Docetaxel extravasation into the normal breast during breast cancer treatment

Nagi S. El Saghir[a] and Zaher K. Otrock[a]

We report a new case of central line extravasation of docetaxel into the normal breast of a patient with metastatic left breast cancer. During the infusion of docetaxel, the patient complained of mild discomfort at the site of a subclavian Port-a-Cath, followed by redness, warmth and itchiness of the entire skin of the right breast beneath the port of entry, and it involved the entire right breast by the next day. Over the following few days, she developed blistering, desquamation and oozing of serous fluid through skin fissures. Anti-histamines and hydrocortisonebased ointment induced partial relief of symptoms. Warm soaks induced skin relief. Reaction resolved over few weeks leaving a brownish pigmentation of the skin of the breast, with clearly demarcated lines, as the only sequlae. *Anti-Cancer Drugs* 15:401–404 © 2004 Lippincott Williams & Wilkins.

Anti-Cancer Drugs 2004, **15**:401–404

Keywords: breast, chemotherapy, docetaxel, extravasation, vesicant

[a]Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon.

Correspondence to N. S. El Saghir, Division of Hematology/Oncology, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon.
Tel: +961 3-827-955; fax: +961 1-747-144;
e-mail: elsaghir@cyberia.net.lb, nagi.saghir@aub.edu.lb

Received 2 September 2003 **Revised form accepted** 17 December 2003

Introduction

Docetaxel has been described to have possible vesicant properties, but little is known about the extent of tissue injury it may cause after extravasation [1]. In this report we present the first case of an accidental central line docetaxel extravasation into the soft tissue of the normal right breast of a patient with metastatic left breast cancer. We present our case from extravasation to recovery and we review the few available reports in the literature.

Case report

F. E. is a 63 year-old lady who had a left breast cancer treated in 1999 with a left modified radical mastectomy and axillary dissection that showed invasive ductal carcinoma with involvement of 12 out of 13 axillary lymph nodes. She had a stage II (T2 N1 M0) breast cancer. She had positive estrogen and progesterone receptors, and HER2/*neu* was not overexpressed. She received adjuvant chemotherapy with 4 cycles of doxorubicin–cyclophosphamide and 4 cycles of paclitaxel using the CALGB 9344 protocol AC-T followed by radiation therapy and adjuvant tamoxifen [2].

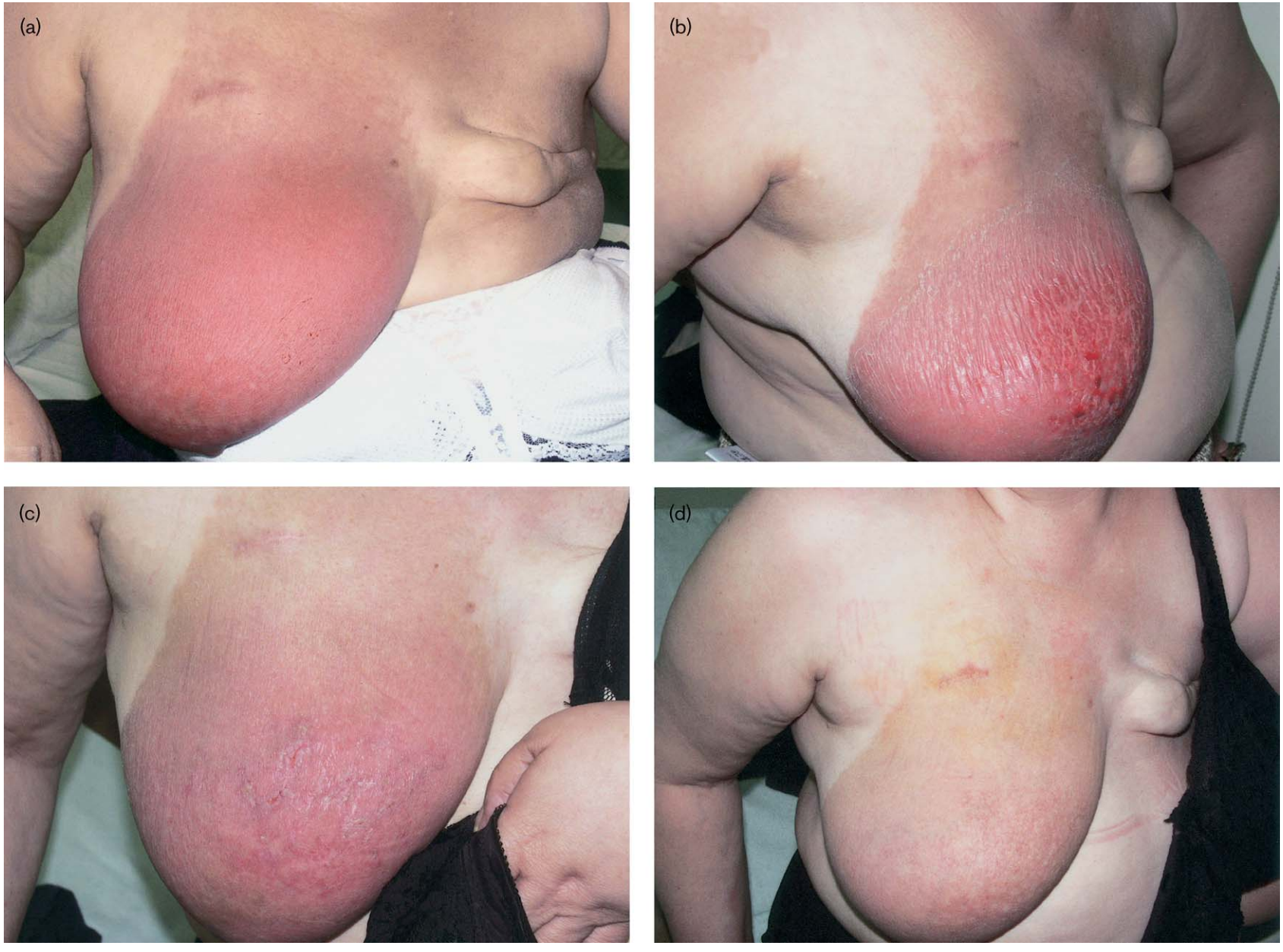
The patient did very well for 3 years. In 2002, she developed a pericardial effusion, the cytology of which was positive for malignancy. Her serum Ca 15.3 was 72.3 U/ml (reference range 0.0–28.0). A suspect bone scan uptake of the femoral head was negative by computed tomography-guided fine needle aspiration biopsy. The patient was therefore diagnosed to have recurrence of breast cancer, and was treated with docetaxel (Taxotere) and capecitabine (Xeloda) [3].

