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CASE REPORT

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Changes in the subcutaneous tissue of catheterization site from the precatheterization state to the onset of anticancer drug-induced induration: A case report

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Abstract

This case showed that anticancer drug administration induces unhealthy subcutaneous tissue (thrombus or edema) without subjective symptoms, abnormal sign by palpation, or inspection, which have an extravasation risk.

KEYWORDS

chemotherapy, induration, injection site reaction, oncology nursing, peripheral venous

1 | INTRODUCTION

This report presents some of the changes in the subcutaneous tissue at the site of catheter insertion of a patient undergoing chemotherapy. The site was observed by ultrasonography at 5 time points, namely, before insertion, immediately after treatment, after 1, 3, and 4 weeks.

Some practice guidelines do not recommend the use of a peripheral intravenous catheter for irritant or vesicant continuous administration to avoid vessel damage.[1,2] However, peripheral intravenous catheters are unavoidably used in some patients for drug administration because of their conditions, such as superior vena cava syndrome, coagulopathy, or compromised condition.

In clinical settings, induration can be observed at the catheterization sites after anticancer drug administration even without obvious signs and symptoms of extravasation such as feelings of tingling, burning, pain, swelling, and redness at the

injection site.[2,3] A previous study reported the incidence of induration after chemotherapy as 17.4%. If induration is found by physicians or nurses, inserting catheter to the affected site is avoided. It can lead to catheter placement in inappropriate sites, such as the hands, near joints, or thin fragile veins.[4] These catheterization sites are reported as risk factors of extravasation. Thus, induration after anticancer drug administration is a clinical challenge for patients who must receive repetitive treatment using a peripheral intravenous catheter; induration occurrence should be prevented. It is important to know the actual condition of induration very well for safe chemotherapy treatment. Ultrasonography is used to observe the condition of the vein or surrounding tissue.[5,6] We already reported actual condition of induration through ultrasonography after obvious extravasation,[7] but the onset process of induration without obvious extravasation was unclear. Here, we report time course observation of the catheterization site from precatheterization to induration development through ultrasonography (Figure 1).

2 | CASE DESCRIPTION

A 77-year-old man with esophagus cancer was receiving chemotherapy, paclitaxel, weekly through a peripheral intravenous catheter at a chemotherapy room in a university hospital in Japan. He was not diabetic and was not on anticoagulants or immunosuppressants. His body mass index was 18.5. Data of patient character and details of drugs administration method were collected from his medical chart.

No abnormal subcutaneous tissue condition was observed at the target site, which was confirmed through ultrasonography, prior to catheterization for the administration anticancer drug; on the second week of paclitaxel administration, diameter of the target vein was 2.4 mm. It was calculated by measuring the minor axis and major axis three times, and measurements were averaged. Then, the average of the minor axis was added to the average of major axis and divided by two. Also, the skin at the site of catheterization did not have any signs of abnormality upon inspection and palpation.

All ultrasound images were obtained by one researcher using a Noblus® with linear array (5-18 MHz) 2D probe (Hitachi, Ltd, Medical). Precatheterization images were obtained by a 5-cm swept probe (peripheral side 2.5 cm; center side 2.5 cm) with short axis over the point that nurses selected as catheterization site, along the vein. Ultrasonographic images were assessed with reference to previous studies;[5,6] unclear superficial fascia at surrounding vein was judged as subcutaneous edema presence, and ununiform echoic area in the intravascular lumen was judged as thrombus.

The nurse inserted a 24G catheter at the patient's cephalic vein on the right forearm. Location of the catheterization site was recorded by a measure and digital camera. Drug administration protocol was as follows: First, the nurse secured the catheterization site by administering normal saline solution; a 6.6 mg of dexamethasone sodium phosphate + 20 mg of famotidine + 5 mg of d-Chlorpheniramine Maleate + 50 mL of normal saline was administered at 300 mL/h for 10 minutes. Next, 50 mL normal saline was administered at 300 mL/h for 10 minutes. Then, 156 mg paclitaxel + 50 mL normal saline was administrated at 300 mL/h for 60 minutes. Lastly, normal saline 30 mL at 300 mL/h for 6 minutes was administered. Thus, total drug administration time was about 90 minutes. Anticancer drug administration was completed without local adverse event or discomfort such as swelling, redness, and pain; however, subcutaneous edema and thrombus were observed through ultrasonography just after finishing anticancer drug administration (Figure 2A, B1, 2). Using ultrasonography, it was confirmed that the catheter tip was located in the vessel without stimulating the vessel wall.

