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Case Report

Severe Photo Toxicity Recalled by Docetaxel

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Keywords

Photo recall toxicity · Docetaxel · Chemotherapy · Breast cancer

Abstract

Photo-recall phenomenon is a rarely recognized adverse event of chemotherapeutic agents. The physiopathology of this entity is unclear. We have reported a 56-year old breast cancer patient with severe photo toxicity recalled 5 months after the initial sunburn by one course of adjuvant docetaxel treatment. However, being given right diagnosis and proper managements the patient could be able to complete her adjuvant chemotherapy according to the planed time schedule, without any delay. Our case may be explained by the theory that long-lived memory T-cells may remember former skin damage and cross-react with cytotoxic drugs. In addition, we have proved that weekly paclitaxel can still be the drug of option after docetaxel recalled severe photo toxicity.

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Case Report

A 56-year-old woman presented to our oncology department in May 2018 with a painful erythematous rash with multiple blisters covering the upper part of her back toward the neck. In January 2018 she had been diagnosed with breast cancer and was in the middle of her adjuvant chemotherapy after partial mastectomy. She was on day 8 after the first course of docetaxel treatment (90 mg/m² in a three-week regimen), which was given after three courses of prior treatments with epirubicin and cyclophosphamide. Earlier on day 3, she started to feel irritation and pain over her upper back and neck. An extensive rash over the area was noticed on day 5 with increasing pain. She visited the emergency room on day 6 and was found neutropenic. Blisters appeared over the erythematous area later that day. The patient suffered from an intensive pain despite maximal dosages of paracetamol and ibuprofen day 8, she showed up in our clinic and presented a confluent, elevated, burning erythema distributed on previously sunburned areas, the neck and the upper back, strictly excluding areas previously covered with clothes and hair. The appearance reminded of an acute sunburn. However, she had not been exposed to the sun for the last weeks. The patient was admitted to the infectious diseases ward for assessment because herpes infection was suspected. One of the blisters was punctured and PCR tests for herpes simplex virus type I (HSV I), herpes simplex virus type II (HSV II) and varicella zoster virus (VZV) were performed. The patient had fever up to 38.3 degree Celsius and the treatment with valaciclovir was initiated. However, the clinical picture was atypical since the erythema was covering several dermatomes while distinctly sparing the parts under her bra straps, rising suspicion of photo toxicity. The patient had not been sun exposed during the period of chemotherapy, but she had undertaken a trip to Vietnam for two weeks 5 months before the docetaxel treatment. Her upper back and neck was sunburned at that time, but to a much lighter degree without skin bullae. The rash progressed with a vesicular erythema and some large blisters followed by shallow erosions. At day 9, the patient was sent for dermatological consultation. A skin biopsy from the back was taken and it revealed a blistering dermatitis with interface changes including basal vacuolar degeneration, apoptotic keratinocytes at all levels, engagement of a sweat gland duct, intraepithelial vesiculation and partial epidermal necrosis. A subepithelial lymphocytic infiltrate with few eosinophils and neutrophils was seen. These findings were similar to erythema multiforme. Immunohistochemistry with antibodies against HSV1/2 and VZV were negative, which were also confirmed by the negative PCR results by serology. Thus, we diagnosed a severe docetaxel-induced photo toxicity which was recalled 5 months after the initial sunburn. The medication of valaciclovir was stopped after two days of administration.

The recall eruption was much more intense than the initial sunburn. Both the clinical (Fig. 1) and pathological (Fig. 2) presentations showed similarities to HSV/VZV infections. Although the erythema was clinically assessed as grade 4, it resolved relatively quickly after 3 days of application with topical corticosteroids (betametasone cream once a day). The erythema faded with a superficial desquamation leaving a hypo- and hyperpigmentation on day 11. Due to this severe skin toxicity, the patient was not continued with docetaxel treatment. Instead, weekly paclitaxel was administrated. Six doses of paclitaxel were given successfully, and no more skin toxicity was observed. The adjuvant chemotherapy was thus completed according to the planned time schedule, without any delay.

Photo-recall phenomenon is a phototoxic eruption occurring on areas of previous ultraviolet-induced solar erythema following a systemic administration of a chemotherapeutic drug. It has been mostly described with methotrexate but remains rare with other antineoplastic drugs. Few cases have been documented with gemcitabine, etoposide, and cyclo-

phosphamide [1–3], but even more rarely cases have been reported with taxane based regimens [3–5]. Droitcourt *et al* described a case of docetaxel-induced photo-recall skin rash on a woman treated for a non-small-cell lung cancer [4]. He et al. reported a case induced by paclitaxel [5].

Apparently, docetaxel seems to be more potent to recall the photo toxicity than other cytotoxic drugs the patient has received. Prior to docetaxel, our patient had already received three repeated courses of epirubicin in combination with cyclophosphamide relatively shortly after the initial sunburn, but no skin toxicity was developed. In addition, she has also received 6 courses of paclitaxel treatment after the docetaxel course, without any occurrence of skin toxicity. Furthermore, the recall occurred 5 months after the initial sun damage, which was far longer than that in other reports (1–8 days), but within the time period of 2–7 days after administration of the triggering drug.

