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Chemotherapy Extravasation

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The Case

A 73-year-old woman with no past medical history was diagnosed with stage IIIA breast cancer. She and her oncologist decided to begin systemic chemotherapy that would involve 6 cycles of treatment, all administered at the outpatient chemotherapy center located at the local hospital.

The patient arrived for her first day of treatment. A nurse who was relatively new to the job had difficulty placing a peripheral IV catheter but was ultimately able to achieve venous access in the left arm. Despite meeting some resistance when infusing saline, the nurse proceeded to infuse the first medication, doxorubicin, a highly toxic chemotherapeutic agent. The patient immediately began complaining of pain at the infusion site. Upon closer examination, the nurse noted that the chemotherapy had infused outside of the vein (extravasated) into the skin.

The nurse removed the IV catheter and placed an ice pack on the site. She had not been given any information about how to manage extravasations nor had she been informed of the location of the "extravasation kit," so she did not know what else needed to be done. Eventually, the IV site was bandaged and the patient was sent home to return later in the week. The patient suffered pain at the site with some mild redness and blistering but had no long-term side effects.

The Commentary

Intravenous chemotherapeutic agents are associated with multiple complications, both local and systemic. Extravasation of the medication into the skin is one of the most dreaded complications that can occur during chemotherapy administration (1), as patients can suffer short-term and long-term consequences. Fortunately, steps can be taken to reduce the risk of extravasation and limit the consequences if it does occur.

Vesicant (causing blisters) chemotherapy agents such as doxorubicin, the agent this patient received, can cause tissue necrosis if they leak from the vein or are inadvertently administered into tissue. Doxorubicin and the other anthracycline vesicants (daunorubicin, epirubicin, idarubicin) cause cell death (necrosis) by

binding to the DNA in healthy tissue cells when they extravasate. In addition, anthracyclines are not easily metabolized by the body; they can remain in the tissues for a substantial period of time. Consequently, these extravasation injuries often become larger, deeper, and more painful over time. Other types of vesicant chemotherapy, such as the plant alkaloids (e.g., vincristine, vinblastine), do not bind to the DNA in healthy cells and are more easily metabolized in the tissues. Therefore, extravasation injuries with these agents generally remain localized, are mildly painful, and improve over time.(2)

Despite the best efforts of nurses and health care facilities, extravasation of vesicants does occur, albeit infrequently. Published incidence rates of chemotherapy extravasation range from 0.01% (3) to 6%.(4) However, many health care providers realize that even one extravasation injury is one too many, particularly since most injuries are preventable.(2)

The severity of a vesicant extravasation injury is influenced by the type of vesicant that extravasates (DNA-binding or non-binding [Table 1]), concentration and amount of vesicant in the tissue, and location.(5) Extravasations in the dorsum of the hand or wrist generally cause more damage than extravasations in other areas, such as the forearm, which was the site of this patient's extravasation. This is because the forearm has more overlying tissue and fewer underlying structures (such as tendons and nerves) than the hand and wrist.

Unlike the patient in this case, who had a minor extravasation and no long-term effects (most likely because the event was detected early), some extravasations may require hospitalization for wound debridement, skin graft or flap placement, and IV antibiotics. Scheduled chemotherapy treatment often must be delayed, which may set back treatment and lead to psychological distress for the patient. Long-term sequelae may include chronic infection, disability, and disfigurement.(5)

Prevention (Table 2) is the most important approach to extravasation management.(1) The Oncology Nursing Society (6) and Infusion Nurses Society (7) have published guidelines for vesicant administration and extravasation management. Institutional policies and procedures used in hospitals, clinics, and office settings should be written in accordance with these guidelines and reviewed annually.

In the case above, the IV device was inserted with some difficulty, and the nurse proceeded with vesicant administration despite meeting resistance when infusing saline. Traumatic IV device insertion can pierce the vein wall and increase the risk of extravasation. Vesicants should only be administered after a peripheral IV device is easily inserted, a blood return is obtained from the IV, saline flows freely, and there is no evidence of redness or swelling. Even when all signs point to a well-placed line, extravasation of chemotherapy delivered peripherally remains a possibility, due to patient movement, inadequately secured IV devices, and prior venipuncture.(8)

Because of the high risk of extravasation associated with peripheral vesicant administration, patients often are advised to have an implanted port placed. Implanted ports (Figure) are usually placed under the skin on the chest wall. A non-coring needle is inserted into the septum of the port, which is connected to tubing that terminates in the superior vena cava. Implanted ports reduce, but do not eliminate, the risk of vesicant extravasation. Extravasation from implanted ports may occur when non-coring needles are incompletely inserted or dislodged, from thrombus formation at the catheter tip that causes backtracking of the vesicant to the puncture site, or from device malfunction or breakage. When a blood return is not obtained from

implanted ports, device patency and placement must be confirmed by other measures (e.g., dye study, successful instillation of a declotting agent, etc.) prior to vesicant administration.(6-9)

If an extravasation occurs or is suspected, steps should be promptly taken to limit the damage. First and foremost, vesicant administration should immediately be stopped. The extravasation site should be assessed and measured, and findings documented. Digital photographs are helpful to assess changes over time. Local cooling (ice pack) is recommended for extravasations of DNA-binding agents to constrict blood vessels and help prevent the vesicant from spreading to adjacent tissues. Doxorubicin is a DNA-binding agent, so applying ice to the patient's extravasation—as was done in this case—was an appropriate action. Local warming (dry heat) is indicated for non–DNA-binding vesicant extravasations to increase blood flow to the area, which helps distribute the vesicant and promote its absorption. Hyaluronidase, an enzyme that degrades hyaluronic acid and breaks subcutaneous tissue bonds, is used as an antidote for extravasation of non–DNA-binding vesicants. It is locally injected to promote drug diffusion and enhance absorption of the vesicant.(1,8)