One week later, no abnormal findings at the catheterization site were noted upon inspection or palpation. However, subcutaneous edema and the remaining thrombus at the site were observed, which were confirmed through ultrasonography. Three weeks later, the site was positively assessed for induration by palpation, and subcutaneous tissue and thrombus were observed through ultrasound. Four weeks later, the induration, thrombus, and subcutaneous edema were still present (Figure 2C-E). No symptoms were observed upon inspection at any one time, and no subjective symptoms such as pain or sensations of burning were reported.

On the post-treatment days, ultrasonographic images were taken same way as precatheterization, using puncture site or induration site as a center point. Evaluation of the presence of induration through palpation was conducted by a clinical nurse and one researcher who had clinical experience as a nurse.

Observation period was from February to March in 2019.

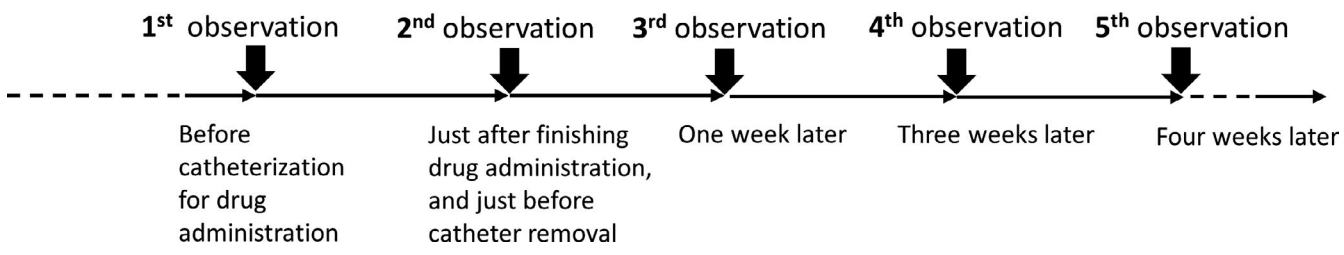

FIGURE 1 None

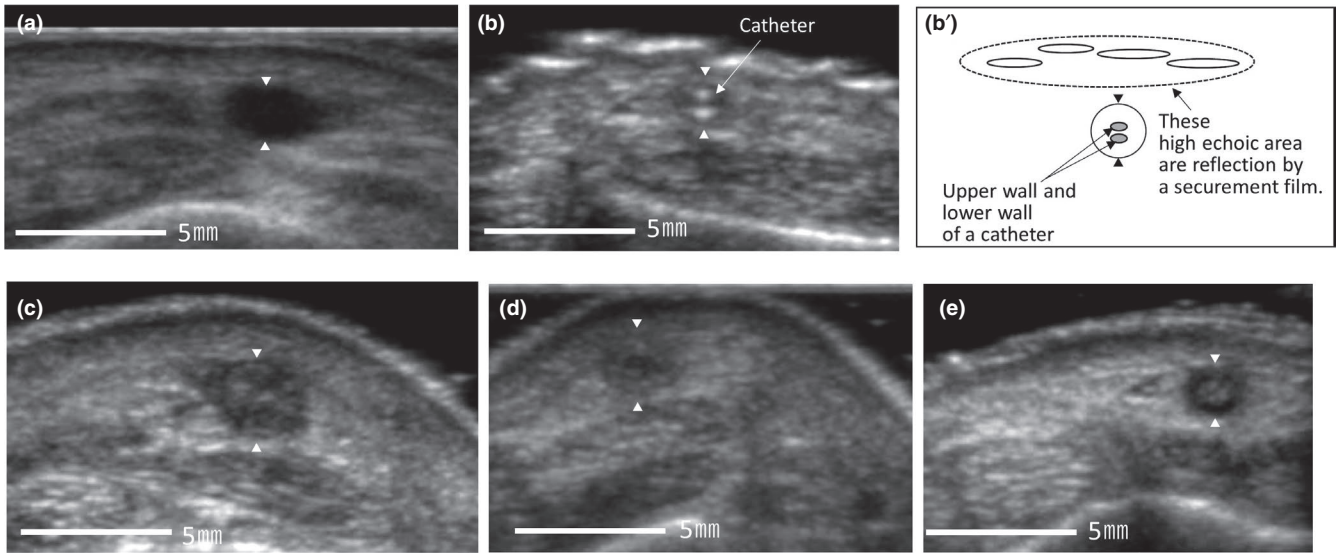

FIGURE 2 A, Just before insertion a catheterization; Vein lumen area was imaged as anechoic area. B, Just after completing anticancer administration, and just before the catheter removal. Two high echo points shown by arrow are upper wall and lower wall of the catheter. Some high echo points at skin surface are reflection by a catheter securement film. (Refer B': Illustration diagram.) There was no anechoic area; instead, vein lumen was imaged as nonuniform echoic area. It was considered thrombus presence. Also, uncleared superficial fascia was observed at the surrounding tissue of the vein. It was considered subcutaneous edema. C, Post-treatment 1 wk; Ununiform echoic area remained in the vein lumen, and subcutaneous edema at surround tissue of the vein. There was nothing abnormal detected by palpation. D, Post-treatment 3 wks; Ununiform echoic area remained in the vein lumen, and subcutaneous edema at surround tissue of the vein. Furthermore, induration was found by palpation in the site. E, Post-treatment 4 wks; Unechoed area become clear in the vein lumen, but there was still remain thrombus and subcutaneous edema. Also, induration remained

3 | DISCUSSION AND CONCLUSION

We observed the target site from precatheterization time until the development of induration caused by chemotherapy drug administration through a peripheral intravenous catheter. This is the first study that reported time course observation of the catheterization site from precatheterization to induration development through ultrasonography.

Reports about peripheral intravenous catheterization-induced induration are few; however, the condition of the subcutaneous tissue (thrombus, subcutaneous edema, and vessel wall thickening) in this case was the same as in a previous report. In that report, the induration sites were observed using ultrasonography, wherein the observation was only conducted on the next treatment day in patients who were receiving chemotherapy via peripheral intravenous catheters.[3]

