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TOXICITY TO TOPICAL DIMETHYL SULFOXIDE IN A PEDIATRIC PATIENT WITH ANTHRACYCLINE EXTRAVASATION

M. E. Llinares, M. Bermúdez, and J. L. Fuster □ Division of Hematology Oncology, Pediatric Department, University Hospital "Virgen de la Arrixaca," Murcia, Spain

M. S. Díaz and C. M. González □ Division of Hematology Oncology, Pharmacy Department, University Hospital "Virgen de la Arrixaca," Murcia, Spain

□ *Accidental extravasation of vesicant chemotherapy may cause important tissue injuries. Nowadays, the majority of authors propose topical dimethyl sulfoxide (DMSO), with or without local cooling, as the treatment of choice for anthracyclines extravasation. No significant toxicity has been reported when DMSO is used as topical treatment. This report describes a case of local toxicity consisting of severe pain after its use in a pediatric patient. An illustration shows the extravasation area.*

Keywords. antidote, DMSO, extravasation

Accidental subcutaneous extravasation of vesicant antineoplasic agents such as vincristine, docetaxel, mitomycin-C, and doxorubicin may cause soft tissue injuries, ranging from minor erythema to severe local necrosis [1]. These changes may not become apparent during the first days or even weeks after the extravasation episode, and when the skin is damaged, worsening may continue for several months, probably due to residual drug diffusion into the adjacent tissue [2]. As the use of central venous lines for administration of chemotherapy has become a general practice, incidence of this problem has been reduced dramatically, but human errors may still occur.

For treating anthracycline extravasation, the topoisomerase II catalytic inhibitor dexrazoxane [2], heparin fractions [3], and subcutaneous GM-CSF [4] have been tested in experimental studies in mice and have been demonstrated to decrease incidence of skin lesion. Furthermore, dexrazoxane has also proven successful in 2 adults patients [5], but today, no randomized trials in humans have been reported. Therefore, recommendations should be based on clinical experience.

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Address correspondence to M. E. Llinares, Unidad de Oncohematologia Pediatrica, Hospital Universitario Virgen de la Arrixaca, Ctra. Madrid-Cartagena s/n El Palmar, Murcia 30005, Spain. E-mail: josel.fuster@carm.es

Tissue inflammation does not play a significant role in the pathophysiology, and local injection or topical administration of corticosteroids has caused contradictory results [2, 10]. Currently, most authors recommend topical DMSO with or without intermittent local cooling as the treatment of choice for anthracyclines extravasation [6–9]. DMSO is one of the most common solvents used for in vivo administration of several water-insoluble substances, and has been applied as part of the treatment of illnesses such as brain edema, amyloidosis, intersticial cystitis, and schizophrenia [9]. No significant toxicity has been previously reported when it is used as topical antidote for vesicant cytotoxic drugs [6, 7].

We report a case of idarubicin extravasation in a pediatric patient whose DMSO administration had to be withdrawn due to secondary effects, consisting of severe pain after each application and intense local skin erythema. No blisters or necrosis developed.

CASE REPORT

A 4-year-old girl was diagnosed of having acute myelogenous leukemia (FAB M2 subtype and AML1/ETO positive). A catheter-type Portacath was placed under general anesthesia by accessing the left subclavian vein via the infraclavicular approach. Induction to remission chemotherapy consisted of cytarabine in continous infusion 100 mg/m^2/day, days 1–7, etoposide 125 mg/m^2/day, days 1–3, and idarubicin 12 mg/m^2/day, days 1–3.

In a second idarubicin dose, an accidental drug extravasation occurred. A total volume of 20 mL containing 8 mg of idarubicin was infused into subcutaneous tissue because the needle was accidentally placed out of the portal system. Immediately, the patient complained of severe pain and developed local erythema. A significant drug volume was drained out before needle was removed, but it could not be pointed out how much drug was delivered into subcutaneous tissue.

