Recovery of symptomatic extravasation of liposomal doxorubicin after dexrazoxane treatment

Filip Yves De Vos[a], Willem Joost Lesterhuis[a], Roger Johannes Brüggemann[b] and Winette Tita van der Graaf[a]

A patient with metastatic ovarian cancer was treated with liposomal doxorubicin and carboplatin. She had an extravasation during liposomal doxorubicin infusion. Initially, she was treated conservatively with cold compresses and topical treatment. However, because of worsening of symptoms, she received dexrazoxane once daily for 3 days after which complete recovery occurred. This is the first casereport on symptomatic extravasation of liposomal doxorubicin treated with dexrazoxane.
***Anti-Cancer Drugs* 23:139–140 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

Anti-Cancer Drugs 2012, **23**:139–140

Keywords: dexrazoxane, extravasation, liposomal doxorubicin

[a]Departments of Medical Oncology and [b]Clinical Pharmacy, Radboud University Nijmegen Medical Center, Nijmegen, the Netherlands

Correspondence to Dr Filip Yves De Vos, PhD, MD, Radboud University Nijmegen Medical Center, P.O. Box 9101, Nijmegen, 6500 HB, The Netherlands
Tel: +0031243613457; fax: +0031243540788;
e-mail: f.devos@onco.umcn.nl

Received 6 April 2011 **Revised form accepted** 12 August 2011

Introduction

Ovarian cancer is the fourth leading cause of cancer death in women in the Western world [1]. As a large number of patients with ovarian cancer will relapse after first-line treatment, second-line liposomal doxorubicin-based therapy is commonly used [2].

Extravasation of intravenously administered anthracyclines can become an oncologic emergency with serious complications, depending on the volume and concentration of the administered cytostatic agent [3]. Standard procedures in the acute phase include intermittent use of cold packs for 15–20 min for 1–2 days and administration of dexraxozane 15 min after the removal of cold packs within 6 h of extravasation into a large vein in the unaffected arm [4–7]. Recommended intravenous dexraxozane dosage is 1000 mg/m^2 once daily on days 1–2 and 500 mg/m^2 on day 3 with a maximum dose of 2000 mg on days 1–2 and 1000 mg on day 3. Consultation of a plastic surgeon for debridement of necrotic tissue and wound rinsing should be considered depending on the severity of extravasation.

Case

A 61-year-old Caucasian woman with distant lymphadenopathy of ovarian cancer received palliative liposomal doxorubicin 30 mg/m^2 and carboplatin with target area under the curve of 5 mgh/l intravenously on day 1 every 4 weeks. Before administering the fifth cycle, the oncology nurse did not detect any abnormalities during routine inspection of the intravenous access site in the distal part of the left arm. However, during liposomal doxorubicin infusion, the patient complained of pain around the intravenous access site, which rapidly spread to the left axilla. A closer examination showed painful edema of the whole arm and axilla. Immediately, the liposomal doxorubicin infusion, 50 ml of which was being administered at a concentration of 50 mg in a total volume of 250 ml saline solution, was halted because of suspected extravasation. A plastic surgeon was consulted and conservative treatment was started with the use of cold compresses. No dimethylsulfoxide was applied because of the small amount of liposomal doxorubicin extravasated and the mild symptoms following the extravasation. Pain subsided quickly and after administration of the liposomal doxorubicin infusion in the contralateral arm, the patient was discharged. However, 3 days later, the patient presented with gradually increasing pain in the left arm and reddening of the skin. As the liposomal structure of the doxorubicin could result in a long-enduring extravascular exposure to the chemotherapeutic agent, she received intravenous administrations of dexrazoxane once daily for three consecutive days at a dose of 1000 mg/m^2 on days 1 and 2 and 500 mg/m^2 on day 3. The symptoms decreased from the second day of dexrazoxane administration without development of skin lesions or loss of function. Because of this complication, she refused a sixth and last course of liposomal doxorubicin and carboplatin. In the follow-up of 3 months, all clinical signs of extravasation disappeared.

Discussion

Although a substantial amount of literature is available regarding the extravasation and treatment of well-known anthracyclines such as doxorubicin and epirubicin, little is known about the side effects and therapy of the extravasation of liposomal doxorubicin [8–10]. Dexrazoxane is a bisdioxopiperazine, which acts as an intracellular iron chelator and specific catalytic inhibitor of DNA

0959-4973 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins DOI: 10.1097/CAD.0b013e32834be51a

topoisomerase II [11]. As the drug is converted intracellularly to an open-ring chelator, it binds iron from the iron–anthracycline complex, thereby preventing the formation of free radicals leading to tissue injury. Other mechanisms of action remain unclear. Two prospective, open-label, single-arm, multicenter studies showed that dexrazoxane was highly effective in preventing complications after anthracycline extravasation [12]. To date, dexrazoxane is a standard antidote for anthracycline extravasation in many guidelines [4–7,13]. Liposomal anthracycline extravasation is mentioned solely in the German working group for supportive care in cancer guidelines, in which the use of cold packs is advised [7]. This case study describes the delayed occurrence of symptoms after extravasation of liposomal doxorubicin and, for the first time, describes the successful use of dexrazoxane in this situation, even when administered days after the extravastion.

Acknowledgments

There are no sources of support for the work in the form of grants, equipment, drugs, or any combination of these to be disclosed, nor was any funding received for this work.

Conflicts of interest

There are no conflicts of interest.

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