The physiopathology of photo-recall phenomenon is still unclear. One hypothesis was that after a sub-erythematous exposure to UV light, the UV-dependent pro-inflammatory factors might be upregulated by the triggering drug to reach the erythematous threshold. However, this theory can hardly explain the recall reported in our patient which occurred 5 months after the initial sun damage. Another theory is that some skin-resident cells remember previous damage, and memory T cells that were primed during the original inflammation may persist at high levels during the asymptomatic phase and evolve into long-lived memory cells that can cross-react with unrelated drug [6]. This theory may explain our case. However, these hypotheses need to be further confirmed in future research.

To our knowledge, this is the first reported case of a breast cancer patient with a rare but severe photo toxicity recalled by an adjuvant docetaxel treatment 5 months after the initial sunburn. We believe this rare and peculiar type of skin eruption induced by docetaxel is worth being recognized by the oncologists as well as dermatologists and pathologists. Paclitaxel can be the drug of option after docetaxel recalled photo toxicity.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to declare.

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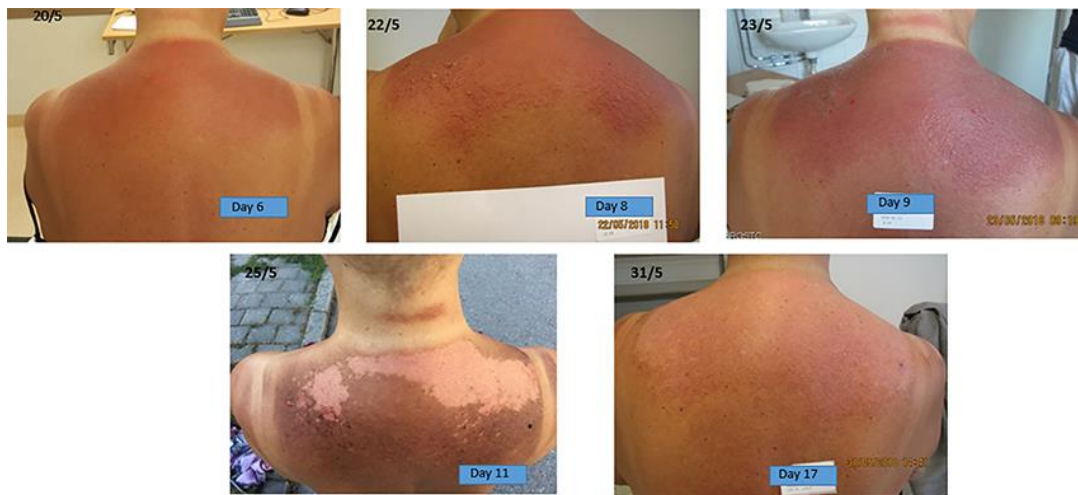


Fig. 1. The development of the photo toxicity recalled by treatment with docetaxel. *Day 6.* Indurated, burning erythema distributed on previously sunburned areas, the neck and the upper back, strictly excluding areas previously covered with clothes and hair. *Day 8.* Progressive, vesicular erythema with some large blisters. *Day 9.* Vesicular erythema with blisters and erosions and superficial desquamation. *Day 11.* Post inflammatory hyperpigmentation and desquamation of areas previously covered by blisters and vesicular erythema. *Day 17.* Hypo- and hyperpigmentation on areas previously affected by vesicular erythema.

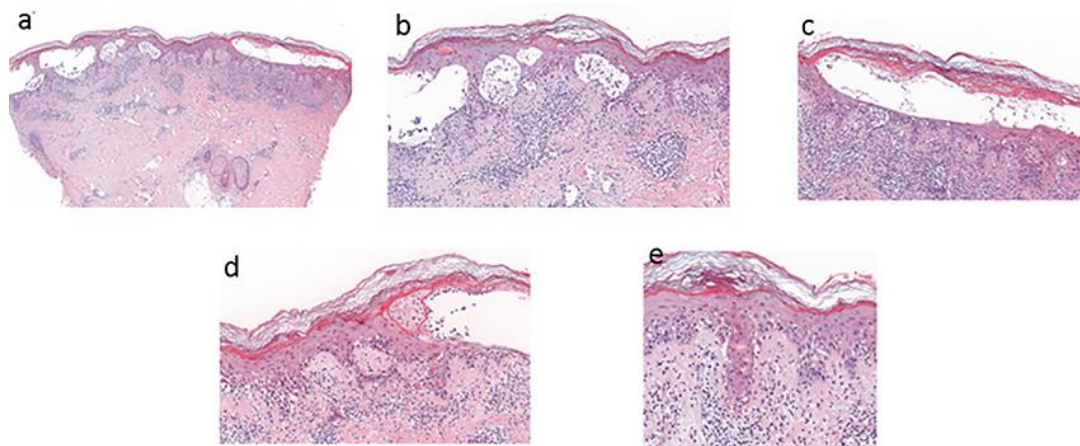


Fig. 2. The morphological picture of the recalled photo toxicity. **(a).** Multiple intraepidermal vesicles HE $\times 5.7$. **(b).** Interface changes with basal and suprabasal apoptosis. Moderate lymphocytic inflammation with few neutrophils and eosinophils, $\times 14$. **(c).** Intraepidermal bulla with necrotic roof. Mainly orthokeratosis, $\times 17$. **(d).** Intravesicular inflammation and group of apoptotic cells and interface changes $\times 18.8$. **(e).** Focal engagement of sweat gland epithelium $\times 27$.