Linear Vesicles and Bulla along the Course of the Cephalic Vein: A Rare Presentation of Vesicant-type Reaction following Intravenous Docetaxel Infusion

Dear Editor,

The extravasation of chemotherapeutic agents during infusion is unfortunate and unpleasant to the patient.[1] Extravasation of chemotherapy can cause tissue damage and necrosis, impairment of function, and sometimes permanent damage. Extravasation of these agents is classified into vesicant (bullous lesions), non-vesicant, and irritant reactions.[2] Docetaxel, a taxane group of chemotherapeutic agents, is used for the treatment of solid tumors of the breasts, lungs, prostate, gastric, and head and neck. However, *per se*, docetaxel has a low incidence of infusion-site reactions and rarely causes vesicant-type reactions.

A 47-year-old female patient presented to the dermatology department with blisters over her left wrist after an intravenous infusion of docetaxel for breast cancer. She was administered the first dose of intravenous docetaxel (135 mg) through the lateral aspect of her left wrist. On the third day of injection, she developed small itchy, reddish-raised lesions over the injection site on the lateral aspect of her left wrist, which gradually increased in size and became clear fluid-filled lesions over the next 2 days and she presented to us on the 10th day after the injection. The patient did not provide a history of any topical application after the infusion. On examination, large bulla measuring 7 × 4 cm with multiple discrete and confluent linear vesicles containing clear fluid on an erythematous base were observed to be distributed on the radial aspect of the left wrist at the site of drug administration along the course of the left cephalic vein [Figure 1]. There were no other skin lesions or systemic symptoms. Acute irritant dermatitis, blister beetle dermatitis, and bullous erythema multiforme were the differentials.

Blood investigations revealed anemia (10.3 g/dL), leukocytosis (16,500/mL) with neutrophilia (85%), and high erythrocyte sedimentation rate (ESR) (65 mm). Liver and renal function tests were normal and viral markers were negative. A skin biopsy from a vesicle showed a subepidermal split [Figure 2], with necrotic and dyskeratotic keratinocytes along with mononuclear dermal infiltrate [Figure 3].

The patient was managed with topical clobetasol cream and fusidic acid cream with a resolution of lesions within 2 weeks. A diagnosis of vesicant-type reaction to docetaxel was made. Subsequent infusions were administered using precautions to prevent extravasation, and the patient completed treatment without a recurrence of blistering.

Its cytotoxic activity results from the stabilization and accumulation of microtubules within cells, causing apoptosis, thus explaining the dyskeratotic cells observed in histopathology in our case.[3] Vesicant drugs have the ability to cause blister formation with or without tissue destruction. There is no consensus regarding whether taxanes are vesicants or irritants.

Docetaxel is more commonly regarded as an irritant with a low vesicant potential, compared to paclitaxel. Docetaxel is classically considered to be an exfoliant with low vesicant capability. It is not clear whether taxanes or the vehicles in which they are dissolved are responsible for the infusion reactions. In the case of docetaxel, the vehicle polysorbate 80 is postulated to cause histamine release, thereby causing

Figure 1: Large bulla and multiple vesicles in a linear pattern along the course of the left cephalic vein

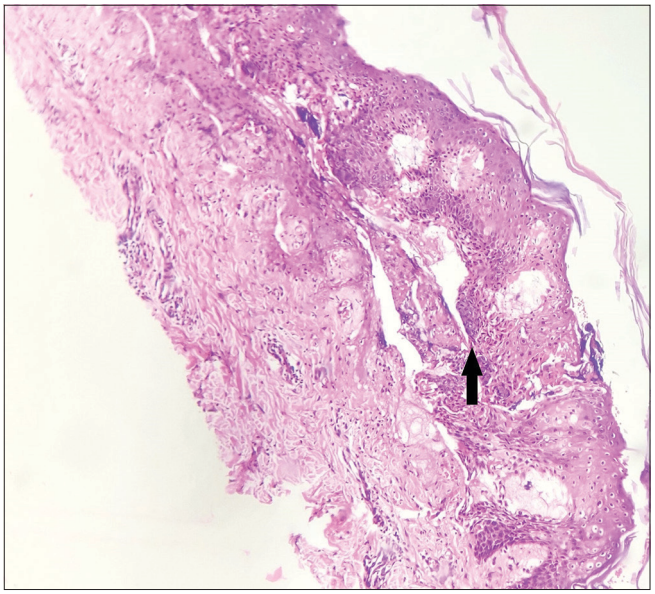

Figure 2: Skin biopsy showing subepidermal cleft (arrow) and mononuclear cells in the dermis, (H and E, ×100)