Docetaxel was infused i.v. through a right chest wall subclavian Port-a-Cath device. After premedication with tropisetron (Navoban), dexamethasone (Decadron), diphenhydramine (Benadryl) and ranitidine (Zantac), and during the administration of her sixth cycle of docetaxel (180 mg diluted in 250 cm^3 NSS over 1 h), the patient complained of mild discomfort at the catheter site located in the upper part of her right breast. The same day, she reported skin redness and warmth of her right breast. The next day, redness became very itchy and increased to involve all her right breast (Fig. 1a). There was no skin induration or s.c. thickening. It was hyperemic and pitting. The patient was initially treated for possible atypical cellulitis with IV Augmentin which was discontinued after 48 h as the patient showed no improvement. The erythema expanded, and covered the area of the polysite and the whole breast with clearly demarcated borders. The patient remained afebrile and her CBC was normal. Superinfection was therefore ruled out and a pure chemical extravasation reaction was entertained. The patient was given oral hydroxyzine hydrochloride (Atarax 25 mg p.o. b.i.d.).

Over the following few days, she developed more irritation and discomfort, blistering, desquamation, and oozing of serosanguinous fluid through minute skin fissures (Fig. 1b). In addition to anti-histamine tablets, a 1% hydrocortisone-based ointment and warm soaks were applied to the involved skin. Skin relief and reduction of skin desquamation was noted gradually (Fig. 1c). The reaction resolved completely over 8 weeks leaving a residual brownish pigmentation of the skin of

0959-4973 © 2004 Lippincott Williams & Wilkins DOI: 10.1097/01.cad.0000124494.74538.76

Fig. 1



(a) Docetaxel extravasation initial skin redness. (b) Desquamation and oozing of serosanguinous fluid. (c) Recovery of skin desquamation. (d) Residual skin pigmentation.

the breast, with well-demarcated borders (Fig. 1d). Over the following months, we noted further resolution of skin and s.c. reaction to docetaxel extravasation with only mild persistent pigmentation of the affected breast skin.

After chemotherapy, the patient was placed on a non-steroidal aromatase inhibitor (Letrozole) and she continues to receive zoledronic acid (Zometa). The patient is in complete remission and was re-evaluated in July 2003 and had no evidence of disease.

Discussion

Despite widespread experience and careful administration of chemotherapeutic agents, extravasation still occasionally occurs and may cause tissue damage. It is an inherent risk of i.v. therapy. The course and the management of extravasation remain subjects of continuing debate [4] and frustration.

The extent and severity of tissue injury is determined by the properties of the agent, the amount extravasated and the concentration in the extravasated fluid. Physiochemical characteristics such as pH, osmolarity and molecular weight also affect the amount of tissue injury. The degree of dissociability of the infusate and the acidity of the reconstituting diluent also contribute to tissue morbidity. The site of the extravasation and its anatomical components, as well as the length of time that the tissues remain exposed to the agent contribute to the severity of injury [5].

