AND THE TREATMENT TEAM

1. Inform patients of the risk for vesicant extravasation. Although the risk for vesicant extravasation is very low, estimated to be in the range of 0.01%–6% [1, 2], patients need to be informed that extravasation may occur each time they receive a vesicant. When a chemotherapy protocol or treatment plan is initially explained to a patient, there is a tendency to emphasize the more common risks, such as myelosuppression, nausea and vomiting, hypersensitivity, and fatigue. The risk for vesicant extravasation is sometimes overlooked or underemphasized. However, in the courtroom, it is recognized that a risk for vesicant chemotherapy is extravasation, and the question of whether or not patients were fully informed of this risk is considered. In some cases, patients have...
responded by saying “nobody ever told me this could happen.”

2. **Recognize that implanted ports reduce—they do not eliminate—the risk for extravasation.** Oncologists often recommend port insertion because of the sclerosing effect of vesicants and other chemotherapy drugs on the peripheral veins. Although implanted ports reduce the risk for extravasation, vesicant extravasations can still occur. Noncoring (e.g., Huber) needles may be incompletely placed into or dislodge from the port septum (Fig. 1). Formation of a thrombus or fibrin sheath at the tip of the catheter can cause backtracking of the vesicant along the catheter to the venotomy site where the vesicant can leak into the tissue. Perforation of the superior vena cava, catheter fracture, and separation of the port from the catheter also can lead to vesicant extravasation into the tissue or other areas such as the mediastinum or pleural space [3, 4].

3. **Never permit or approve the use of an implanted port that “flushes easily” but does not have a blood return.** If a port lacks a blood return but flushes easily, vesicant chemotherapy should not be given without further investigation; a blood return or other evidence of correct port placement and patency (e.g., dye study) is needed before a vesicant is administered. The patient should be placed in a supine or lateral decubitus position and another attempt made to obtain a blood return. This simple maneuver is successful in many patients, especially outpatients, who are seated upright during the initial attempt to obtain a blood return. If repositioning is not successful, a 10-ml syringe with normal saline can be used with a gentle “push-pull” motion to flush the port. In a study conducted in Belgium, a blood return was achieved in 53% of 8,685 ports that lacked a blood return after simply changing the patient’s position and/or additional flushing [5]. Implanted port catheter tips typically accumulate a coat of fibrin that can act as a one-way valve, permitting infusion of fluids but not the withdrawal of blood. Catheter tips also can be occluded by thrombi. Instillation of a thrombolytic agent (e.g., tissue plasminogen activator [TPA]) should restore a blood return from the port when partial (withdrawal occlusion) or total occlusion occurs. In the Cardiovascular Thrombolytic to Open Occluded Lines (COOL) efficacy trial, alteplase (TPA injection) restored catheter function 90% of the time [6].

A chest x-ray can ascertain proper catheter placement and may detect a fractured or severed catheter. However, chest x-ray does not ascertain catheter patency. A chest x-ray that includes the cervical spine is indicated when there is suspicion of catheter migration (e.g., when patients feel or “hear” something on one side of the neck) (Fig. 2). A dye study (cathetergram) assesses both placement and patency. Extravasations can occur when catheters detach from or break at the junction of the catheter and port septum, when catheters fracture, and, rarely, when catheters are nicked, sliced, or pierced prior to or during port insertion (Fig. 3).

Vesicant administration should only proceed when there is a blood return from the port or there is other evidence of correct placement and patency, such as a dye study.

4. **Know that despite nurses’ best efforts, vesicant extravasations sometimes occur.** Although nurses take great care to prevent extravasations by closely monitoring patients during vesicant administration, extravasations sometimes occur. Patient movement may cause a peripheral i.v. catheter to perforate the vein wall. Accidental tugging on i.v. tubing may cause the catheter to dislodge. Mechanical failure of the vascular access device is yet another example

![Figure 1. Doxorubicin-induced tissue necrosis that occurred after a needle dislodged from an implanted port.](image1)

![Figure 2. X-ray of the cervical spine showing migration and impending fracture of the port catheter.](image2)
of a situation that cannot always be prevented; instead, extravasations must be detected promptly.

5. Admit that a vesicant extravasation has occurred. Extravasation is a known risk of vesicant administration. When this complication occurs, or is suspected, be truthful and avoid minimizing the situation—or worse, fabricating an explanation for the extravasation.

6. Avoid the “blame game.” Patients often seek explanations for why their extravasations occurred. It is tempting to criticize the nurse for poor technique or imply that the patient moved or in some way caused or contributed to the extravasation occurring. Instead, various factors should be examined, and most importantly, the information that was present at the time of the extravasation must be considered. Once an extravasation injury is apparent, “Monday morning quarterbacks” can find fault, point fingers, and, with great authority, state what should have been done differently. However, what information was present at the time of the extravasation? Was a blood return obtained? How and how often was the patient monitored? Was the staffing level sufficient to care for the number and acuity of the patients treated that day? Did anything unusual occur (e.g., inadvertently tugging on the tubing)? Did the patient complain of pain at the i.v. site? Each extravasation is unique and must be considered in the context in which it occurs. Like medication errors, there are usually multiple factors that cause or contribute to the occurrence of a vesicant extravasation.