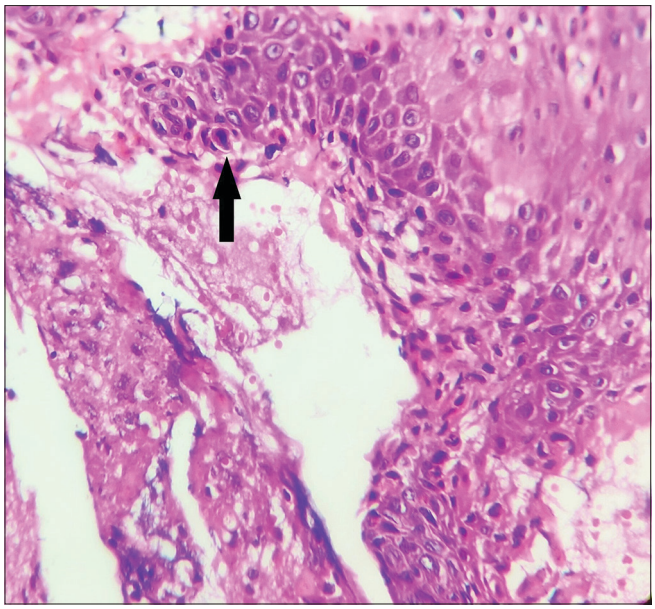

Figure 3: Skin biopsy showing dyskeratotic cells (arrow) in the epidermis with a subepidermal cleft, (H and E, ×400)

infusion reactions; however, this has not been validated in the laboratory.[4] The pH and osmolarity of the agent also contribute to the vesicant reaction. The symptoms of extravasation reactions can range from mild pain to localized tissue inflammation, leading to necrosis, ulceration, and sloughing of skin and deeper tissues. The risk factors for extravasation include small veins, obesity, old age, and the presence of skin diseases such as eczemas and psoriasis. Bullous formation at the infusion site occurred 5 days later in this report, which is consistent with other reports (range: 3–10 days) of extravasations involving a small amount of vesicant leakage, followed by dermatological findings in the following days or weeks. The exact mechanism of action is not known; however, the development of a bullous reaction could be due to direct cellular toxicity.[3,4] Bullous irritant contact dermatitis presents as an area of erythema and blistering with no particular pattern, whereas vesicant reaction presents with blisters in a linear pattern along the course of the veins [Figure 1]. The earliest sign of vesicant reaction due to extravasation is itching and erythema at the infusion site. The infusion can be immediately stopped and local cold compresses can be given. Thus, careful monitoring by the nursing staff during infusion goes a long way to prevent such reactions. Paclitaxel, 5-fluorouracil, doxorubicin, cyclophosphamide, and vinca alkaloids are also known to cause vesicant-type reactions. Based on the few reports of docetaxel extravasations, different treatments have been proposed, including elevation and resting of the affected area, local cold compresses (preferred as it can reduce inflammation due to vasoconstriction), and hot compresses, whereas the specific therapy is hyaluronidase injection at the extravasated site.[5]

Bullae formation after docetaxel infusion has been reported in only 10 cases to the best of our knowledge, and specific histopathological findings have not been described in most cases, unlike the present case.[3-5] This is another highlight of our case. Health workers who administer docetaxel infusions should be aware of its potential vesicant properties and closely monitor for signs and symptoms of extravasation to avoid extravasation-related complications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

Vinayak Visvanath, Pradeep Nair S

Department of Dermatology and Venereology, Government Medical College Trivandrum, Kerala, India

Address for correspondence:
Dr. Pradeep Nair S,
Department of Dermatology and Venereology, Government Medical College Trivandrum - 695 011, Kerala, India.
E-mail: dvmchtvm@yahoo.co.in

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