Although docetaxel is a member of the taxane family, it seems to have different properties from paclitaxel during tissue extravasation. Docetaxel has been reported to cause variable extravasation effects. Ascherman *et al.* reported five patients who experienced extravasation injuries during peripheral i.v. administration of docetaxel. Initial mild pain and swelling at the site of infiltration were followed by marked edema and erythema, increased tenderness, and blister formation [6]. Treatment consisted of warm soaks, elevation and active range-of-motion exercises. Two of their patients developed residual changes in skin pigmentation and one patient noted mildly decreased sensation of the affected extremity after 18 months [6]. Berghammer *et al.* reported an accidental extravasation of docetaxel that caused residual discoloration [7]. Their patient was treated with isotonic saline, topical dimethylsulfoxide and local hypothermia. The patient was left with mild brownish skin discoloration [7]. Raley *et al.* reported a case of docetaxel extravasation that caused delayed tissue injury consisting of skin blistering and desquamation. The patient was given non-steroidal anti-inflammatory agents and mild opioids for the pain [1].

Here, we reported the first case of docetaxel extravasation into the soft tissues of a breast and chest wall from Port-a-Cath entry of a central line. Our patient complained of mild discomfort at the catheter site during the infusion of docetaxel. She then experienced redness and warmth of her right breast. The redness increased to involve all her outer right breast. She developed skin desquamation and blisters, but she had no deep tissue necrosis. She only had residual hyperpigmentation of the skin. The reaction and pigmentation showed very clear borders that were well delineated. Docetaxel seems to have spread by gravity into the entire breast tissue and diffused easily into s.c. breast tissue.

Extravasated docetaxel did not produce tissue necrosis or any major sequalae. Oral anti-histamines, topical ointment containing 1% hydrocortisone and warm soaks were used. Recovery was complete, with mild residual brownish pigmentation of the skin of the breast, with clearly demarcated borders.

Although docetaxel did not cause deep tissue injury and necrosis, it was capable of causing superficial tissue injury, irritation, blisters, desquamation, serosanguinous fluid oozing and hyperpigmentation. Those properties can be considered superficial vesicant properties. In the literature docetaxel was listed as an irritant [8]. Our report demonstrates that docetaxel is more than an irritant. It is a vesicant or at least a superficial vesicant.

It is clear that prevention remains essential to avoid extravasation. Nurses must also demonstrate knowledge of vesicants, and of the initial symptoms and signs of chemotherapy extravasation such as pain, swelling and erythema [9,10]. Huber needles of central Port-a-Cath access should be always carefully assessed at the beginning and during infusion of docetaxel for possible dislodgement. Before a continuous infusion of a vesicant agent is initiated, the venous access should be assessed for good patency and normal flow. The infusion site should always be monitored and observed frequently during the administration of docetaxel and all chemotherapeutic agents.

References

1 Raley J, Geisler JP, Buekers TE, Sorosky JI. Docetaxel extravasation causing significant delayed tissue injury. *Gynecol Oncol* 2000; **78**:259–260.
2 Henderson IC, Berry DA, Demetri GD, Cirrincione CT, Goldstein LJ, Martino S, *et al.* Improved outcomes from adding sequential Paclitaxel but not from escalating Doxorubicin dose in an adjuvant chemotherapy regimen for patients with node-positive primary breast cancer. *J Clin Oncol* 2003; **21**: 963-964.
3 O'Shaughnessy J, Miles D, Vukelja S, Moiseyenko V, Ayoub J-P, Cervantes G, *et al.* Superior survival with capecitabine plus docetaxel combination therapy in anthracycline-pretreated patients with advanced breast cancer: phase III trial results. *J Clin Oncol* 2002; **20**:2812–2823.
4 Langstein HN, Duman H, Seelig D, Butler CE, Evans GR. Retrospective study of the management of chemotherapeutic extravasation injury. *Ann Plastic Surg* 2002; **49**:369–374.

5 Boyle DM, Engelking C. Vesicant extravasation: myths and realities. *Oncol Nursing Forum* 1995; **22**:57–67.
6 Ascherman JA, Knowles SL, Attkiss K. Docetaxel (Taxotere) extravasation: a report of five cases with treatment recommendations. *Ann Plastic Surg* 2000; **45**:438–441.
7 Berghammer P, Pohnl R, Baur M, Dittrich C. Docetaxel extravasation. *Supp Care Cancer* 2001; **9**:131–134.
8 Armand JP. *Attitude pratique en cas d'extravasation des anticancereux. Medicaments utilises en cancerologie*, 4eme edn. Dossier du Centre National Hospitalier d'Information sur le Medicament; 2001, pp. 38–43.
9 Chrystal C. Administering continuous vesicant chemotherapy in the ambulatory setting. *J Intravenous Nursing* 1997; **20**:78–88.
10 Camp-Sorrell D. Developing extravasation protocols and monitoring outcomes. *J Intravenous Nursing* 1998; **21**:232–239.