During precatheterization, no abnormal findings were observed on the skin and subcutaneous tissues including veins, and its diameter was enough to insert a 24G catheter.[8] In addition, the patient was not diabetic, was nonobese, and was not on any anticoagulants or immunosuppressants. Thus, we did not suspect a slow wound healing factor. There was no complication during drug administration, but subcutaneous edema and thrombus were confirmed upon finishing administration. A week later, induration was not observed at the site, even with the presence of subcutaneous edema and thrombus. However, induration with edema or thrombus was observed 3 weeks later. Above these reasons, induration caused by anticancer drug administration was due to the fibrotic subcutaneous tissue formation, which was a result of mild inflammation that did not induce pain, swelling, and erythema.

Inflammation may be induced by chemotherapy or catheter tip irritation to vessel walls. In this case, chemotherapeutic drugs might have induced induration due to inflammation. There are two reasons why we hold this clinical opinion. One, the catheter tip position was not in an irritating position to the vessel wall. The other reason is paclitaxel, which has been reported as a high stimulation drug, compared with other taxanes, such as docetaxel and nab-paclitaxel.[9]

Fibrosis which is the last part of inflammation reaction is formed gradually and lasts about a few weeks.[10] Thus, we consider that fibrosis had still not become advanced at 1-week postchemotherapy. It means that in short treatment interval chemotherapy, there is possibility of anticancer drug administration using the site that has subcutaneous edema or thrombus as catheter placement site because nurses cannot detect abnormal tissue condition by palpation only.

"Unhealthy subcutaneous tissue" is one of the extravasation risk factors.[4] This case showed that anticancer drug administration through a peripheral intravenous catheter induces

the development of unhealthy subcutaneous tissue (thrombus or edema) without subjective symptoms, abnormal sign by palpation, or inspection. Also, this case showed how subsequent anticancer drugs, including vesicants, may be infused at vulnerable sites. Continuous administration of irritants or vesicants via a central vein is recommended. However, for patients who unavoidably require peripheral intravenous catheters, the catheterization site must be carefully selected. Short-term interval therapy such as a weekly chemotherapy has especially high risk for anticancer drug infusion at risky sites. Future researchers should consider the possibility of these risky sites when selecting appropriate catheterization site.

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CONFLICT OF INTEREST

MA and RM belong to the laboratory supported by Terumo Co. CK and HS have no conflict of interest.

AUTHOR CONTRIBUTIONS

MA: designed the research. MA and CK: contributed to data collection. MA: drafted the manuscript. RM and HS: critically reviewed the manuscript and supervised the whole study process. All authors read and approved the final manuscript.

ETHICAL APPROVAL

This observation was conducted in accordance with the Declaration of Helsinki, and study protocol was approved by the Research Ethics Committee of the facility where researchers belong (No. 11650-1). Using images and information for report was permitted by the patient.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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