Other chemical agents can also be used to limit tissue damage after extravasation in some circumstances. For example, dimethyl sulfoxide (DMSO), a free radical scavenger that is applied topically to an extravasation area, has been used to treat anthracycline extravasations. In one study, application of a 99% DMSO solution every 6 hours for 2 weeks in patients with suspected vesicant extravasations prevented tissue necrosis in 16 patients.(10) In another study, only 1 of 57 patients treated with DMSO (every 8 hours for 1 week) with suspected vesicant extravasations developed necrosis.(11) DMSO side effects include mild burning and scaling at the extravasation site and malodorous breath. The only medical grade DMSO product available in the United States is a 50% solution, which may not be as efficacious as the 99% solutions used in many trials.

In two clinical trials conducted in Europe, patients with suspected extravasations (confirmed by biopsies showing that anthracyclines were present) were treated with dexrazoxane, an agent that is indicated to prevent anthracycline-induced cardiac toxicity.(12) Dexrazoxane's mechanism of action is unknown, but some evidence suggests that it inhibits topoisomerase II reversibly and reduces anthracycline tissue damage.(13) One of 57 patients with biopsy-verified anthracycline extravasations developed tissue necrosis (overall efficacy 98.2%), and the majority of the patients were able to continue chemotherapy as scheduled.(12) This IV treatment must be initiated as soon as possible and within 6 hours of an anthracycline extravasation. Totect (dexrazoxane for injection) is packaged as an extravasation treatment kit for single patient use and recently became commercially available in the United States.(13,14)

Despite advances in IV device technology, the risk of extravasation during vesicant administration cannot be completely eliminated. Patients need to be informed of this risk, and nurses must implement risk reduction strategies such as those outlined in Table 2. In addition, health care providers need to be aware of the latest advances in extravasation management so they can promptly initiate appropriate treatment.

Take-Home Points

- Vesicant chemotherapy agents are known to cause tissue necrosis if they leak from the vein or are inadvertently administered into the tissue.
- Extravasation is a known risk of vesicant administration.

- Implanted ports reduce, but do not eliminate, the risk of vesicant extravasation.
- Vesicants should only be administered after a blood return is obtained, saline flows freely, and there is no evidence of redness or swelling.

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Tables

Table 1. Vesicant Chemotherapy Agents

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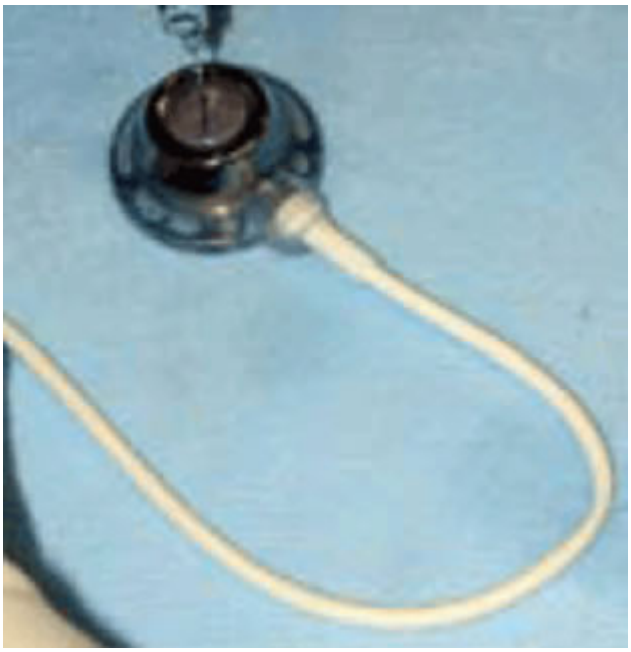
Classification	Examples
DNA Binding	
Alkylating agents	Mechlorethamine (nitrogen mustard)
Anthracycline antibiotics	Daunorubicin, doxorubicin, epirubicin, idarubicin
Other anticancer antibiotics	Dactinomycin, mitomycin, mitoxantrone
Non-DNA Binding	
Alkylators	Amsacrine
Plant alkaloids	Vinblastine, vincristine, vindesine, vinorelbine
Taxanes	Docetaxel, paclitaxel (note: considered to be mild vesicants)

Table 2. Extravasation Prevention Strategies

Inform the patient that extravasation is a risk of vesicant administration.
Instruct the patient to avoid movement during vesicant administration and to immediately report pain, burning, or other symptoms.
Insert a new IV device immediately prior to peripheral vesicant administration.
Use a large vein in the forearm for peripheral vesicant administration.
Do not administer a vesicant in a vein below a recent venipuncture site.
If insertion of an IV device is difficult, requires probing, or causes pain, restart the IV in another location.
Refer patients at high risk for peripheral extravasation for central line placement. High-risk patients include those with small, fragile veins or limited peripheral access due to lymphedema, cerebral vascular accident, or other causes; cognitively impaired patients; and active young children.
Stabilize and secure the IV device and cover the site with a transparent dressing to aid in visualization of the site.
Obtain a blood return prior to, and during, vesicant administration.
Immediately stop vesicant administration if there is a loss of blood return from the IV device, the patient reports stinging or pain, or redness or swelling develops.

Figure

Figure. Example of Implanted Port.



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