7. Discard the “it can’t happen here” mentality. Extravasations can occur wherever vesicants are administered, even in settings where highly experienced oncology nurses give hundreds of doses of vesicants each day. And just be-

cause an extravasation hasn’t ever occurred in a particular facility doesn’t mean that an extravasation can’t occur. One could occur this afternoon or tomorrow. Extravasations cannot always be prevented.

8. Be familiar with the signs and symptoms of a vesicant extravasation. Fortunately, vesicant extravasations do not occur every day. In fact, they occur so rarely that some oncologists have never seen one personally. Signs and symptoms of a vesicant extravasation include swelling (common), redness, discomfort (may or may not be present and is often described as stinging or burning), lack of a blood return from the i.v. device, and an infusion that slows or stops [7–9]. When in doubt, it is best to presume that an extravasation has occurred and initiate appropriate treatment.

Initial workup following a suspected vesicant extravasation should include estimating the amount and concentration of the vesicant that may have extravasated into the tissue, evaluating the symptoms reported by the patient, assessing the administration site (including measuring and photographing the area in accordance with institutional protocol), and assessing the extremity (if applicable) for range of motion and discomfort with movement. Treatment of the extravasation should then be initiated promptly.

**TREATMENT OPTIONS FOR VESICANT EXTRAVASATIONS**

Oncologists practicing in the 1970s likely recall the early published reports and photographs of vesicant extravasation injuries. Despite a significant amount of research (mostly animal) on antidotes and treatments, extravasation management—until recently—was not much different than it was 30 years ago. Anthracycline (e.g., daunorubicin, doxorubicin, epirubicin, idarubicin) extravasations have been initially managed by cooling the area (ice packs), and the ensuing tissue necrosis generally has required debridement and skin grafting or flap placement. Plant alkaloid
(vincristine, vinblastine, vinorelbine) extravasations have been managed by heat application and local injection of hyaluronidase; however, in 2001–2004, hyaluronidase was commercially unavailable [10].

In December 2005, the FDA approved Hylenex® recombinant (hyaluronidase human injection, Baxter, Deerfield, IL) for use as an adjuvant agent to increase the absorption and dispersion of other injected drugs. Hyaluronidase increases the permeability of connective tissue through the hydrolysis of hyaluronic acid, a polysaccharide found in the intercellular matrix of connective tissue. Hylenex® recombinant is a purified preparation of the enzyme recombinant human hyaluronidase. Other formulations of hyaluronidase are derived from animal products. Amphadase™ (Amphastar Pharmaceuticals, Rancho Cucamonga, CA) is a bovine-derived preparation and Vitrase® (ISTA Pharmaceuticals, Irvine, CA) is an ovine-derived preparation [10].

Hyaluronidase is locally injected into the extravasation sites of plant alkaloids. A 1-ml solution of hyaluronidase is injected as five 0.2-ml injections using a 25-gauge or smaller needle. The needle is changed with each injection. Hyaluronidase is stored under refrigeration [10].

In September 2007, the FDA approved Totect™ (dexrazoxane for injection, TopoTarget USA, Rockaway, NJ) for the treatment of extravasation resulting from i.v. anthracycline chemotherapy (Fig. 4). (There is currently no therapeutic equivalent of Totect; see FDA [11].) The mechanism by which dexrazoxane diminishes tissue damage is unknown. Totect is supplied as a treatment kit for single patient use and is a systemic treatment that is infused over 1–2 hours each day for 3 days in a large vein in an area away from the extravasation site. Totect dosing is based on the patient’s body surface area (BSA), from the extravasation site (e.g., the opposite arm). Totect treatment is managed by heat application and local injection of hyaluronidase; however, in 2001–2004, hyaluronidase was commercially unavailable [10].

Mechlorethamine (nitrogen mustard) extravasations have been and continue to be treated with the antidote sodium thiosulfate. Sodium thiosulfate neutralizes mechlorethamine to form nontoxic thioesters that are excreted in urine. The manufacturer of mechlorethamine recommends application of ice for 6–12 hours following the local injection of sodium thiosulfate into the extravasation area. A dose of 2 ml of sodium thiosulfate solution for each milligram of mechlorethamine suspected to have extravasated is injected s.c. into the extravasation site using a 25-gauge or smaller needle. The needle is changed with each injection [15].

Taxane (paclitaxel, docetaxel) extravasations cause mild tissue necrosis, and topical cooling is the only recommended treatment [16]. Patients should be instructed to monitor the extravasation site and report blistering, skin sloughing, fever, chills, and worsening pain at the extravasation site.

**SUMMARY**

Vesicant extravasations are a litigious area in oncology practice. Oncologists can reduce the risk for litigation as well as optimize patient care by promptly recognizing and treating extravasations. Advances in vesicant extravasation treatment are improving outcomes for patients; tissue necrosis can now be reduced and, in some cases, entirely prevented. Oncologists need to be aware of vesicant extravasation antidotes and new extravasation treatments, such as Totect, which is indicated for the treatment of anthracycline extravasations.

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**REFERENCES**


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