Treatment consisted of topical administration of DMSO and intermittent cooling. Topical DMSO application was started approximately 1 h after the accident. It was provided in a 99% solution and was applied over the affected skin with a wide margin around it, 4 times per day. Local ice pack was applied before DMSO solution for 1 h for 3 days. During and after each DMSO application the patient complained of severe pain in the extravasation area. She was treated with first-level analgesics and then with opioids for pain control without any improvement. So, 5 days after beginning with DMSO solution, treatment had to be withdrawn because of severe pain related with DMSO application and important erythematous area in every place where the solution was applied (wider than the idarubicin extravasation area). After that, we only applied antiseptic solution because the skin developed exudative areas. Later, when lesions became dry, we also applied a moisturizing cream.

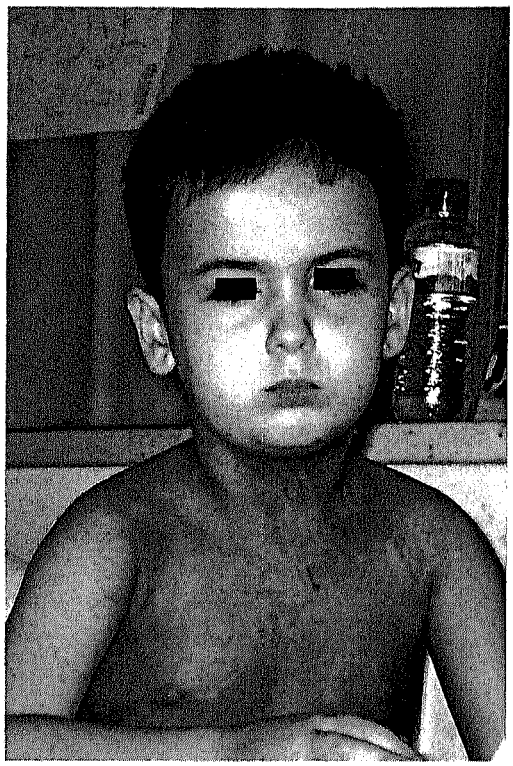

FIGURE 1 The extravasation area.

Figure 1 shows the extravasation area and was taken 13 days after the event (8 days after stopping treatment with DMSO). Skin is erythematous but does not present any disruption area. No blisters are present.

Chemotherapy induction was continued by an external central venous line. Four weeks after the event, the skin was ad integrum and only loss of pigmentation and focal induration was patent at the area affected by the extravasation. The Portacath was canalized and a catheterography study showed a correct placement and connection of the portal to the tube line.

DISCUSSION

Chemotherapy extravasation is a rare event but unfortunately it still occurs. Children are especially at risk given that they are almost continuously moving. Displacing of the needle out of the portal system is not an uncommon event in young children with Portacath central venous devices. One should verify the correct function of the system before infusing chemotherapy to prevent its extravasation into the subcutaneous tissue.

Several guidelines for the safe handling of different chemotherapy agents are available.

Topical DMSO solution is now commonly accepted as the best choice for anthraciclyne extravasation. Our local policy recommends this treatment for 14 days.

Severe pain after DMSO application is reported in a minority of patients [11]. Our patient experienced idarubicin extravasation and acute pain with each DMSO application. Neither first-level analgesics nor opioids before each application proved to be effective for pain control, and for this reason DMSO treatment was withdrawn after 5 days. Thereafter, she did not require any more analgesia.

We present a case of idarubicin extravasation successfully managed with only 5 days of DMSO treatment. Short-time contact of idarubicin with subcutaneous tissue as well as rapid application of DMSO solution are probably involved as causes for a favorable outcome in our patient. As far as we know, only 1 case of severe pain secondary to DMSO treatment has been reported before. A 19-year-old boy experienced skin redness and pain after daunorubicin infusion, although the authors pointed out that anthracycline extravasation was not clearly proven [10].

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